別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該時評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合論（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0001	M. Zuo, I. Gamache, K. Fagbemi, F. R. Day, K. K. Ong and D. Manousaki	2025	The causal role of endocrine disrupting chemicals in pubertal timing: a Mendelian randomization study	OBJECTIVES: Endocrine disrupting chemicals (EDCs) interfere with hormonal homeostasis, and have been observationally linked to altered pubertal timing, defined by the age at menarche (AAM) in girls and the age at voice change (VAC) in boys. However, the causality of these associations remains unclear. We used Mendelian randomization (MR) to investigate if genetically altered serum EDC levels affect pubertal timing. METHODS: We selected genetic instruments for 11 EDCs (bisphenol A (BPA), BP-3, BP-8, BP-1, BP-2, BP-4, BP-5, BP-6, BP-9, BP-10, and BP-12) from a GWAS of 1,720 children. Two-sample MR was conducted to examine mediating effects of body mass index (BMI). RESULTS: We found causal MR associations with AAM for three phenol-containing EDCs: BPA (-0.10 SD [-0.19,-0.01], 95% CI 0.9 [0.83, 0.99], p=0.03), PCR (-0.11 SD [-0.20, -0.03], 95% CI 0.9 [0.82, 0.97], p=0.01), and PCR (-0.10 SD [-0.19, -0.01], 95% CI 0.9 [0.83, 0.99], p=0.03). See MR association was found with AAC for bisphenol A (BPA, -0.11 SD [-0.20, -0.02], 95% CI 0.9 [0.82, 0.98], p=0.02) and for dibutyl phthalate (DBP, -

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統合_0014	R. Zhou, Z. Chen, T. Yang, H. Gu, X. Yang and S. Cheng	2024	Vitamin D Deficiency Exacerbates Poor Sleep Outcomes with Endocrine-Disrupting Chemicals Exposure: A Large American Population Study	Phthalate and bisphenol A are recognized as the predominant endocrine-disrupting substances (EDCs) in the environment, but their impact on sleep health remains unclear. Vitamin D has often been reported to play a role in sleep regulation. However, the interaction between vitamin D and EDCs on sleep health remains unexplored. This study aimed to investigate the associations between environmental EDCs and sleep duration through modeling various exposures. Furthermore, it emphasizes the importance of vitamin D in this present scenario. Preliminary analyses suggested that vitamin D-deficient individuals generally slept shorter than individuals with normal vitamin D (p < 0.05). Exposure to three vinyl phthalate (MEP), mixtures (TPH), and three benzyl phthalate (BCPP), either alone or in combination, was associated with reduced sleep duration and a greater risk of vitamin D deficiency. Individuals with low vitamin D levels exposed to TPH experienced shorter sleep duration than those with normal vitamin D levels (p < 0.05). TPH and BCPP were identified as crucial factors in patient outcomes, where evaluating mixed exposures (p < 0.05). The results provide new data supporting a link between exposure to EDCs and insufficient sleep length. Additionally, they imply that a vitamin D shortage may worsen the sleep problems induced by EDCs.	Nutrients. 2024 Apr 26;16(9):1291.	10.3390/nu16091291	38732537	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0015	Y. Zhou, Z. Jin, L. Zhu, F. Huang, A. Ye and C. Hou	2022	A preliminary study on the relationship between environmental endocrine disruptors and precocious puberty in girls	OBJECTIVES: To explore the associations of environmental endocrine disruptors on precocious puberty in girls. METHODS: This was a case-control study in which 30 girls with precocious puberty and 30 age- and sex-matched controls were enrolled. The concentrations of 20 environment endocrine disruptors (bisphenol A, bisphenol B, bisphenol S, propylparaben, butylparaben, methyl paraben, mono-2-ethylhexyl phthalate, monoethyl phthalate, and monomethyl phthalate) in urine and 10 steroid hormones (dihydrotestosterone, androstenedione, hydrocortisone, 11-deoxycortisol, 17-α-hydroxyprogesterone, 4-androstenedione, testosterone, progesterone, and estradiol) in serum were measured by ultra-performance liquid chromatography-tandem mass spectrometry. The associations of maternal urinary BPA, BPF, and BPS, urinary levels of bisphenol A, monobutyl phthalate, and monoisononyl phthalate were significantly higher in the precocious group than in the prepubertal group. As to blood hormones, 11-deoxycortisol, corticosterone, deoxycorticosterone, and progesterone were significantly lower in the precocious group than in the prepubertal group (p<0.05, VIP>1). CONCLUSIONS: Our findings confirm the association between phthalate exposure and the incidence of precocious puberty in girls. Control and reduction of children exposure to phthalate esters should be considered as a health priority.	J Pediatr Endocrinol Metab. 2022 Jun 14;35(6):989-997.	10.1515/jpem-2021-0691	35692072	ヒト	生殖発生	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0016	B. Zhou, P. Yang, Y. L. Deng, Q. Zeng, W. Q. Luo and S. R. Mei	2020	Prenatal exposure to bisphenol a and its analogues (bisphenol F and S) and ultrasound parameters of fetal growth	BACKGROUND: Bisphenol A (BPA) has been shown to affect normal fetal growth, but human evidence on its analogues, BPF and BPS, is limited. OBJECT: To examine the associations between prenatal exposure to BPA and its analogues, BPF and BPS, and ultrasound parameters of fetal growth. METHODS: We measured urinary BPA, BPF, and BPS concentrations among 321 pregnant women during late pregnancy from a cohort study in Wuhan, China. Fetal biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC) were measured by ultrasonography. The associations of maternal urinary BPA, BPF, and BPS concentrations with fetal ultrasound parameters were examined using linear regression models. RESULTS: Maternal urinary BPA concentrations were associated with a decrease of 0.20 mm (95%CI: -0.39, -0.01) in HC (p for interaction = 0.003), such as with increase in maternal urinary BPA concentrations was associated with a mean decrease of 0.20 mm (95%CI: -0.39, -0.01) among boys and a mean increase of 0.21 mm (95%CI: 0.03, 0.39) among girls for HC. The associations were robust for urinary BPA concentrations modelled as tertiles or including urinary BPA, BPF, and BPS into mutual adjustment models. We did not observe robust associations between maternal urinary BPF and BPS concentrations and ultrasound parameters of fetal growth. Though in inverse association with HC and a positive association with FL were estimated for maternal urinary BPF concentrations modelled as continuous variables. CONCLUSIONS: Prenatal exposure to BPA but not BPF and BPS was sex-specifically associated with certain fetal growth parameters.	Chemosphere. 2020 May;246:125805.	10.1016/j.chemosphere.2019.125805	31918106	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0017	R. Zhang, H. Ma, M. Jin, Z. Lu, Y. Deng, C. Liu, N. Shen, J. Li, H. Wang, P. Ying, B. Li, Q. Zeng, Q. Lu, L. Cheng, Y. Zhu, X. Miao and J. Tian	2022	Genome-wide gene–bisphenol A, F and triclosan interaction analyses on urinary oxidative stress markers	BACKGROUND: Bisphenols and triclosan (TCS) are common endocrine disruptors (EDCs) that may induce oxidative stress. However, there is limited information as to whether these EDCs, indexed with genetic variants, modify the levels of oxidative stress on a genome-wide scale. METHODS: We first performed a genome-wide scan among a Chinese population and also measured three urinary EDCs, including bisphenol A (BPA), bisphenol F (BPF), and TCS, and 8-hydroxy-2′-deoxyguanosine (8-OHdG), a biomarker of oxidative stress. Then, we validated the significant findings in a Taiwanese population. RESULTS: Unfortunately, we examined interactions between three urinary EDCs and nearly 0.8 million genetic variants on three urinary oxidative stress markers by the improved linear mixed (ILM) models. Only urinary BPA, BPF, and TCS were positively associated with 8-OHdG (β, 95% CI: 0.0252, 0.0123, 0.0377; p = 0.0001, 0.0001, 0.0001, respectively). We identified 2 SNPs, rs1229984 (ADH1B) and rs4988235 (MCM6), showing significant gene-TCS interactions on 8-OHdG (all P < 5 × 10−8). The gene-level analysis found significant interactions between SNUH1 and TCS for 8-oxoPG (all P values (P = 2.02 × 10−6). CONCLUSION: Our results identify several gene–EDCs interactions for oxidative stress, highlighting that EDCs may modify the effect of genetic variants on oxidative stress.	Sci Total Environ. 2022 Feb 10;807(Pt 1):150753.	10.1016/j.scitotenv.2021.150753	34619205	ヒト	その他(酸化ストレス)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0018	Q. Zhong, M. Peng, J. He, W. Yang and F. Huang	2020	Association of prenatal exposure to phenols and parabens with birth size: A systematic review and meta-analysis	Phenols and parabens are endocrine-disrupting chemicals and are widely used in daily life products due to their antibacterial action. Previous studies suggest associations of prenatal exposure to phenols and parabens with fetal development; however, such findings are not well-summarized. The aim of this review and meta-analysis is to summarize the associations between maternal exposure to phenols and parabens and birth size. We identified 21 relevant studies that met the inclusion criteria through databases of PubMed, Cochrane, EMBASE and QuickMedian. The last search was in July 2, 2019. The heterogeneity and possibility of publication bias among included studies were examined by Q-statistic and Begg's tests, respectively. Meta-analysis revealed that prenatal exposure to mixed phenols (β = 0.08, 95% confidence interval (CI): -0.138, 0.301), benzophenone-3 (β = -16, β = -0.052, 95% CI: -0.833, 0.023), bisphenol A (n = 9, β = -0.004 g, 95% CI: -0.191, 0.102), 2-4-dichlorophenols (n = 6, β = -12.126 g, 95% CI: -29.071, 4.819), methyl paraben (n = 4, β = -0.004 g, 95% CI: -0.191, 0.102), and propyl paraben (n = 4, β = -0.004 g, 95% CI: -0.191, 0.102) were not associated with birth size. However, prenatal exposure to triclosan (n = 5, β = -0.001 g, 95% CI: -0.002, 0.000) was associated with decreased birth size. Subgroup analysis suggested that heterogeneity in our meta-analysis was mainly attributable to the studies conducted in developed countries and samples collected in the second trimester. Insignificant and controversial associations of maternal exposure to phenols and parabens with birth size were observed in our study. The study design and methods of the included studies are inconsistent, and the effects of environmental pollutants on human health are complex. Further cohort studies with large samples and a consistent approach are thus required to evaluate the associations of maternal exposure to phenols and parabens with birth size.	Sci Total Environ. 2020 Feb 10:703:134720.	10.1016/j.scitotenv.2019.134720	31731171	ヒト	生殖発生/メタアナリシス	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0019	J. Zheng, J. E. Reynolds, M. Long, C. Ostertag, T. Pollock, M. Hamilton, J. F. Dunn, J. Liu, J. Martin, M. Gibbs, B. Landman, Y. Huo, D. Dewey, O. Kurmasch and C. Lebel	2022	The effects of prenatal bisphenol A exposure on brain volume of children and young mice	Bisphenol A (BPA) is a synthetic chemical used for the manufacturing of plastics, epoxy resin, and many personal care products. This ubiquitous endocrine disruptor is detectable in the urine of over 80% of North Americans. Although adverse neurodevelopmental outcomes have been observed in children with high prenatal and postnatal exposure to BPA, the effects of prenatal BPA on brain structure are unclear. Here, using magnetic resonance imaging (MRI), we studied the associations of maternal BPA exposure with children's brain structure, as well as the impact of comparable BPA levels in a mouse model. Our human data showed that most maternal BPA exposure effects on brain volume outcomes occurred, with the largest effects observed in the caudate region of the inferior frontal gyrus (p = 0.016), superior occipital gyrus (p = 0.006), and paracentral gyrus (p = 0.080). In mice, gestational exposure to an equivalent level of BPA (2.25 μg BPA/kg body/day) induced structural alterations in brain regions including the superior olivary complex (SOC) and bed nucleus of the stria terminalis (BNST). Behavioral tests revealed that BPA-exposed mice displayed hyperactivity and impaired sensorimotor gating. We performed the primary endpoint analysis. Combined, these human and mouse data suggest that gestational exposure to low levels of BPA may have some impacts on the developing brain at the resolution of MRI.	Environ Res. 2022 Nov;214(Pt 3):114040.	10.1016/j.envres.2022.114040	35952745	ヒト、動物	発達神経	1	不明	1	不明	0	2.25 μg BPA/kg体重/日	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0020	Y. Zhao, Y. Yu, H. Liu, X. Ruan, Y. Guo and J. Wu	2025	Infant urinary bisphenol A concentrations in relation to child neurodevelopment at 2 years of age	Prenatal and childhood bisphenol A (BPA) exposures are known to negatively affect neurodevelopment, but the impact of exposure during the infancy period remains unclear. This study aimed to investigate BPA exposure in infancy and its association with neurodevelopment at 2 years of age. A total of 1,000 mother-infant pairs were recruited from Ma'anshan Maternal and Child Health Hospital between 2021 and 2023. Urine samples were collected from infants at 1 and 6 months, followed by neurodevelopmental assessments at 2 years of age. Of the 748 and 732 urine samples collected at 1 and 6 months, unconjugated BPA was detected via liquid chromatography-tandem mass spectrometry in 57.7 and 90.8%, with median concentrations of 2.79 and 6.61 μg/L, respectively. At the 1 month assessment, no statistically significant associations were observed between urinary BPA concentrations and any neurodevelopmental outcomes in either male or female infants (all adjusted P > 0.05). However, at the 6 month assessment, female infants' receptive language abilities were identified exclusively in female infants. Specifically, higher urinary BPA concentrations at 6 months were independently associated with lower scores in the gross motor domain (adjusted β = -3.32; 95 % CI: -6.16, -0.48; P = 0.022) and the total score (adjusted β = -3.32; 95 % CI: -6.16, -0.48; P = 0.022). Additionally, a 10-fold increase in urinary BPA concentration was associated with a 3.32-point decrease in the total score (adjusted β = -3.32; 95 % CI: -6.16, -0.48; P = 0.022) after controlling for relevant confounders. In contrast, no significant associations were detected between 6-month BPA concentrations and neurobehavioral outcomes in male infants (all adjusted P > 0.05). Our study identified neurodevelopmental effects of BPA as specific to both exposure timing and infant sex, highlighting for the finding that exposure at 6 months was negatively associated with neurobehavioral scores in females.	Ecotoxicol Environ Saf. 2025 Sep 15:303:118896.	10.1016/j.ecoenv.2025.118896	40840092	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0021	Y. Zhang, Z. Zhang, F. Zhou, G. Xu, W. Huang, M. Wang, Y. Lan, W. Zhang, Z. Liu, S. Cheng, S. Qiu, F. Qi and Z. Wei	2025	Association between endocrine disrupting chemicals exposure and the risk of all-cause mortality in individuals with diabetes mellitus or its complications: A prospective cohort study	OBJECTIVE: To investigate the association between exposure to endocrine-disrupting chemicals (EDCs) and all-cause mortality in individuals with diabetes mellitus (DM) in U.S., including those with diabetic complications. METHODS: This prospective cohort study included participants with DM in the 1999-2018 National Health and Nutritional Examination Survey. Data on mortality were obtained from the National Death records up to December 31, 2019. Cox regression, WQS regression and g-BKMR regression were constructed to examine the associations between EDCs and all-cause mortality in individuals with DM or its complications, adjusted for potential confounders. Restricted cubic spline analysis was used to investigate linear relationships. Subgroup analyses were also tested to pinpoint high-risk populations. RESULTS: The study included 2,265 participants. Mean (7 of) of 9 (ethylhexyl) phthalate (MEHHP), mono (2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono (7-ethyl-5-carboxyheptyl) phthalate (MECPP) showed positive associations with all-cause mortality in the WQS regression model (HR 1.24 (95 % CI: 1.08, 1.42), HR 1.24 (95 % CI: 1.08, 1.42), and HR 1.24 (95 % CI: 1.08, 1.42), respectively). Similar results were observed in the g-BKMR model (HR 1.24 (95 % CI: 1.08, 1.42), HR 1.24 (95 % CI: 1.08, 1.42), and HR 1.24 (95 % CI: 1.08, 1.42), respectively). Bayesian kernel machine regression (BKMR) models revealed a similar relative contribution of optimal MEHHP, MEOHP, and mono (7-ethyl-5-carboxyheptyl) phthalate (MECPP) toward positive associations with all-cause mortality in the diabetic population. Stratified analyses revealed that the associations between EDCs and all-cause mortality in individuals with DM or its complications were significantly stronger among those with female infants only. Preterm birth risk may be compound, sex, and window-specific. Given the limited sample size of this cohort, results should be confirmed in larger studies, including birth populations.	Environ Int. 2025 Jun;200:109556.	10.1016/j.envint.2025.109556	40446755	ヒト	その他(死亡率)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0022	Y. Zhang, V. Mustieles, P. L. Williams, J. Yland, J. Souter, J. M. Braun, A. M. Calafat, R. Hauser and C. Messerlian	2021	Prenatal urinary concentrations of phenols and risk of preterm birth: exploring windows of vulnerability	OBJECTIVE: To explore windows of vulnerability to prenatal urinary phenol concentrations and preterm birth. DESIGN: Prospective cohort. SETTING: A large fertility center in Boston, Massachusetts. PATIENT(S): A total of 586 mothers who sought fertility treatment and gave birth to a singleton between 2005 and 2018. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Gestational age at birth and preterm birth (<37 completed weeks). RESULT(S): Compared with women with term preterm births, urinary bisphenol A (BPA) concentrations were higher among preterm births (including early and late preterm), and among those with female infants. Second-trimester BPA concentrations were associated with preterm birth (Risk Ratio [RR] 1.23; 95%CI: 0.92, 1.65), which was primarily driven by female RR 1.65; 95%CI: 1.03, 1.89). Second-trimester BPA concentrations were associated with early preterm birth (RR 1.61; 95%CI: 1.01, 2.56) and late preterm birth (RR 1.66; 95%CI: 1.01, 2.73) among female infants only. Second-trimester bisphenol S concentrations showed a suggestive risk of preterm birth (RR 1.26; 95%CI: 0.82, 1.95), although the small case numbers precluded sex-specific examination. CONCLUSION(S): We found preliminary evidence of associations between mid-to-late pregnancy BPA and early pregnancy paraben concentrations with preterm birth among those with female infants only. Preterm birth risk may be compound, sex, and window-specific. Given the limited sample size of this cohort, results should be confirmed in larger studies, including birth populations.	Fertil Steril. 2021 Sep;116(3):820-832.	10.1016/j.fertnstert.2021.03.053	34238571	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0023	Y. Zhang, V. Mustieles, P. L. Williams, B. J. Wylie, I. Souter, A. M. Calafat, M. Danielsboiku, A. Lee, S. Vagios, R. Hauser and C. Messerlian	2021	Parental preconception exposure to phenol and phthalate mixtures and the risk of preterm birth	BACKGROUND: Parental preconception exposure to select phenols and phthalates was previously associated with increased risk of preterm birth in single chemical analyses. However, the joint effect of phenol and phthalate mixtures on preterm birth is unknown. METHODS: We included 380 female and 211 male (383 couples) participants seeking infertility treatment in the Environment and Reproductive Health (EARTH) Study who gave birth to 386 singleton infants between 2005 and 2016. Nine preconception urinary concentrations of bisphenol A (BPA), parabens, and seven phthalate biomarkers, including di-2-ethylhexyl phthalate (DEHP) metabolites, were examined. We used principal component analysis (PCA) with log-Poisson regression and Probit-Bayesian Kernel Machine Regression (BKMR) with hierarchical variable selection to examine maternal and paternal preconception mixtures and preterm birth (<37 completed weeks of gestation). We also examined couple-level exposure to mixtures of BPA, parabens, and DEHP metabolites. RESULTS: In maternal and paternal preconception mixtures, PCA1 was positively associated with preterm birth. Maternal PCA1 scores (adjusted Risk Ratio (aRR): 1.16; 95%CI: 1.08, 1.24) and paternal (aRR: 1.17; 95%CI: 1.08, 1.27) preconception DEHP-BPA factor was positively associated with preterm birth. Maternal and paternal BKMR models consistently presented the DEHP-BPA factor with the highest group Posterior Inclusion Probability (PIP). BKMR models further showed that maternal DEHP-BPA mixtures were linearly associated with increased preterm birth risk when all exposures were above the 60th percentile. Maternal DEHP metabolites were the largest contributors, with BPA and paraben metabolites contributing little to the mixture effect. Couple-based BKMR models showed a similar relative contribution of paternal DEHP-BPA and maternal DEHP-BPA preconception mixtures on preterm birth. We found a positive joint effect on preterm birth across increasing quantiles of couples' total mixture concentrations. CONCLUSION: In this prospective cohort of subfertile couples, maternal DEHP and DEHP- and paternal DEHP-exposure before conception were positively associated with preterm birth. Both parental windows jointly contributed to the outcome. These results suggest that preterm birth may be a couple-based pregnancy outcome.	Environ Int. 2021 Jun;151:106440.	10.1016/j.envint.2021.106440	33640694	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0024	Y. Zhang, V. Mustieles, P. L. Williams, I. Souter, A. M. Calafat, M. Danielsboiku, A. Lee, S. Vagios, R. Hauser and C. Messerlian	2022	Association of preconception mixtures of phenol and phthalate metabolites with birthweight among subfertile couples	Although parental preconception exposure to some phenols and phthalates have been associated with reduced birthweight, few studies have examined those chemicals as complex mixtures. METHODS: We included 386 mothers and 211 fathers (383 couples) who gave birth to 386 singletons from a prospective cohort of couples seeking fertility evaluation. Urinary concentrations of bisphenol A (BPA), parabens, and 11 phthalate metabolites, including those of di(2-ethylhexyl) phthalate (DEHP) were examined. Birthweight was abstracted from delivery records. We used principal component analysis and Bayesian Kernel Machine Regression (BKMR) with hierarchical variable selection to examine maternal and paternal preconception mixtures and birthweight. We also examined couple-level exposure to mixtures of BPA, parabens, and DEHP metabolites. RESULTS: In maternal and paternal preconception mixtures, PCA1 scores were positively associated with birthweight. In BKMR models, the DEHP-BPA factor had the highest group Posterior Inclusion Probability (PIP). BKMR models further showed that maternal preconception mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), a DEHP metabolite, and paternal preconception mono-n-butyl phthalate concentrations were inversely associated with birthweight when the remaining mixture components were held at their median concentrations. In couple-based BKMR models, paternal preconception parabens contributed more to couples' joint effect on birthweight compared to maternal preconception biomarkers. A decreasing trend of birthweight was observed across quantiles of maternal, paternal, and couples' total preconception mixture concentrations, respectively. CONCLUSION: Results suggest that preconception exposure to mixtures of DEHP metabolites in couples suggest a complex interplay between paternal and maternal preconception exposure to mixtures of nonpersistent chemicals, with both parental windows of exposure jointly contributing to reduced birthweight.	Environ Epidemiol. 2022 Aug 31;6(5):e222.	10.1097/ee9.0000000000000222	36249269	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0025	X. Zhang, G. Zhao, J. Ma, F. Tao, C. W. Pan, F. Zhang, Y. Wang, W. Yang, Y. Xiang, X. Wang, Y. Tian, J. Yang, W. Du and Y. Zhou	2023	Design, methodology, and baseline of eastern China student health and wellbeing cohort study	PURPOSE: To describe the study design, methodology, and cohort profile of the Eastern China Student Health and Wellbeing Cohort Study. The cohort baseline includes 1) targeted disease (myopia, obesity, elevated blood pressure, and dental caries) and 2) lifestyle behaviors (physical activity, sedentary behavior, and sleep). PARTICIPANTS: Primary and secondary schools in Shandong province, China, have been recruited and conducted annual health examinations and questionnaire surveys. Data collection and monitoring have been carried out in the study population in the first stage (2020-2021), a total of 6,588 students in primary schools are enrolled in the cohort study. FINDINGS TO DATE: Of all the cohort participants, the ratio of male to female is 1.16 among a total of 6,588 students participants, of which 2,728 (41.4%) students are from developed regions and 3,778 (58.1%) students are from developing regions. The initial age of participants ranges from 6 to 15 years old, with a mean age of 10.2 ± 2.4 years old. The prevalence of myopia, obesity, elevated blood pressure, and dental caries in developed regions and in developing regions, the prevalence of myopia, obesity, and elevated blood pressure is 39.7%, 17.9%, and 12.9% in the first three, respectively. The corresponding prevalence in developing regions is 21.6 ± 9.6 in developed regions, 11.6 ± 9.0 in developed regions, 10 Exposures: 11 The first aspect of individual behaviors in the questionnaire survey includes diet, physical exercise, bullying, and family. 2) The second aspect of environment and metabolomics. the average time (hours/day) is 1.03 (0.58-1.61) (41.1%), and the average likelihood (hours/week) is 3.61 (0.138-10.5) (42.1.5%). Metabolomics. Xiao bisphenol A in the urine is 0.750 ng/ml. 2) The third aspect of gene and epigenetics. 100% (rs420345, rs2350823, rs2350824, rs2350825, rs2350826, rs2350827, rs2350828, rs2350829, rs2350830, rs2350831, rs2350832, rs2350833, rs2350834, rs2350835, rs2350836, rs2350837, rs2350838, rs2350839, rs2350840, rs2350841, rs2350842, rs2350843, rs2350844, rs2350845, rs2350846, rs2350847, rs2350848, rs2350849, rs2350850, rs2350851, rs2350852, rs2350853, rs2350854, rs2350855, rs2350856, rs2350857, rs2350858, rs2350859, rs2350860, rs2350861, rs2350862, rs2350863, rs2350864, rs2350865, rs2350866, rs2350867, rs2350868, rs2350869, rs2350870, rs2350871, rs2350872, rs2350873, rs2350874, rs2350875, rs2350876, rs2350877, rs2350878, rs2350879, rs2350880, rs2350881, rs2350882, rs2350883, rs2350884, rs2350885, rs2350886, rs2350887, rs2350888, rs2350889, rs2350890, rs2350891, rs2350892, rs2350893, rs2350894, rs2350895, rs2350896, rs2350897, rs2350898, rs2350899, rs2350900, rs2350901, rs2350902, rs2350903, 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rs2350995, rs2350996, rs2350997, rs2350998, rs2350999, rs2351000, rs2351001, rs2351002, rs2351003, rs2351004, rs2351005, rs2351006, rs2351007, rs2351008, rs2351009, rs2351010, rs2351011, rs2351012, rs2351013, rs2351014, rs2351015, rs2351016, rs2351017, rs2351018, rs2351019, rs2351020, rs2351021, rs2351022, rs2351023, rs2351024, rs2351025, rs2351026, rs2351027, rs2351028, rs2351029, rs2351030, rs2351031, rs2351032, rs2351033, rs2351034, rs2351035, rs2351036, rs2351037, rs2351038, rs2351039, rs2351040, rs2351041, rs2351042, rs2351043, rs2351044, rs2351045, rs2351046, rs2351047, rs2351048, rs2351049, rs2351050, rs2351051, rs2351052, rs2351053, rs2351054, rs2351055, rs2351056, rs2351057, rs2351058, rs2351059, rs2351060, rs2351061, rs2351062, rs2351063, rs2351064, rs2351065, rs2351066, rs2351067, rs2351068, rs2351069, rs2351070, rs2351071, rs2351072, rs2351073, rs2351074, rs2351075, rs2351076, rs2351077, rs2351078, rs2351079, rs2351080, rs2351081, rs2351082, rs2351083, rs2351084, rs2351085, rs2351086, rs2351087, rs2351088, rs2351089, rs2351090, rs2351091, rs2351092, rs2351093, rs2351094, rs2351095, rs2351096, rs2351097, rs2351098, rs2351099, rs2351100, rs2351101, rs2351102, rs2351103, rs2351104, rs2351105, rs2351106, rs2351107, rs2351108, rs2351109, rs2351110, rs2351111, rs2351112, rs2351113, rs2351114, rs2351115, rs2351116, rs2351117, rs2351118, rs2351119, rs2351120, rs2351121, rs2351122, rs2351123, rs2351124, rs2351125, rs2351126, rs2351127, rs2351128, rs2351129, rs2351130, rs2351131, rs2351132, rs2351133, rs2351134, rs2351135, rs2351136, rs2351137, rs2351138, rs2351139, rs2351140, rs2351141, rs2351142, rs2351143, rs2351144, rs2351145, rs2351146, rs2351147, rs2351148, rs2351149, rs2351150, rs2351151, rs2351152, rs2351153, rs2351154, rs2351155, rs2351156, rs2351157, rs2351158, rs2351159, rs2351160, rs2351161, rs2351162, rs2351163, rs2351164, rs2351165, rs2351166, rs2351167, rs2351168, rs2351169, rs2351170, rs2351171, rs2351172, rs2351173, rs2351174, rs2351175, rs2351176, 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別添-2　統合文献リスト

通称性評価（動物）1：該当、0：該当しない　通称性評価（疫学）1：該当、0：該当しない　通称性評価（in vitro）1：該当、0：該当しない　通称性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通称性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で除害に基づき除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通称性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0027	W. Zhang, Y. Li, T. Wang, X. Zhang, J. Zhang, X. Ji and L. Lu	2024	Distribution and potential risk factors of bisphenol a in serum and urine among Chinese from 2004 to 2019	BACKGROUND: Bisphenol A (BPA) is an oil-derived, large-market-volume chemical with endocrine-disrupting properties and reproductive toxicity. Moreover, BPA is frequently used in food-contact materials, has been extensively researched recently, and widespread exposure in the general population has been reported worldwide. However, national information on BPA levels in general Chinese people is lacking. METHODS: This study collected and analyzed 128 1263 in urine and 61 in serum) research articles published between 2003 and 2021 to reflect the BPA internal exposure levels in Chinese populations. The Monte Carlo simulation method is...	Front Public Health Vol.12 Pages 1196248	10.3389/fpubh.2024.1196248	38379678	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0028	S. Zhang, L. Dai, Z. Wan, Z. Huang, M. Zou and H. Guan	2024	Sex-specific associations of bisphenol A and its substitutes with body fat distribution among US adults: NHANES 2011-2016	Bisphenol A (BPA) and its structural analogs (bisphenol S (BPS) and bisphenol F (BPF)) are widely consumed endocrine disrupting chemicals that may contribute to the etiology of obesity. To date, few studies have directly investigated the sex-related associations between bisphenols and body fat distribution in adults. In this study, we included 2569 participants from the National Health and Nutrition Examination Survey (NHANES) 2011-2016 to explore the associations between urinary bisphenols and body fat...	Environ Sci Pollut Res Int. 2024 Jan;31(5):7948-7958.	10.1007/s11356-023-31589-z	38172318	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0029	N. Zhang, Y. Zhao, L. Zhai, Y. Bai, W. Wei, Q. Sun and L. Jia	2024	Urinary concentrations of bisphenol A and its alternatives: Potential predictors of and associations with antral follicle count among women from an infertility clinic in Northern China	BACKGROUND: Experimental studies have suggested exposure to bisphenol A (BPA) and its alternatives, such as bisphenol F (BPF) and bisphenol S (BPS), may exert adverse effects on ovarian reserve, but human evidence is limited. Moreover, the potential predictors of exposure to bisphenols among women seeking infertility treatment have not been reported. OBJECTIVE: To explore whether individual or mixture of BPA, BPF, and BPS exposure is associated with antral follicle count (AFC) and to identify potential predictors of exposure to bisphenols. METHODS: A total of 1,...	Environ Res. 2024 May 15:249:118433.	10.1016/j.envres.2024.118433	38331151	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0030	N. Zhang, Y. Zhao, L. Zhai, Y. Bai and L. Jia	2023	Urinary bisphenol A and S are associated with diminished ovarian reserve in women from an infertility clinic in Northern China	Bisphenol A (BPA) has been demonstrated to cause ovarian toxicity including disruption of steroidogenesis and inhibition of follicle growth. Still, human evidence is lacking on its analogs, such as bisphenol F (BPF) and bisphenol S (BPS). In this study, we aimed to investigate the associations between exposure to BPA, BPF, and BPS with ovarian reserve in women of childbearing age. We recruited 311 women from an infertility clinic in Northern China between 2019 and 2020. Urinary concentrations of BPA, BPF, and BPS were measured using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Antral follicle count (AFC) was used to assess the associations between urinary BPA, BPF, and BPS levels and indicators of ovarian reserve and DOR, respectively. Restricted cubic spline (RCS) models were further utilized to explore potential non-linear associations. Our results showed that urinary BPS concentrations were negatively associated with AFC (β = -0.083; 95%CI: -0.172, -0.005). Analysis of their dual-high urinary concentrations of BPF, BPS, and total bisphenols (2 BPs) from women who did not, and age was related to increased urinary BPF concentrations. CONCLUSION: Our findings indicated that exposure to individual BPA, BPF, BPS and bisphenols mixtures were associated with impaired ovarian reserve. Furthermore, the intake of fried food, as identified in this study, could serve as an important bisphenols exposure route for reproductive-aged women.	Ecotoxicol Environ Saf. 2023 May:256:114867.	10.1016/j.ecoenv.2023.114867	37027940	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0031	L. Zhang, J. Zhang, S. Fan, Y. Zhang, J. Li, Y. Zhao, S. Ni, J. Liu and Y. Wu	2023	A case-control study of urinary concentrations of bisphenol A, bisphenol F, and bisphenol S and the risk of papillary thyroid cancer	The incidence of thyroid cancer (TC), especially papillary thyroid cancer (PTC), has dramatically increased globally. Whereas some endocrine disruptors have been linked to neoplastic processes, the associations between human exposure to bisphenol analogs and the risk of TC remain unclear. This present case-control study examined the associations between the urinary concentrations of BPA and other bisphenol analogs, namely bisphenol F (BPF) and bisphenol S (BPS), and the risk of PTC. After adjusting for confounders and creatinine standardization, significantly positive associations were observed for BPF (odds ratio [OR] = 1.80, 95% confidence interval [CI]: 1.27-2.56), but negative associations were observed for BPS (OR = 0.58, 95% CI: 0.41-0.83) and total bisphenols (OR = 0.72, 95% CI: 0.52-0.99). Moreover, the significant associations remained robust in the stratified analyses by sex, age, and body mass index. Additionally, additional significance was observed only in non-smoking women, suggesting the inherent effects of BPF exposure on PTC risk, especially in women. These findings require replication and confirmation in further research.	Chemosphere. 2023 Jan;312(Pt 1):137162.	10.1016/j.chemosphere.2022.137162	36347349	ヒト	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0032	J. Zhang, M. Yuan, Y. Liu, X. Zhong, J. Wu and W. Chen	2025	Bisphenol A exposure and neurodevelopmental disorders and problems in children under 12 years of age: A systematic review and meta-analysis	BACKGROUND: Bisphenol A (BPA) exposure may lead to neurodevelopmental disorders, and problems (NDPs) in children under 12 years old. In recent years, the number of relevant studies has increased, but the evidence remains inconsistent. OBJECTIVES: To systematically review and meta-analyze the associations between BPA exposure and NDPs in children under 12 years old. METHODS: A systematic search was conducted in eight bibliographic databases for peer-reviewed research articles published from database inception to October 31, 2024. Eligible studies were epidemiological observational studies in children under 12 years old, which evaluated the associations between BPA of biosamples and NDPs. The converted effect sizes were synthesized using multilevel random-effects meta-analysis models. Meta-regression analysis, sensitivity analysis, unmeasured confounding bias, and publication bias tests were examined to substantiate the results. RESULTS: The search identified 1880 unique studies, 32 of which met the criteria including 25,880 participants were finally included in the meta-analysis. The meta-analysis showed that BPA exposure was associated with intellectual disability (Cohen's d = 0.14, 95 %CI = 0.06-0.22), autism spectrum disorder (ASD, Cohen's d = 0.12, 95 %CI = 0.04-0.20), and attention-deficit/hyperactivity disorder (ADHD, Cohen's d = 0.10, 95 %CI = 0.03-0.17). Subgroup analyses revealed that the associations between urine BPA was associated with intellectual disability, ASD, ADHD, and motor disorders. Urine, and with intellectual disability and ADHD in girls. CONCLUSION: This study indicated that BPA exposure was associated with an increased risk of NDPs. In children, particularly in boys, underscoring the importance of considering BPA exposure as a potential risk factor for children's brain health.	J Hazard Mater. 2025 Jun 15:490:137731.	10.1016/j.jhazmat.2025.137731	40054188	ヒト	-	-	-	-	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0033	H. Zhang, S. Feng, S. Song, Q. Zhao, Y. Gao and T. Zhang	2025	First evidence in the association of phenolic endocrine-disrupting chemicals with secondary non-alcoholic fatty liver disease: A case-control study in South China	The presence of phenolic endocrine-disrupting chemicals (EDCs) in patients with secondary non-alcoholic fatty liver disease (S-NAFLD) and their associations with S-NAFLD incidence have not been previously documented. In this study, serum concentrations of 12 phenolic EDCs, including parabens, benzophenone-type (2-) EDCs, bisphenols, and bisphenol A diglycidyl ether derivatives, were detected in patients with S-NAFLD (n = 100) and healthy controls (n = 100) from South China. Bisphenol A (BPA) was the predominant phenolic EDC in both groups, with significantly higher concentrations in patients with S-NAFLD compared to those in the healthy population. Through multiple modeling analyses, we observed that parabens and bisphenols, which are commonly associated with S-NAFLD incidence. A risk of high-risk EDCs for S-NAFLD-related diseases was identified, including propyl paraben (PrP), butyl paraben (BuP), bisphenol S (BPS), and bisphenol AF (BPAF). Furthermore, significant positive correlations were found between the serum levels of these high-risk analytes and liver clinic indices. To the best of our knowledge, this study firstly examined the serum levels of multiple phenolic EDCs in patients with S-NAFLD, aiming to provide novel insights into high-risk EDCs associated with S-NAFLD incidence and their associations with clinic liver indices.	Environ Pollut. 2025 May 15:373:126086.	10.1016/j.envpol.2025.126086	40118363	ヒト	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0034	D. Zhang, K. Zhao, T. Han, X. Zhang, X. Xu, Z. Liu, X. Ren, X. Zhang, Z. Lu and C. Qin	2024	Bisphenol A promote the cell proliferation and invasion ability of prostate cancer cells via regulating the androgen receptor	A synthetic organic substance called bisphenol A (BPA) is used to make polycarbo- nate resin, polysulfate, and polyurethane plastic. BPA exposure via regular basis has increased the risk of developing cancer. Recent study has found that BPA exposure is linked to the development of prostate cancer (PCa). Androgen receptor (AR) is a crucial factor in the development of PCa. The purpose of this study was to investigate the prostate cancer cohort were obtained using the cBioPortal algorithm. The analysis of Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment was used to investigate probable pathways that are closely related to the genes. Additionally, the BPA-based risk model was built using regression analysis. Additionally, the molecular docking method was employed to assess BPA's capacity to attach to important genes. Finally, our team was able to successfully pair the BPA cohort settings for prostate cancer patients. Additionally, the KEGG enrichment study showed that of the neighbors related to BPA, prostate cancer is the most highly enriched. In a group of men with prostate cancer, the BPA-related prognostic prediction model exhibits good predictive value. The BPA demonstrated strong and efficient binding to the androgen receptor, according to the molecular docking studies. According to cell proliferation and invasion experiments, exposing prostate cancer cells to BPA at a dosage of 10(-7) mM could greatly enhance their ability to proliferate and invade.	Ecotoxicol Environ Saf. 2024 Jan 1:269:115818	10.1016/j.ecoenv.2023.115818	38091676	in vitro	-	-	-	-	1	0	10^{-7}μM	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0035	D. Zhang, X. Liu, Q. Xiao, L. Han, J. Yang, K. Li, J. Xu, Q. Zheng, F. Ma, J. Chen and S. Lu	2024	Co-Exposure to Bisphenols, Parabens, and Antimicrobials and Association with Coronary Heart Disease: Oxidative Stress as a Potential Mediating Factor?	Coronary heart disease (CHD) is the leading cause of global mortality, but the effects of plasticizers and antimicrobial additives on CHD is unknown. Here, we conducted a case-control study to investigate the mediating role of oxidative stress. In the association between co-exposure to seven bisphenols, four parabens, triclocarban (TCC), triclosan (TCS), triclocarbon, and CHD risk in Guangzhou, China. Generalized linear models and weighted quantile sum regression were used to analyze mixture outcome associations. Quantile-based g-computation showed a positive joint effect of a decile increase in exposure to all examined pollutants on CHD risk (OR: 1.62; 95% CI: 1.08, 2.43). Bisphenol A (BPA) (OR: 1.49; 95% CI: 1.01, 2.20) and TCC (OR: 1.49; 95% CI: 1.01, 2.20) were the major contributors. Urinary BPA concentrations were positively correlated with a 2,3-hydroxybutyl BPA (1.1-1.1) ng/mL) elevation of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a pro-BuP, TCC, bisphenol AP (BPAP), and BPP contributed to increased 8-OHdG. Mediation analysis revealed that 8-OHdG mediated the relationship between BPA, BPP, BPAP, and TCS, and CHD risk. Moreover, the mediating role of high-density lipoprotein (HDL) between several bisphenols and CHD was also identified. It is yet to be verified, but bisphenols may elevate CHD risk by reducing HDL values and increasing oxidative stress.	Environ Sci Technol. 2023 Jan 10;57(1):531-538.	10.1021/acs.est.2c06488	36534741	ヒト	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0036	C. Zhang, Y. Luo, S. Qiu, X. Huang, K. Jin, J. Li, M. Yang, G. Hu, K. Zhang, Z. Jiang, M. Wang, X. Zou and Q. Wei	2022	Associations between urinary concentrations of bisphenols and serum concentrations of sex hormones among US. Males	BACKGROUND: Bisphenol A (BPA) exposure and its structural analogs (BPS and BPF) might cause endocrine alterations and adverse physiological effects. Few studies to date have directly explored the association between BPA and its analogs and sex hormones in males. METHODS: We included 2,569 participants (aged 20-80 years) with available information on urinary bisphenols and sex hormones from the U.S. National Health and Nutrition Examination Survey 2011-2016. We included participants without data available on sex hormones and urinary bisphenols. Furthermore, participants consuming sex hormone medications were excluded. Multivariable regression models were performed to assess the association between bisphenols and sex hormones. RESULTS: In this study, 2387 participants were included. Of 2387 participants, 1,194 were males. Urinary BPA was detected in 92.7% of participants, BPS in 52.1%, and BPF in 39.2%. Urinary BPA was positively associated with total testosterone (TT) (β = 0.062, 95% CI: 0.016, 0.108, P = 0.011) and free testosterone (FT) (β = 0.062, 95% CI: 0.016, 0.108, P = 0.011) in males. However, no associations were observed between BPA and TT in females. Furthermore, increased BPA and BPF levels were associated with higher levels of sex hormone binding globulin (SHBG) (Model 2: β = 0.062, 95% CI: 0.016, 0.108, P = 0.011; β = 0.05, 95% CI: 0.015, 0.085, respectively). Additionally, participants in the highest BPA exposure quartile (quartile 4) had 0.833 nmol/L higher levels of SHBG than those in quartile 1 (Model 2: 95% CI: 0.156, 1.507, P = 0.021). Prior-level (0.085). Both BPA and BPS were negatively associated with free testosterone (FT, nmol/L) after full adjustment (Model 2: β = -0.015, P = 0.011; Model 2: β = -0.014, P = 0.008, respectively). However, BPF was positively associated with FT (Model 2: β = 0.02095, P = 0.018). CONCLUSION: Our study indicated that exposure to both BPA and its substitutions could alter sex hormone levels. This finding supports the possibility that human exposure to bisphenols at environmental levels might affect the endogenous hormone balance.	Environ Health Vol.21 Issue 1 Pages 135	10.1186/s12940-022-00949-6	36550468	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0037	B. Zhang, Y. He, H. Zhu, X. Huang, X. Bai, K. Kannan and T. Zhang	2020	Concentrations of bisphenol A and its alternatives in paired maternal-fetal urine, serum and amniotic fluid from an e-waste dismantling area in China	Bisphenol A (BPA) and its alternatives are suspected endocrine disruptors. However, prenatal exposure and transplacental transfer of bisphenols (BPs) is still limited. Therefore, BPA and its six alternatives in maternal serum (MS), maternal urine (MU), cord serum (CS), and amniotic fluid (AF) samples collected from 305 maternal-fetal pairs in an e-waste dismantling site in Southern China were determined. Bisphenol AF (BPAF) and bisphenol S (BPS) were the dominant BPA alternatives detected in MS and CS, and the geometric mean (GM) concentration of BPAF (0.02 ng/mL) in MS, 0.097 ng/mL in CS and BPS (0.09 ng/mL in MU, 0.08 ng/mL in CS) in MS and CS was lower than that of BPA (0.6 ng/mL in MS, 0.05 ng/mL in CS). The ratios of BPA concentrations between MU and MS (MU/MS ratio) were over three times higher than those of AF and CS. GM CS-AF concentration ratios between bisphenols were similar to those in MS and CS. The GM CS-AF concentration ratio of BPA (1.4) was significantly lower than that of BPAF (2.9), BPS (1.9), and BPB (1.5). Results suggest that BPs and its alternatives can pass through the placental barrier. The placental transfer rates of BPs are partially related to molecular weight or log K(ow) values. This finding indicates that structure transport is responsible for the placental transfer of BPs.	Environ Int Vol.136 Pages 105407	10.1016/j.envint.2019.105407	31955035	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0038	W. Zhao, H. Yang, J. Zhang and Q. Chen	2022	Association between co-exposure to phenols and phthalates mixture and infertility risk in women	BACKGROUND: Exposure to phenols and phthalates has been separately linked to increased risks of infertility in women of reproductive age. However, the combined effect of phenols and phthalates exposure on infertility has not been explored. METHODS: Data from the National Health and Nutrition Examination Survey (NHANES) were used. A total of 897 women of reproductive age (18-45 years) with available information on urinary phenol and phthalate metabolites, reproductive questionnaires, and covariates were included in the present study. The definition of infertility was based on self-reports. Multivariable logistic regression, principal component analysis (PCA), and weighted quantile sum (WQS) regression were used to assess the associations between co-exposure to phenols and phthalates mixture and risk of infertility among women of reproductive age. RESULTS: The PCA results for urinary concentrations of phenols and phthalates revealed that bisphenol A (BPA), mono(3-carboxypropyl) phthalate (MCPP), and monoethyl phthalate (MEP) metabolites, [mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP) and mono(2-ethyl-5-carboxypentyl) phthalate (MECPP)] were positively associated with infertility. PCA revealed that the DEHP-MPB factor (-97, none was significantly positively related to the likelihood of infertility [adjusted odds ratio (aOR) = 1.05; 1.00, 1.10]. The DEHP-MPB component consistently had the highest group posterior inclusion probability (PIP) in BKMR models. The BKMR model also found that MEOHP, MEHHP, and BPA were positively associated with infertility risk when the remaining combination concentrations were held at their median values. In addition, we observed that the probability of infertility increased dramatically as the quantile of total mixture concentration increased. CONCLUSION: Our findings indicate that a combination of phenol and phthalate metabolites is linked to infertility among reproductive-age women. BPA and DEHP, in particular, are significantly related to the risk of infertility.	Environ Res Vol.215 Issue Pt 1 Pages 114244	10.1016/j.envres.2022.114244	36058272	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0039	W. Zhao, W. Tang, X. Shen, H. Xu and J. Zhang	2023	Exposure to bisphenol A and its analogs and polycystic ovarian syndrome in women of childbearing age: A multicenter case-control study	BACKGROUND/OBJECTIVES: In recent years, the reproductive toxicity of new bisphenol analogs has garnered much interest, but it remains to be determined whether bisphenol analogs affect polycystic ovarian syndrome (PCOS). We investigated the associations between urinary concentrations of bisphenol A (BPA) and its analogs and PCOS in women of childbearing age. METHODS: A total of 1,000 PCOS cases and 1,0 controls were included in the current analysis. We quantified seven bisphenol analogs in urine samples, including bisphenol S (BPS), bisphenol AF (BPAF), bisphenol AP (BPAP), bisphenol B (BPB), bisphenol F (BPF), and bisphenol Z (BPZ). Spearman correlation and generalized linear regression were used to assessing the relationship between bisphenol analogs and hormonal parameters. To examine the associations of bisphenol analogs with odds of PCOS, multiple logistic regression, and two multi-pollutant models [quantile-based g-computation (QGC) and extreme gradient boosting (XGBoost) methods] were used. RESULTS: After covariates adjustment, BPA, BPS, and BPAP were positively correlated with testosterone (T) in the control group (P < 0.05). Dose–response relationships were observed between BPA, BPS, BPAP, and T (P-nonlinear < 0.05). Compared with the lowest quartile, the highest quartile of BPA (OR = 1.52, 95% CI: 1.16, 1.99), BPS (OR = 1.34, 95% CI: 1.03, 1.75), and BPAP (OR = 1.32, 95% CI: 1.01, 1.72) were associated with higher odds of PCOS. The QGC index was also positively related to PCOS (OR = 1.27, 95% CI: 1.03, 1.57), with BPA (weight = 0.52), BPS (weight = 0.28), and BPAP (weight = 0.20) likewise, the same overweight or obese tended to have a stronger association between bisphenol analogs and PCOS than normal-weight women. CONCLUSIONS: Environmental exposure to bisphenol analogs was associated with increased odds of PCOS in this case-control study. This association was stronger among obese and overweight women.	Chemosphere. 2023 Feb:313:137463.	10.1016/j.chemosphere.2022.137463	36470355	ヒト	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

曝露性評価（動物）1：該当、0：該当しない

曝露性評価（疫学）1：該当、0：該当しない

曝露性評価（in vitro）1：該当、0：該当しない

曝露性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに曝露性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で排除に基づき排除。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	曝露性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0040	J. Y. Zeng, M. Zhang, K. H. Chen, C. Liu, Y. L. Deng, P. P. Chen, Y. Miao, F. P. Cui, T. Shi, T. T. Lu, X. Y. Liu, Y. Wu, C. R. Li, C. J. Liu and Q. Zeng	2024	Prenatal exposures to phthalates and bisphenols in relation to oxidative stress: single pollutant and mixtures analyses	Prenatal exposures to phthalates and bisphenols have been shown to be linked with adverse birth outcomes. Oxidative stress (OS) is considered a potential mechanism. The objective of this study was to explore the individual and mixtures of prenatal exposures to phthalates and bisphenols in associations with OS biomarkers. We measured eight phthalate metabolites and three bisphenols in the urine samples from 335 pregnant women in the Wuhan-Zhuhan cohort. Urinary concentrations of 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 8-iso-prostaglandin F2α (8-iso-PGF2α) were measured as OS biomarkers. In associations with the individual chemicals, we estimated by linear regression models and restricted cubic spline (RCS) models, and their associations with the chemical mixtures were explored by quantile g-computation (qg-comp) models. In single pollutant analyses, five phthalate metabolites including monoethyl phthalate (MEP), monoethyl phthalate (MEP), mono (2-ethylhexyl) phthalate (MEHP), (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and (2-ethyl-5-oxohexyl) phthalate (MEOHP) and three bisphenols including monomethyl phthalate (MMP), monoethyl phthalate (MEP), mono (2-ethylhexyl) phthalate (MEHP), (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), (2-ethyl-5-oxohexyl) phthalate (MEOHP) and monobenzyl phthalate (MBzP) were positively associated with 8-OHdG levels in the fully adjusted models and were risen 3% in overall association in GLM and P for non-linear association (P-NL) in restricted cubic spline (RCS) models. In mixture analyses, qg-comp models showed that a one-quartile increase in the chemical mixtures of phthalate metabolites and bisphenols was positively associated with urinary levels of 8-OHdG and 8-iso-PGF2α (+), and bisphenol A (BPA) and bisphenol F (BPF) were the most contributing chemicals, respectively. Prenatal exposures to individual phthalates and mixtures of phthalates and bisphenols were associated with higher OS levels.	Environ Sci Pollut Res Int Vol.31 Issue 9 Pages 13954-13964	10.1007/s11356-024-32032-7	38267646	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0041	J. Y. Zeng, P. P. Chen, C. Liu, Y. L. Deng, Y. Miao, M. Zhang, F. P. Cui, T. T. Lu, T. Shi, K. D. Yang, C. J. Liu and Q. Zeng	2022	Bisphenol A analogues in associations with serum hormone levels among reproductive-aged Chinese men	BACKGROUND: Bisphenol A (BPA) as an endocrine disrupting chemical has been shown to alter reproductive endocrine function, but little is known on its analogues such as bisphenol F (BPF) and bisphenol S (BPS) with increasing usage and exposure. OBJECTIVE: To explore the associations between exposure to BPA, BPF and BPS and serum reproductive hormones among reproductive-aged Chinese men. METHODS: We measured BPA, BPF and BPS concentrations in urine samples from 335 reproductive-aged men in the Wuhan-Zhuhan cohort. Serum hormone levels including testosterone (T), estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and sex hormone-binding globulin (SHBG) were detected in serums. We used restricted cubic spline (RCS) models and multivariate linear regression models to examine the associations between exposure to BPA, BPF and BPS and serum hormone levels, and mixed linear regression models were utilized to explore associations between these associations. We also examined potential modifying effects by age and body mass index (BMI). RESULTS: There was little evidence of associations between BPA exposure and altered reproductive hormones. However, we found that elevated BPF and BPS exposures were in negative associations with estrogen (E2) levels and E2/T level (estradiol/testosterone ratio) (all P for trends < 0.05), and that elevated BPS exposure was negatively associated with SHBG levels (P for trend = 0.09). Based on the RCS models, these linear negative associations mixed that between BPS exposure and E2/T ratio were further confirmed. In stratified analyses, BPA exposure was positively associated with T levels among men with BMI < 24 kg/m2 (P for interaction = 0.02). CONCLUSIONS: Our findings suggested that BPA exposure was not associated with reproductive hormones. Elevated BPF and BPS exposures were negatively associated with male serum E2/T ratio and SHBG levels, and these associations varied by age and BMI.	Environ Int. 2022 Sep;167:107446.	10.1016/j.envint.2022.107446	35940031	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0042	M. Zbucka-Krętowska, U. Lisowek, W. Miltyk, I. Sidakiewicz, P. Pierzyński, B. Mikwski, S. Wal czyński and J. Ciesiacki	2019	Simultaneous analysis of bisphenol A fractions in maternal and fetal compartments in early second trimester of pregnancy	Background:Bisphenol A (BPA) is an estrogenic, endocrine disrupting compound widely used in the industry. It is also a ubiquitous environmental pollutant. Its presence was confirmed in human fetuses, which results from maternal exposure during pregnancy. The mechanisms behind maternal-fetal transfer, and relationships between pregnant women and fetal exposures remain unclear. The aim of this study was to assess the impact of maternal exposure to BPA on the exposure of the fetus. Methods:Maternal plasma and amniotic fluid samples were collected from 52 pregnant women undergoing amniocentesis for prenatal diagnosis of chromosomal aberrations in the 15th-18th gestational week. Concentrations of BPA in the samples were measured by high-performance liquid chromatography with fluorescence detection. Results:The number of BPA-positive samples in amniotic fluid was 42 (81%) and in maternal plasma 41 (79%). The median concentration of maternal plasma BPA was 8 times higher than the total BPA concentration in the amniotic fluid (0.69 ng/mL, range 0.05-49.76 ng/mL vs. median 0.08 ng/mL, range 0.3 ng/mL - 0.61 ng/mL). There was no direct relationship between the levels of BPA in maternal plasma and amniotic fluid levels. The permeability factor, in turn, negatively correlated with fetal development (body weight: P = 0.03, P = 0.001). Conclusions:Our results suggest that the risk of fetal BPA exposure depends on placental BPA permeability, rather than the levels of maternal BPA plasma concentration and support general recommendations to become aware and avoid BPA-containing products.	J Perinat Med Vol.47 Issue 7 Pages 765-770	10.1515/jpm-2019-0040	31348763	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0043	A. N. Zamora, E. Marchlewicz, M. M. Téllez-Rojo, C. F. Baccarelli, P. X. K. Song, A. Mercado, D. C. Dolinoy and K. E. Peterson	2022	Trimester two gestational exposure to bisphenol A and adherence to mediterranean diet are associated with adolescent offspring oxidative stress and metabolic syndrome risk in a sex-specific manner	BACKGROUND: Exposure to prenatal bisphenol A (BPA) and Mediterranean Diet Score (MDS) has been linked to metabolic risk in child offspring. It remains unclear if independent and interactive effects persist in adolescence. METHODS: We examined prenatal BPA and MDS on adolescent offspring metabolic syndrome risk score (MRS) and 8-isoprostane (8-iso), a biomarker of oxidative stress. Data from maternal adolescent pairs (n = 148) in the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) cohort in Mexico City were used. Second trimester urine BPA and first trimester MDS were measured during pregnancy. MRS and 8-iso were obtained during adolescence. We used linear regression models to examine associations between maternal-specific BPA, MDS, and MRS and offspring 8-iso outcomes. We then stratified analyses by sex. We identified a significant association between MDS with increased 8-iso (β = -0.066, p = 0.05), and a marginal association between trimester two BPA with increased 8-iso (β = 0.215, p=0.06). MDS modified the marginal association between BPA and 8-iso in females (β = 0.060). A negative, marginal association was observed between trimester two BPA and MRS (β = -0.106) while BPA*T1 MDS was significantly positively associated with MRS (β = 0.102 × males. CONCLUSIONS: Study findings indicate that trimester two prenatal BPA and maternal adherence to a Mediterranean diet may have sexually dimorphic effects on adolescent offspring oxidative stress, and metabolic syndrome risk.	Front Nutr. 2022 Oct 5:9:961082.	10.3389/fnut.2022.961082	36276834	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0044	A. N. Zamora, E. C. Jansen, J. M. Goodrich, M. M. Téllez-Rojo, P. X. K. Song, J. D. Meeker, D. C. Dolinoy, A.-T.-O. L. A. Cantonwine and K. E. Peterson	2023	Cross-sectional associations between phthalates, phenols, and parabens with metabolic syndrome risk during early-to-mid adolescence among a cohort of Mexican youth	BACKGROUND: Epidemiological studies on children and adults have linked exposures from plastics and personal care products to metabolic disruption. Yet, the impact of endocrine disrupting chemicals (EDCs) on adolescent metabolic syndrome (MetS) risk during early and mid-adolescence is unclear. METHODS: To examine the link between exposure to EDCs and MetS risk in this transitional window, cross-sectional data from 505 Mexican youth in early to mid-adolescence (10-12 years) were analyzed. Urinary biomarker concentrations of phthalates, phenol, and paraben analytes were measured from a single spot-urine sample collected in 2019, study personnel obtained anthropometric and metabolic measures. We examined associations between exposure to phthalates and metabolites, phenol, and paraben analytes with MetS scores using linear regression adjusted for specific gravity, sex, age, pubertal status, smoking, alcohol intake, physical activity level, and screen time. As a secondary aim, mediation analysis was conducted to evaluate the role of hormones in the relationship between EDC exposure and MetS risk. RESULTS: Of the 505 youth, 11.3% (n = 57) had MetS. Urinary concentrations of 2,5-dichlorophenol (2,5-DCP), 2,4-dichlorophenol (2,4-DCP), phthalates/base analytes were, including 3- (MHP) (β = 0.23 (95% CI: 0.06, 0.37), p = 0.01), phthalates/base analytes (mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP)) among males. Among females, BPA (β = 0.26 (95% CI: 0.03, 0.49), p = 0.03) was positively associated with MetS risk-a score and was placed 2.5 DCP (β = 0.09 (95% CI: 0.02, 0.16), p = 0.01) was associated with increased waist circumference z-score. Results showed no evidence of mediation by hormone concentrations in the association between summary phthalates with lipids, ratio or MetS risk z-scores. CONCLUSION: Higher EDC exposure was positively associated with serum lipids during adolescence, particularly among males.	Environ Res Vol.236 Issue Pt 1 Pages 116706	10.1016/j.envres.2023.116706	37474091	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0045	Ö. Yuruker, C. Dalkan, M. Uccu, Ö. Yetkin, A. Bahaygül and N. N. Bahcecilar	2023	High fetal bisphenol A exposure enhances IL22 secretion: A proinflammatory cytokine	BACKGROUND: Bisphenol A (BPA) is an industrial product, widely used in human-consumed types of equipment that can be transmitted orally, by inhalation or through dermal absorption and is detectable in nearly body fluids including umbilical. A correlation between BPA concentration in maternal serum and cord blood has been demonstrated previously, suggesting a possible transfer of BPA from the hemoplacental unit. OBJECTIVE: Our objective is to determine the impact of cord blood BPA level on cytokine responses. METHODS: In this cross-sectional study, healthy pregnant women who delivered healthy newborns followed by the Obstetrics and Gynecology Department of Ankara Yildirim Beyazit University between January 2019 and January 2020 were included in the study. Cord blood samples were collected from 100 healthy newborns. For cytokine examination, cord blood cells (PBMC) were isolated by Ficoll-Hypaque density gradient centrifugation. Cells were cultured in the presence or absence of phytohemagglutinin (PHA) (5 μg/mL) for 48 hours. Cytokine concentrations in the supernatants were determined by ELISA. RESULTS: Among 107 deliveries, 7 (6.5%) were excluded in the study, due to lack of cut-off value. BPA levels were classified as percentiles. No statistically significant difference was detected in the comparison of cytokine levels based on BPA concentrations below and above the 25th and 50th percentile. Significantly higher IL22 levels (p = 0.007) and lower IL-17/IL-22 (p = 0.01) were detected in those with BPA level above 75th percentile (> 0.51 ng/ml) compared to the below group. CONCLUSIONS: This is the real life study demonstrated that very high BPA levels in cord blood of expectant mothers enhances IL22 secretion in cord blood which is a proinflammatory cytokine. Studies evaluating long-term immunological effects on these highly exposed newborns are recommended.	Asian Pac J Allergy Immunol Vol.41 Issue 4 Pages 396-400	10.12932/ap-020320-0778	33386784	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0046	B. Yue, S. Ning, H. Miao, C. Fang, J. Li, L. Zhang, Y. Bao, S. Fan, Y. Zhao and Y. Wu	2023	Human exposure to a mixture of endocrine disruptors and serum levels of thyroid hormones: A cross-sectional study	Exposure to endocrine disrupters (EDCs) could disrupt thyroid hormone homeostasis. However, human epidemiological studies reported inconsistent observations, and scarce information on the effect of a mixture of chemicals. The aim of the present study was to examine the associations of multiple chemicals with thyroid hormones among adults from China. We measured seven kinds of thyroid hormones and urinary levels of 11 EDCs, including six phthalate metabolites, bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), para-hydroxybenzoic, and triclosan among 1717 healthy adults without occupational exposure. Associations of multiple urinary EDCs with thyroid hormones were assessed by multivariate linear regression models and Bayesian kernel machine regression (BKMR) models. Multivariate linear regression models showed that for all free hormones, an interquartile range (IQR) significantly associated with lower thyroxine (T4) (β = -0.27, 95% confidence interval (CI) (-0.41, -0.13)), total triiodothyronine (TT3) (β = -0.03, 95% CI (-0.05, -0.01)), free T4 (FT4) (β = -0.02, 95% CI (-0.03, -0.01)), and free T3 FT3 (β = -0.04, 95% CI (-0.07, -0.02)), and mono (2-ethyl-5-oxohexyl) phthalate (MEOHP) and monoethyl phthalate (MEP) positively associated with FT4 (β = 0.01, 95% CI (0.01, 0.02)) and FT3 (β = 0.02, 95% CI (0.01, 0.03)), respectively. Moreover, we observed significant dose-response relationships between FT3 and the mixture of 11 EDCs, and MEP was the main contributor to the mixture effect, suggesting the priority of potential effect of MEP on disrupting thyroid function under a real scenario of human exposure to multiple EDCs. Our findings supported the hypothesis that human exposure to low levels of EDCs could alter thyroid hormones homeostasis, among non-occupational healthy adults.	J Environ Sci (China) Vol.125 Pages 641-649	10.1016/j.jes.2022.01.017	36375946	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0047	Y. Yuan, Q. Chen, X. Ding, Q. Zhang and X. Zhong	2024	Endocrine disrupting chemical Bisphenol A and its association with cancer mortality: a prospective cohort study of NHANES	INTRODUCTION: There is evidence suggesting that Bisphenol A (BPA) is associated with increased all-cause mortality in adults. However, the specific causes of the relationship between BPA exposure and cause-specific mortality remain unclear. METHODS: Bisphenol A (BPA) was measured in urine samples from participants in the National Health and Nutrition Examination Survey (NHANES) using high-performance liquid chromatography-mass spectrometry (LC-MS). Through the use of multivariable Cox proportional hazard regression and restricted cubic splines, the relationships between urine BPA and death from all causes and cancer were investigated. RESULTS: This study has a total of 8,836 participants, and 337 died from cancers after a 7.5-year follow-up. The median level of BPA was 2.8 ng/mL. Urinary BPA levels were not independently associated with all-cause mortality. For cancer mortality, the second quartile, multivariable-adjusted hazard ratio was 0.52 (95% confidence interval: 0.30 to 0.88; p = 0.02) compared to the lowest quartile. The restricted cubic spline, showed that the association was nonlinear (p for nonlinearity = 0.028) and the inflection point was 5.49 ng/mL. CONCLUSION: Urinary BPA exposure was U-shaped associated with the risk of cancer mortality, and a lower level of BPA less than 5.49 ng/mL was associated with a higher risk of cancer mortality.	Front Public Health. 2024 Feb 23:12:1341789.	10.3389/fpubh.2024.1341789	38584917	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0048	S. Yuan, K. Du, H. Liu, X. Guo, B. Zhang, Y. Wang, B. Wang, H. Zhang and H. Guo	2023	Association between bisphenol A exposure and thyroid dysfunction in adults: a systematic review and meta-analysis	The occurrence of thyroid dysfunction is affected by environmental factors, and BPA is a ubiquitous environmental pollutant with the potential to cause thyroid dysfunction. However, the limited epidemiological evidence shows an inconsistent association between BPA exposure and thyroid dysfunction. Therefore, the literature on the impact of BPA on thyroid was sorted and analyzed to study the relationship between BPA and adult thyroid function. The studies published as or before 23rd May 2022 from PubMed, Web of Science, and Scopus were collected and pooling the association between BPA exposure and the levels of thyroid hormones. The methodological quality of each study was assessed, the sensitivity analysis and subgroup analysis based on study population and gender were also performed, and publication bias was evaluated. A total of 2988 literatures were identified, and 14 studies were included in the meta-analysis. The pooled results showed that BPA exposure was positively correlated with TSH (β = 0.03, 95% confidence interval (CI): 0.01, 0.05), and the coefficients between BPA and FT3/FT4 were -0.01 (95%CI: -0.03 ~ 0.00) and -0.00 (95%CI: -0.11 ~ 0.10), BPA concentration was positively correlated with TSH in females, and the pooled correlation coefficient was 0.08 (95%CI: 0.02–0.08). The effects of BPA on thyroid hormone levels were significantly different between males and females. BPA may significantly decrease the levels of FT3 and TSH in males but increase the levels of FT3 in females. Considering the high heterogeneity among studies and the limited investigations, the subgroups, the relationship between BPA exposure and thyroid dysfunction needs to be further investigated.	Toxicol Ind Health. 2023 Apr;39(4):188-203.	10.1177/07482337231156284	36772983	ヒト	-	-	-	-	-	-	システマティックレビュー・メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0049	N. Yuan, J. Sun, X. Zhao and W. Li	2024	Relationship between bisphenol A and autoimmune thyroid disease in women of childbearing age	BACKGROUND: Autoimmune thyroid disease (AITD) is the main cause of hypothyroidism in women of childbearing age. Bisphenol A (BPA) is an environmental factor affecting AITD. This study aims to investigate relationship between BPA and AITD in women of childbearing age, thereby providing a reference for the prevention of hypothyroidism in this specific demographic. METHODS: A total of 330 women of childbearing age were enrolled in this study, including the euthyroid group (matched 90 women with euthyroidism and thyroid autoantibodies negativity) and the AITD group (matched 90 women with euthyroidism and at least one thyroid autoantibody positivity). Urinary BPA concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Thyroid autoantibodies and BPA's endocrine were detected. The difference of BPA levels between the two groups was compared. Logistic regression was used to analyze the correlation between BPA and AITD. RESULTS: The proportion of multivariate and serum thyroid-stimulating hormone levels were significantly higher in the AITD group compared to the euthyroid group. Logistic regression analysis revealed that BPA levels did not exhibit a statistically significant association with AITD. Spearman correlation analysis revealed a statistically significant correlation between BPA and urinary iodine levels (r = 0.16, P < 0.05), as well as a correlation between urinary BPA and free triiodothyronine (FT3) levels (r = 0.29, P < 0.05). CONCLUSION: This study revealed a correlation between urinary BPA levels and FT3 levels. However, it did not establish a relationship between BPA and AITD in women of childbearing age.	Front Endocrinol (Lausanne). 2024 Jan 29:15:1333915.	10.3389/fendo.2024.1333915	38348416	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0050	K. Y. Yuan, Y. H. Gu, Y. H. Pei, S. Y. Yu, T. Z. Li, T. Feng, Y. Liu, J. Tian, X. Miao, J. Kong, M. Hu and B. F. Yuan	2025	Comprehensive analysis of transplacental transfer of environmental pollutants detected in paired maternal and cord serums	Prenatal exposure to hazardous environmental pollutants is a critical global concern due to their confirmed presence in umbilical cord blood, indicating the ability of pollutants to cross the placental barrier and expose the fetus to harmful compounds. However, the transplacental transfer efficiencies (TTEs) of many pollutants remain underexplored. Herein, we developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method to quantitatively analyze 95 environmental pollutants, including 13 bisphenols (BPs), 18 organophosphorus flame retardants (OPFRs), 7 brominated and other flame retardants (BFRs), 36 phthalates (PAEs), and 11 per- and polyfluoroalkyl substances (PFASs), in paired maternal serum and cord serum samples from 100 mother-infant pairs in Tianjin, China. The TTEs of pollutants ranged from 0.01 (bisphenol A (BPA) and bisphenol S (BPS)) to the highest concentration (500–8,000 pg/mL in maternal serums and 12.66 ng/mL in cord serums), followed by 4-cumyl-2,6-di-tert-butylphenol (TTCDTBP) (median TTE = 0.93) and 3,3′,5,5′-tetrachloro-4,4′-biphenol bisphenol (BPHC). The exposure concentrations of the same type of pollutants were highly correlated between maternal and cord serums. Perfluorohexanoic acid (PFHxA) had the highest TTE value (0.59), while perfluorooctane sulfonic acid (PFOS) had the lowest (0.28). TTEs of PFOS and perfluorooctanoic acid (PFOA) were higher for linear isomers, whereas TTEs of perfluoroalkanesulfonic acid (PFHxS) and perfluorodecane sulfonic acid (PFDS) were higher for male newborns. Moreover, the expression levels of the transplacental transporters ABCA1, ABCC1, ABCC3, ABCC4, ABCG1, SLCO2B1, and SLCO4A1 were significantly correlated with the TTEs of pollutants. Molecular docking revealed that pollutants with higher TTEs exhibited stronger binding affinities to ABCC4 and SLCO4A1. Further research is essential to unveil the mechanisms involved in the transplacental transfer of environmental pollutants, ultimately fostering our comprehension of their impact on fetal health and child outcomes.	J Hazard Mater Vol.486 Pages 136970	10.1016/j.jhazmat.2024.136970	39740555	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0051	S. I. Yoo, H. Joo, D. Kim, M. H. Lim, E. Kim, M. Ha, H. J. Kwon, K. C. Park and M. M. Kim	2020	Associations between Exposure to Bisphenol A and Behavioral and Cognitive Function in Children with Attention-deficit/Hyperactivity Disorder: A Case-control Study	OBJECTIVE: Bisphenol A (BPA) is a widely produced synthetic chemical used to manufacture polycarbonate plastics and epoxy resins. We aimed to investigate the association between exposure to BPA and behavioral and cognitive function in children with attention-deficit/hyperactivity disorder (ADHD) and healthy controls. METHODS: The study included 182 children aged from 6 to 15 years. The ADHD and control groups included 116 and 66 children, respectively. Urinary BPA concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Cognitive function was examined using the Continuous Performance Test (CPT, NEUROSpace, Seoul, Korea). Participants were investigated with the Korean Dimensional Assessment Scale for Children (KDSC). Multivariate logistic regression models were used to examine the associations between BPA and ADHD. RESULTS: Participants were investigated with the Korean Dimensional Assessment Scale for Children (KDSC). Multivariate logistic regression models were used to examine the associations between BPA and ADHD. Participants were investigated with the Korean Dimensional Assessment Scale for Children (KDSC).

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0053	D. Yeum, S. Ju, K. J. Cox, Y. Zhang, J. B. Stanford and C. A. Porucznik	2019	Association between peri-conceptional bisphenol A exposure in women and men and time to pregnancy- The HOPE study	BACKGROUND: Bisphenol A (BPA) is a non-persistent endocrine disrupting chemical with nearly ubiquitous, involuntary exposure. Previous studies have shown that BPA causes reproductive dysfunction in animal models, but there are limited data regarding the effects of BPA exposure on time to pregnancy (TTP) in humans. OBJECTIVE: To evaluate whether peri-conceptional BPA exposure of women and men is associated with couples' TTP. METHODS: The Home Observation for Pregnancy Environment (HOPE) study is a prospective pregnancy cohort study of couples trying to conceive in Utah. Urine samples were collected and were followed up to 12 months. Women collected first morning urine samples starting at the beginning of the fertile window and continued until the result of menses or 35 days after the estimated date of ovulation (EDO-35 days). The time to pregnancy (TTP) after the enrollment was self-reported and used for the analysis. Discrete time Cox proportional hazards models were performed to generate fecundability odds ratio (FOR) between BPA and TTP after adjusting for education and age, accounting for right-censoring and prior number of cycles trying to conceive. RESULTS: Among 344 couples, 125 couples became pregnant during the study. There was no association between TTP and peri-conceptional BPA exposure for both men (FOR 1.02, 95% CI: 0.72, 1.47) and women (FOR 1.07, 95% CI: 0.76, 1.52) after adjusting for education and age. CONCLUSIONS: No association was found between peri-conceptional BPA exposure and fecundability in this peri-conception cohort of relatively young, healthy pregnancy planners.	Paediatr Perinat Epidemiol. 2019 Nov;33(6):397-404.	10.1111/ppe.12578	31468552	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0054	O. Yesildemir, Y. Akdevelioglu, A. Duyan Camurdan, B. Cuhaci Cakir, S. B. Eskenazi Kose, D. Arca Cakir, A. Yilun, A. Balci Ozyurt, S. Saburoglu and P. Erkekoglu	2024	Estimated exposure to bisphenol A in breastfed and breastfed plus formula-fed infants in Turkey: a comparison study	This study aimed to estimate and compare dietary exposure to bisphenol A (BPA) in exclusively breastfed (EBF) and breastfed plus formula-fed (BF + FF) infants. A total of 70 mothers and their 0.5-month-old infants (35 EBF and 35 BF + FF) were recruited. Breast milk samples were collected from mothers, and urine samples were collected from infants. Breast milk samples were collected in polypropylene tubes and stored at -20 °C until analysis. Urine samples were collected in sterile polypropylene cups and stored at -80 °C until analysis. Total BPA levels in breast milk, infant formula, and infant urine samples were analyzed by the liquid chromatography (HPLC). While BPA was detected in 42.5% of the breast milk samples, it was in the BF group (mean ± SD = 0.09 ± 0.29 ng/mL). BPA was detected in all of the breast milk samples in the BF + FF group (mean ± SD= 0.72 ± 0.72 ng/mL) (p< 0.05). Similarly, 100% of the infant formula samples in the BF + FF group had detectable levels of BPA (mean ± SD = 1.10 ± 1.17 ng/g formula). The mean urinary BPA levels in the EBF infants (3.31 ± 1.08 µg/L creatinine) were not significantly different from the BF + FF infants (3.83 ± 0.3 µg/g creatinine) (p = 0.23). The average daily BPA intake in EBF infants (0.18 ± 0.11 µg/kg body weight (bw)/day) was found to be significantly higher than in BF + FF infants (0.12 ± 0.09 µg/kg bw/day) (p = 0.05). The estimated daily BPA intake for infants in both groups were below the temporary tolerable daily intake (t-TDI: 4 µg/kg bw/day). Consequently, BPA intake of EBF and BF + FF infants were within safe daily limits during the first six months of life.	Drug Chem Toxicol Vol.47 Issue 3 Pages 253-263	10.1080/01480545.2022.2160456	36571147	ヒト	バイオモニタリング	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0055	K. E. Yeo, S. Lim, A. Kim, Y. B. Lim, C. R. Lee, J. J. Kim and B. N. Kim	2025	Association Between Endocrine-Disrupting Chemicals Exposure and Attention-Deficit/Hyperactivity Disorder Symptoms in Children With Attention-Deficit/Hyperactivity Disorder	OBJECTIVES: This study investigated the relationship between exposure to endocrine-disrupting chemicals (EDCs), specifically phthalates, bisphenol A, bisphenol F, and bisphenol S, and the severity of attention-deficit/hyperactivity disorder (ADHD) symptoms using neuropsychological tests in children diagnosed with ADHD. METHODS: This study included 87 medication-naive children with ADHD aged 6-16 years. The urinary concentrations of EDCs were measured, and ADHD symptom severity was evaluated using neuropsychological tests and clinical symptom scale measurements. The Jonckheere Terpstra test, Pearson and Spearman correlation analyses, linear regression models, and multiple regression models were used to examine the relationships between EDC exposure and ADHD symptoms. RESULTS: A significant correlation was observed between urinary phthalate metabolite concentrations and commission error T scores in the visual Advanced Test of Attention test. No significant associations were found with other neuropsychological indicators or bisphenol levels. CONCLUSIONS: Phthalate exposure affects impulsivity in children with ADHD, which is consistent with the results of previous studies that used parental surveys. However, bisphenols are not clearly associated with ADHD symptoms, which is consistent with the results of previous studies.	J Korean Acad Child Adolesc Psychiatry. 2025 Jan 1;36(1):18-25.	10.5765/jkacap.240035	39811025	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0056	N. N. Yenigül, S. Dilbaz, B. Dilbaz, İ. Kaplanoğlu, F. Güçlü, G. Aldemir, E. Baser, R. Ozaki and O. Mosalioğlu Yaklı	2021	The effect of plastic bottled water consumption on outcomes of ICSI cycles undertaken for unexplained infertility	RESEARCH QUESTION: Do bisphenol A (BPA) levels in maternal urine, serum and follicular fluid affect embryo quality and intracytoplasmic sperm injection (ICSI) cycle outcomes in women with unexplained infertility? DESIGN: Prospective study conducted between 1 April 2019 and 30 September 2020. The study cohort consisted of 92 women aged between 23 and 37 years who underwent intracytoplasmic sperm injection owing to unexplained infertility. Urine samples were collected on the day of oocyte retrieval, and serum and follicular fluid samples were collected during oocyte retrieval. Demographic features and IVF outcomes of the patients were collected. RESULTS: Among the 92 women who underwent ICSI, 50 (54.3%) patients drank only bottled water and 42 (45.7%) patients drank other tap water/boiled water/filtered water/mineral water. Only water consumption was defined as bottled water consumption. Patients who consumed tap water had statistically significantly lower BPA values in their body fluids compared with patients who consumed plastic bottled water (all P < 0.001). Women who had given birth (1 embryo transferred had lower serum BPA values than women who had given birth (2 embryos transferred (3.02 ± 1.17 versus 26.9 ± 37 ng/ml, P = 0.001). Serum and follicular fluid BPA levels were statistically significantly higher in women who failed to achieve clinical pregnancy (P < 0.001, P = 0.008, respectively) and values of a live birth (both P < 0.001). CONCLUSIONS: A negative relationship was found between serum and follicular fluid BPA levels and embryo quality, clinical pregnancy and live birth in these women. In addition, the BPA levels of women who consume tap water at home were lower than those who use plastic bottled water.	Reprod Biomed Online. 2021 Jul;43(1):91-99	10.1016/j.rbmo.2021.04.010	34001442	ヒト	生殖(不妊)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0057	J. F. Yap, K. S. Wan, M. F. M. Yusoff, Y. C. Lim and R. K. Supramani	2025	Challenges in diagnosing occupational allergic contact dermatitis: a case report	BACKGROUND: In Malaysia, occupational allergic contact dermatitis (OCD) is often under-reported. This case report describes a chemical engineer who developed possible ACD, likely due to workplace allergen exposure. CASE PRESENTATION: A 30-year-old male chemical engineer presented with a 3-month history of recurrent, pruritic, erythematous rashes on his hands and forearms. He had worked at his current workplace for eight months. A clinical and occupational history was taken, including fragrance use, and a comprehensive physical examination was conducted. Skin testing was not performed. However, among these, only 'bisphenol A diglycidyl ether', a component of 'epoxy resin,' was listed in the safety data sheet as a confirmed occupational exposure. In accordance with its local regulations, this case was reported as an occupational dermatitis' to the Department of Occupational Safety and Health. The patient was prescribed symptomatic topical treatments, including emollients and topical steroids. Additionally, he was advised to switch to hypoallergenic products. On follow-up, his chronic inflammatory skin lesions showed improvement. CONCLUSIONS: Through occupational history taking and patch testing are successful for diagnosing ACD. Personalized health education and regular follow-ups, is crucial in monitoring lesion resolution and evaluating the effectiveness of preventive measures. In workplace settings.	Ann Occup Environ Med. 2025 Apr:37:e7.	10.35371/aoem.2025.37.e7	40394836	ヒト	免疫	-	-	-	-	-	-	症例報告	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0058	J. Yao, F. Wang, Y. Zhang, Z. Zhang, J. Bi, J. Ha, P. Li, X. Han, Y. Wei, X. Zhang, H. Guo and M. Ha	2022	Association of serum BPA levels with changes in lipid levels and dyslipidemia risk in middle-aged and elderly Chinese	Previous evidences exploring the associations of BPA with lipid changes and dyslipidemia did not obtain consistent results. To evaluate whether serum BPA concentration was associated with changes in blood lipid levels and incident dyslipidemia risk in middle-elderly Chinese adults, we conducted a prospective study with 1880 participants (average 62.65 years old) derived from the Dongfeng-Tongji cohort which was founded in 2008 and followed up each 3 years. Serum BPA levels were measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Changes in lipid levels were calculated as Δ (wide which equal to 1 and 2013) - 1 and 2008). The diagnosis of dyslipidemia was according to Chinese Guidelines on Prevention and Treatment of Dyslipidemia in 2016. We used multivariable linear regression and Logistic regression to explore the associations of serum BPA with changes in lipid levels and incident dyslipidemia risk, respectively. Restricted cubic spline was performed to model the dose-response relationship. Results: 1880 individuals developed with hypercholesterolemia, 87 with hypertriglyceridemia, 30 with high-LDL-cholesterolemia, 76 with low-HDL-cholesterolemia, and 1196 with dyslipidemia. Serum BPA levels were significantly related to TC, LDL-c, and Non-HDL-c levels. In the prospective study, each ln-BPA increase was associated with 0.05 (95% CI: 0.02, 0.08) mmol/L increase in TC, 0.07 (95% CI:0.03, 0.11) mmol/L increase in Non-HDL-c, 0.05 (95% CI: 0.01, 0.08) increase in lg TC/HDL-c, and 0.04 (95% CI: 0.00, 0.08) increase in lg Non-HDL-c (P < 0.05). We only observed significant associations in females but not in males. Besides, serum BPA levels were positively associated with hypercholesterolemia (OR=1.2, 95% CI: 1.01, 1.43). The restricted cubic splines showed similar results. In conclusion, serum BPA was associated TC and Non-HDL-c changes, and BPA was also associated with increased risk of hypercholesterolemia. Further prospective studies with large sample size are warranted to validate our findings.	Ecotoxicol Environ Saf. 2022 Aug:241:113819.	10.1016/j.ecoenv.2022.113819	36068747	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0059	Z. Yang, H. Liu, J. Wei, R. Liu, J. Zhang, M. Sun, C. Shen, J. Liu, K. Mao, Y. Chen, X. Yang, P. Yu, L. Chen and N. J. Tang	2024	Bisphenol mixtures, metal mixtures and type 2 diabetes mellitus: Insights from metabolite profiling	BACKGROUND: Little is known about the combined effect of bisphenol mixtures and metal mixtures on type 2 diabetes mellitus (T2DM) risk, and the mediating roles of metabolites. METHODS: The study included 886 participants from the Dongfeng-Tongji cohort. Urinary bisphenols and metals were measured by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) and inductively coupled plasma mass spectrometry (ICP-MS), respectively. Widely targeted metabolomics was employed to obtain the serum metabolomic profiles. Conditional logistic regression models were used to assess the single associations of bisphenols and metals with T2DM risk after multivariable adjustment. Additionally, the joint effects of bisphenol mixtures and metal mixtures were examined using quantile-based g-computation (QG-C) models. Furthermore, differential metabolites associated with T2DM were identified, and metabolic analyses were performed to explore the role of metabolites in the associations of bisphenols and metals with T2DM risk. RESULTS: The results showed bisphenol mixtures were associated with an increased T2DM risk, with bisphenol S (BPS) contributing the most. Metal mixtures were also associated with an increased T2DM risk, with cobalt (Co) contributing the most. Moreover, 42 differential metabolites were screened between the T2DM cases and controls. Mediation analyses indicated that 9 metabolites mediated the association between BPS and T2DM, while 1 alone mediated the association between Co and T2DM risk. CONCLUSIONS: The study indicated that BPS, Co, Fe, and Zn were the primary contributors to increased T2DM risk, and metabolites played a mediating role in the associations of BPS and Co with the risk of T2DM. Our findings contribute to a better understanding of the mechanisms underlying the associations of bisphenols and metals with T2DM.	Environ Int. 2024 Aug:190:108921.	10.1016/j.envint.2024.108921	39098088	ヒト	代謝	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0060	Y. Yang, X. Bai, J. Lu, R. Zou, R. Ding and X. Hu	2023	Assessment of five typical environmental endocrine disruptors and thyroid cancer risk: a meta-analysis	INTRODUCTION: There are conflicting results on the association between environmental endocrine disruptors (EEDs) and thyroid cancer. This meta-analysis aimed to elucidate the relationship between EEDs and thyroid cancer. METHODS: We searched for epidemiological studies on EEDs and thyroid cancer published in PubMed and Web of Science up to December 2022. We then screened the studies that could extract data on EEDs concentration levels in both thyroid cancer patients and healthy controls. We excluded articles that could not calculate effect sizes, focused on other thyroid diseases, or lacked controls. Standardized mean difference (SMD) was calculated to analyze the association between EEDs and thyroid cancer. We measured the heterogeneity among the included studies using Q- and I-squared (I2) tests and Begg's test, and evaluated article quality using the Newcastle-Ottawa Quality Score (NOS). In the end, fifteen eligible case-control studies were included. RESULTS: Our comprehensive analysis revealed that polychlorinated biphenyls (PCBs) (SMD = 0.61, 95%CI = 0.34, 0.87, P < 0.001), polybrominated diphenyl ethers (PBDEs) (SMD = 0.49, 95%CI = 0.22, 0.76, P < 0.001), and bisphenol A (BPA) (SMD = 0.21, 95%CI = 0.01, 0.41, P = 0.042) were significantly associated with thyroid cancer.PFASs (SMD = -0.22, 95%CI = -0.50, 0.07, P = 0.137) and PAHs (SMD = -0.08, 95%CI = -0.50, 0.33, P = 0.693) had no significant association with thyroid cancer. Sensitivity analysis indicated that the findings were stable. Publication bias was found for PCBs (Egger's test, P = 0.041), but not for BPA (P = 0.602). The study also found that exposure to certain EEDs, such as PBDEs, PAHs, and heavy metals, increases the risk of thyroid cancer. However, further large-scale epidemiological studies and mechanism studies are needed to verify these potential relationships and understand the underlying biological mechanisms.	Front Endocrinol (Lausanne). 2023 Oct 30:14:1283087.	10.3389/fendo.2023.1283087	38027118	ヒト	甲状腺(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0061	P. Yang, B. G. Liu, B. Zhou, W. C. Cao, P. P. Chen, Y. L. Deng, J. Hou, S. Z. Sun, T. Z. Zhang, W. Q. Lu, L. M. Cheng, W. J. Zeng and Q. Zeng	2021	Sex-specific associations of prenatal exposure to bisphenol A and its alternatives with fetal growth parameters and gestational age	BACKGROUND: Bisphenol A (BPA) can cause detrimental effects on fetal growth. However, the effects of BPA alternatives, such as bisphenol F (BPF) and bisphenol S (BPS), on fetal growth are less known. OBJECTIVE: To investigate the relationships of prenatal BPA, BPF, and BPS exposures with fetal growth parameters and gestational age. METHODS: Urinary BPA, BPF, and BPS were measured in 1,347 pregnant women before delivery in a Chinese cohort. The associations of prenatal exposure to BPA, BPF, and BPS with fetal growth parameters and gestational age were examined, and covariates stratified by fetal sex were also considered. We used a restricted cubic splines (RCS) model to examine the dose-response associations between exposures and outcomes. RESULTS: Maternal urinary BPA and BPF were negatively related to birth length (-0.50 cm, 95% CI: -0.97, -0.03 comparing the extreme exposure groups, p for trend = 0.03) and ponderal index (-0.08 kg/m3, 95% CI: -0.15, -0.01, p for trend = 0.03), respectively. Maternal urinary BPA was positively related to gestational age (0.28 weeks, 95% CI: 0.03, 0.53, p for trend = 0.03). Dose-response relationships were nonlinear for BPA and BPS, but linear for BPF. Maternal urinary BPA and BPF were also positively related to birth weight (-102.99 g, 95% CI: -203.98, -2.00 comparing the extreme exposure groups, p for trend = 0.05) and ponderal index (-0.29 kg/m3, 95% CI: -0.57, -0.01 comparing the extreme exposure groups, p for trend = 0.04), respectively, both p for trends < 0.05), and maternal urinary BPS was associated with shorter gestational age (-0.35 weeks, 95% CI: -0.67, -0.03 comparing the extreme exposure groups, p for trend = 0.03). These associations were only observed in girls and exhibited a linear dose-response relationship. CONCLUSIONS: Prenatal BPA, BPF, and BPS exposures were associated with detrimental effects on fetal growth parameters, and stronger effects were noted in female infants.	Environ Int. 2021 Jan:146:106305.	10.1016/j.envint.2020.106305	33395947	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0062	L. Yang, Y. Liu, H. Zhang, Y. Zhao, G. Zhang, Y. Cao, Z. Wang, H. Liang, M. Miao, T. Zhang and J. Xue	2025	Interpretable machine learning-based insights into early-life endocrine disruptor exposure and small vulnerable newborns	Early life exposure to endocrine disrupting chemicals (EDCs) may contribute to small vulnerable newborns, including conditions such as being small for gestational age (SGA) and preterm birth (PTB), yet evidence remains limited. This study, within it, based on 735 mother-infant pairs in the Chinese Jiaozuo Birth Cohort (2018–2020), including 78 SGA and 56 PTB cases, employed interpretable machine learning to elucidate isolated effects of 36 EDCs on SGA and PTB risk and sex interactions in a multi-substance exposure context. Extra Trees and CatBoost classifiers performed best for SGA and PTB, respectively, achieving sensitivities of 0.667 and 0.750 and AUC-ROC values of 0.747 and 0.824. Bisphenol A (BPA), bisphenol S (BPS), and 2,4-dichlorophenol (2,4-DCP) were identified as key contributors to SGA risk, while BPA, BPS, and 2,5-dichlorophenol (2,5-DCP) were linked to PTB. Sex-specific effects were evident, with BPA and BPS associated with increased SGA risk in females (SHAP values: 0.0028 and 0.0026, respectively), while 2,5-DCP and 2,4-DCP showed stronger associations with PTB in males (SHAP values: 0.0022 and 0.0020). Dose–response relationships revealed nonlinear patterns, with BPA and BPS exceeding 2.0 ng/mL increasing SGA risk by 1.8- and 1.6-fold, respectively, and 2,5-DCP and 2,4-DCP above 0.5 ng/mL raising PTB risk by 2.1- and 1.9-fold, respectively. Co-exposure to BPA and BPS further amplified SGA risk (OR = 2.3), while 2,5-DCP and 2,4-DCP co-exposure increased PTB risk (OR = 2.5). Mediation analysis revealed that BPA and BPS partially mediated the effects of 2,5-DCP and 2,4-DCP on PTB, with mediation proportions ranging from 12% to 18%. These findings underscore the critical role of early-life exposure to EDC mixtures in adverse birth outcomes and highlight the sex-specific vulnerabilities of newborns. The integration of interpretable machine learning with traditional epidemiological approaches offers a powerful framework for identifying high-risk exposure patterns and informing targeted public health interventions.	J Hazard Mater. 2025 Jul 15:492:138067.	10.1016/j.jhazmat.2025.138067	40158502	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0063	J. Yang, H. Wang, H. Du, L. Xu, S. Liu, J. Yi, Y. Chen, Q. Jiang and G. He	2021	Serum Bisphenol A, glucose homeostasis, and gestational diabetes mellitus in Chinese pregnant women: a prospective study	Lab studies have suggested that exposure to Bisphenol A (BPA) could disturb glucose homeostasis, but epidemiologic studies are limited and show inconsistent results. For pregnant women. For this, 338 pregnant women were selected from a pregnant women cohort established in Tangshan City in North China between 2013 and 2014. Serum concentrations of BPA were measured in the early terms of pregnancy, and testing glucose and lipid levels were also measured in the same period. Gestational diabetes mellitus (GDM) was diagnosed between 24 and 28 weeks of gestation. Logistic regression was used to estimate the risk of GDM in terms of pregnancy. BPA was detected in 47.63% of pregnant women with a median of 0.49 ng/mL. Natural log-transformed BPA (Ln-BPA) was positively associated with fasting blood glucose (0.039; 95% CI: 0.003, 0.076) and triglycerides (0.099; 0.009–0.222), and homeostasis model insulin resistance index (HOMA-IR) (0.226; 0.087–0.365) in the middle term of pregnancy by multiple linear regression model after adjusting for potential confounders. After serum BPA levels were divided into three groups (low, middle, and high), BPA showed a positive dose–response relationship with fasting glucose, insulin, and HOMA-IR in the middle term of pregnancy. Increased BPA concentration tended to increase the RR of GDM although not statistically significant (risk ratio: 2.10; 95% CI: 0.88–5.00 for high vs. low tertile of BPA concentrations). These findings suggested that exposure to BPA might affect glucose homeostasis and the middle term of pregnancy was a potentially sensitive period.	Environ Sci Pollut Res Int. 2021 Mar;28(10):12546-12554.	10.1007/s11356-020-11263-4	33083951	ヒト	生殖発生(妊娠糖尿病)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0064	C. F. Yang, W. J. J. Kamsaun, C. C. Yang, M. L. Chan and J. I. Wang	2020	Bisphenol a Exposure, DNA Methylation, and Asthma in Children	Epidemiological studies have reported the relationship between bisphenol A (BPA) exposure and increased prevalence of asthma, but the mechanisms remain unclear. Here, we investigated whether BPA exposure and DNA methylation related to asthma in children. We collected urinary and blood samples from 226 children (Childhood Environment and Allergic Diseases Study cohort aged 5 years. Thirty-three candidate genes potentially related to asthma were selected for methylation analysis. Urinary BPA was measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Genome-wide DNA methylation levels were analyzed by Infinium MethylationEPIC BeadChip. Multivariate linear regression was used to examine the relationship between DNA methylation and BPA exposure and asthma risk. Associations between the methylation percentage and BPA exposure were also examined. Accordingly to our findings, MAPK1 showed differential methylation and was further investigated in 226 children. Adjusting for confounders, urinary BPA glucuronide (BPAG) had inversely correlated with MAPK1 promoter methylation (β = -0.08, p = 0.003). For the logistic regression analysis, MAPK1 methylation status was dichotomized into higher methylated and lower methylated groups with cut-off values of the median methylation percentage (78%) while performing the analysis. MAPK1 methylation was lower in children with asthma than in children without asthma (mean ± SD, 84.82 ± 1.68% vs. 79.82 ± 5.96%) (p = 0.001). Mediation analysis suggested that MAPK1 methylation acts as a mediation variable between BPA exposure and asthma. The mechanism of BPA exposure on childhood asthma might, therefore, be through the alteration of MAPK1 methylation. The mechanism of BPA exposure on childhood asthma might, therefore, be through the alteration of MAPK1 methylation.	Int J Environ Res Public Health. 2020 Jan 1;17(1):298.	10.3390/ijerph17010298	31906378	ヒト	免疫	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0065	S. S. Yalçın, E. Okmen, B. B. Kuykınmaz, S. Yalçın, O. Aykut and D. U. Gel-Nkaya	2025	Engraftment after pediatric hematopoietic stem cell transplantation and its association with recipient and donor phthalate and bisphenol A exposure levels: A cohort study	Phthalates and bisphenols, ubiquitous compounds found in various everyday products, have garnered attention due to their potential health-disrupting effects. This study aimed to (1) investigate urinary phthalate metabolite and bisphenol A (BPA) levels in pediatric hematopoietic stem cell transplantation (HSCT) recipients and their donors before and after transplantation, and (2) examine their time-dependent changes. Spot urine samples, collected before the conditioning regimen (day 0), day 5, day 7, day 14, day 21, day 42, and 12 months after transplantation, were analyzed for phthalate metabolites and BPA using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Urine samples from patients' recipients and donors were collected for analysis of phthalate metabolites and BPA in 30 donor-recipient pairs. Monoethyl phthalate metabolite was not detectable in any of the urine samples. A notable increase in phthalate metabolites and BPA levels was observed in recipients starting from day 28. Granulocyte engraftment time showed a positive correlation with donor urinary levels of mono-n-butyl phthalate (MBP), mono-(2-ethylhexyl) phthalate (MEHP), and monobenzyl phthalate metabolites, with recipient MBP levels measured on day 0. Moreover, donor urinary MBP and MEHP levels were also linked to delayed platelet engraftment. No relationship was observed between engraftment timing and the urine levels of neonatal/infantile/childhood exposure to phthalates and BPA. Overall, this study suggests that HSCT may increase exposure to phthalates and BPA in recipients, and that the timing of engraftment may be influenced by the urine levels of phthalate metabolites and the levels of urine phthalate metabolites or BPA. These findings highlight the potential role of preclinician exposure in influencing engraftment outcomes, although no significant associations were found between MBP or BPA levels and engraftment.	Environ Toxicol Pharmacol. 2025 Mar:114:104625.	10.1016/j.etap.2024.104625	39734026	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0066	S. S. Yalçın, I. Erol, B. Oğuz-ar and A. Ozcova	2022	Association of urine phthalate metabolites, bisphenol A levels and serum electrolytes with 24-h blood pressure profile in adolescents	BACKGROUND: Among the possible causes of hypertension in adolescence, electrolyte imbalances and environmental pollutants are drawing increasing attention. We aimed to examine the relationship between bisphenol A (BPA), phthalate metabolites, and serum electrolytes and blood pressure. METHODS: Eighty-six participants aged 12–16 years were included in the study. Body mass index (BMI), office blood pressure and 24-h ambulatory blood pressure measurements (ABPM), and carotid intima-media thickness were determined. Blood samples were taken for hemogram, renal function tests, and serum electrolytes. Urine and total BPA and phthalate metabolites were measured by LC-MS/MS. RESULTS: Mean age was 14.2 ± 1.4 years, and 52.3% were girls. Mean BMI was 21.2 ± 4.3 kg/m2. Forty-two (48.8%) adolescents in ABPM hypertension groups had higher BMI standard deviation score (SDS), glucose, cholesterol, insulin, fat mass/ lean mass ratio, compared to the normal blood pressure profile group. The percentage of adolescents with abnormal urinary mono- benzyl phthalate (MBzP) was higher in ABPM hypertensive (32.1%) and MCHT groups (33.3%), compared to the normal blood pressure profile group (6.9%, p = 0.002). Urinary BPA was detected in 72.1% of the participants. Urinary BPA concentrations were significantly higher in the ABPM hypertensive group (p = 0.001). Urinary mono-benzyl phthalate and 'albumin-corrected calcium-corrected per product' compared to others. Adolescents with abnormally urinary MBzP levels had higher blood pressure profiles, systolic blood pressure (SBP) daytime hypotatic blood pressure (SDS), and night-time/ linear arterial pressure SDS, systolic blood pressure SDS, and diastolic blood pressure (DBP) measurements, compared to others. MCHT was found to be associated negatively with incrementally phthalate and the sum of dibutyl phthalate metabolites and ABPM HT with BCPM. There was no significant association between blood pressure profiles and liver- and total BPA status. CONCLUSION: MBzP was associated with adverse blood pressure profiles. In adolescence. Additive follow- up studies are necessary for cause-effect relations.	BMC Nephrol Vol.23 Issue 1 Pages 141	10.1186/s12882-022-02774-y	35410150	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0067	Y. J. Xu, H. L. Gao, H. Liu, N. W. Zhao, Q. Cheng, F. R. Zhang, J. Yu, A. Q. Wang, Y. J. Dou, B. Ma, F. Zhu, X. L. Xu, C. J. Li, J. Wu, N. Shen and B. Xue	2021	Urinary levels of dimethoate, bisphenol A and benzo[a]pyrene in first-year students of Hohai University from different geographical regions	BACKGROUND: The objective of this study was to detect the urinary levels of dimethoate, benzo[a] pyrene (BaP), and bisphenol A (BPA) in first-year Hohai University students with different geographic origins. METHODS: First-morning urine samples were collected from 569 freshmen aged 16–19 years. Considering their living environment, 31 glucuronidase/sulfatase was combined with solid-phase extraction and liquid chromatography tandem mass spectrometry based method. Geometric means (GMs) of these three chemicals are presented by body mass index (BMI) and location in a volume based and creatinine-standardized way. RESULTS: The detection frequencies of dimethoate, BaP, and BPA were 100%, 100%, and 99.8%, respectively. The GMs of dimethoate, BaP, and BPA were 0.5, 0.2, and 1.3 μg/L, respectively. The GM of dimethoate in males was significantly higher than that in females. The individuals born in 2001 had higher GM concentrations of dimethoate, BPA, and 3-OHBaP. The individuals of Southwest China had significantly lower GM concentrations of dimethoate, BPA, and 3-OHBaP than those who lived in other locations in China. CONCLUSION: The average level of environmental chemical accumulation in freshmen is lower in Southwest China and differs in youth who live in different regions. In addition, obesity is correlated with higher toxic levels in youth.	BMC Public Health Vol.21 Issue 1 Pages 1692	10.1186/s12889-021-11726-4	34530795	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0068	Y. Xu, H. Gao, Z. Du, H. Liu, Q. Cheng, F. Zhang, J. Yu, A. Wang, Y. Dou, B. Ma, N. Zhao, F. Zhu, X. Xu, N. Shen, J. Wu and B. Xue	2022	A new approach for reducing pollutants level: a longitudinal cohort study of physical exercises in young people	BACKGROUND: The present study aimed to evaluate the elimination of three common pollutants (dimethoate, benzo[a]pyrene (BaP) and bisphenol A (BPA)) by different physical exercises and to assess the possible factors which could affect the pollutants elimination. METHODS: A total of 282 individuals who chose different kinds of exercises in accordance to their own wish were recruited. The levels of urinary pollutants were measured using β-glucuronidase/sulfatase hydrolysis followed by a high-performance liquid chromatography tandem mass spectrometry based method. RESULTS: Totally, the levels of dimethoate, BaP and BPA were reduced after physical exercises (all p < 0.05). Among the three pollutants, the elimination of BPA was the most significant (p < 0.001). Multivariate linear regression analysis showed that the level and BMI change was associated factor affecting the improvement effect of dimethoate, BaP and BPA while BMI (body mass index) was a risk factor. Nonetheless, the duration of Southwest China had significantly lower GM concentrations of dimethoate, BPA, and 3-OHBaP than those who lived in other locations in China. CONCLUSION: The present findings indicate that physical exercises can be considered as a novel approach to eliminate pollutants level in human body and can also give suggestions for choosing specific physical exercises to male and female individuals. Moreover, those who are with higher BMI need to lose weight before eliminating pollutant level through physical exercises.	BMC Public Health Vol.22 Issue 1 Pages 223	10.1186/s12889-022-12621-2	35114971	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0069	S. Xu, X. Yuan, Y. Wang, Z. Fu, K. Chen, Z. Cui, L. Xu, H. Zhang, D. Xia and Y. Wu	2025	Bisphenols exposure at environmentally relevant dose promoted ovarian cancer progression and modulated tumor microenvironment through β-catenin/SPP1 axis	Bisphenol A (BPA) and its substitute, Bisphenol S (BPS) are typical endocrine-disrupting chemicals used in plastics, but their cancer-promoting effects has remained controversial. Here, we investigated the effects of environmentally relevant doses of BPA/BPS exposure on the tumor microenvironment (TME) in ovarian cancer. BPA exposure boosts was exhibiting a declining trend and BPS showing an ascending trend in the female population. Moreover, BPA and BPS exposure (0.5 μg/L, 5 μg/L, 50 μg/L) significantly promoted ovarian cancer progression in vivo and in vitro. Mechanistically, BPA and BPS activated the Wnt/β-catenin signaling pathway, thereby both inducing the SPP1 gene transcription. Notably, low dose BPA/BPS facilitated ovarian cancer cells to secrete SPP1 protein to adapt to the TME growth, subsequently fostering the transformation of fibroblasts into cancer-associated fibroblasts (CAFs), which could reshape the TME of ovarian cancer. Two in vivo experiments established with nude mice and SPP1(-/-) mice respectively, both confirmed that low dose BPA/BPS exposure increased the incidence of tumor metastasis accompanied by CAF infiltration, while administration of SPP1-neutralizing antibodies effectively blocked these effects. Our results indicated that exposure to either BPA or its substitute BPS could promote the release of secreted protein SPP1 into the β-catenin/SPP1 axis, ultimately modulating the TME and enhancing the progression of ovarian cancer, providing new evidence and potential intervention strategies for the toxicological assessment and management of bisphenols.	J Hazard Mater. 2025 Jun 15:490:137824.	10.1016/j.jhazmat.2025.137824	40054195	動物、in vitro	1	1	単離＋増殖あり	マイクロウェル、SPPシャドウ	0	50 μg/kg.1	-	-	-	-	1	0	不明	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0070	Y. Xiong, S. Xu, Z. Wang, Z. Wang, S. Li, M. Zhang and Y. Zhang	2024	BPA-free? Exploring the reproductive toxicity of BPA substitutes BPS and BPF on endometrial decidualization	Bisphenol A (BPA) exposure is linked to multiple adverse health outcomes, prompting the rise of "BPA-free" products. However, substitutes like Bisphenol S (BPS) and Bisphenol F (BPF) are equally prevalent, with detection frequencies and concentrations rivaling BPA. Our research previously identified BPS as an endocrine disruptor affecting reproductive and developmental systems. This study explores the impact of BPS, BPF, and BPF on endometrial decidualization and receptivity. We detected these bisphenols in serum samples from infertile women undergoing assisted reproductive technology (ART) treatment whose average age was 31.58 years. Human endometrial stromal cells were exposed to varying concentrations (1, 10, 50, 100, 500, and 1,000 μM) of BPA, BPS, and BPF, following hormonal induction of decidualization (0.5 mM 8-bromo-cAMP (8-Br-cAMP) and 10 μM medroxyprogesterone acetate) for 6 days). Methods including CCK-8, EdU, qPCR, untargeted metabolomics, and transcriptome sequencing assessed cell proliferation, decidualization markers, and metabolic changes. Results indicated that BPS and BPF exposure significantly reduced cell proliferation (p < 0.05) and impaired decidualization. Differential cell proliferation and reduced decidualization markers. Differential metabolites (FC, 1.5; 1.5) and gene expression (GSE6, NAB1, LEF1) were observed with BPS, BPF, and BPE exposure, respectively. Enriched pathways included glutathione metabolism, arginine biosynthesis, ABC transporters, cAMP signaling, and glycogen signaling. Metabolomics and transcriptome analyses unveiled the reproductive toxic effects of BPS and its substitutes, suggesting significant impacts on endometrial decidualization through diverse signaling pathways.	Ecotoxicol Environ Saf. 2024 Nov 15:287:117275.	10.1016/j.ecoenv.2024.117275	39536566	in vitro	子宮	-	-	-	-	-	-	1	0	10, 1 mM, 10 mM, 100 mM, 1 μM	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0071	Y. Xiong, Z. Li, X. Xiong, Z. Luo, K. Zhong, J. Hu, S. Sun and C. Chen	2025	Associations between phenol and paraben exposure and the risk of developing breast cancer in adult women: a cross-sectional study	Increasing evidence suggests that endocrine-disrupting chemicals (EDCs) have adverse effects on breast cancer (BC). The aim of this study was to assess the association between exposure to prevalent EDCs (phenol, paraben) and the risk of developing BC in adult women. Data from 2,000 female participants aged ≥ 20 years with BC information in the National Health and Nutrition Examination Survey (NHANES) database were obtained from the 2005–2018 National Health and Nutrition Examination Survey. A total of 4,000 subjects were included in this cross-sectional study. The researchers first employed multivariable regression models to indicated that exposure to elevated concentrations of TRS increased the risk of developing BC by 2.32 (OR 95% CI = 1.05–5.76, p = 0.032) and 3.56 times (OR 95% CI = 1.23–10.86, p = 0.006), respectively. The nonlinear association between TRS concentrations and the risk of developing BC was statistically significant (P nonlinear = 0.007), and this nonlinear dose–response relationship was examined using restricted cubic splines (RCS) curve modeling on the natural log-transformed TRS concentrations. The association between TRS concentrations and the risk of developing BC was more pronounced among overweight individuals (BMI ≥ 25 kg/m2), those aged ≥ 60 years, and white individuals. Weighted quantile sum (WQS) and quantile-based g-computation (qgcomp) models revealed that exposure to TRS was significantly positively associated with BC risk (OR 95% CI = 1.19–1.68, p < 0.001). Furthermore, in the WQS model, 3,4-dichlorophenol, a chlorinated phenol, exhibited the highest weight (0.61). Sensitivity analyses confirmed that TRS, particularly in overweight individuals (BMI ≥ 25 kg/m2), those aged ≥ 60 years, and white individuals.	Sci Rep Vol.15 Issue 1 Pages 4038	10.1038/s41598-025-88765-z	39900803	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0072	C. Xiong, L. Xu, X. Dong, Z. Cao, Y. Wang, K. Chen, M. Gao, S. Xu, Y. Li, W. Xia and A. Zhou	2023	Trimester-specific associations of maternal exposure to bisphenols with neonatal thyroid stimulating hormone levels: A birth cohort study	BACKGROUND: Growing evidence suggests that exposure to bisphenol A (BPA) during pregnancy could interfere with neonatal thyroid function. Bisphenol F (BPF) and bisphenol S (BPS) are increasingly used as the substitutes for BPA, but little is known about their potential thyroid disrupting effects. METHODS: We measured the urinary levels of BPA, BPF, and BPS in both maternal samples in the first, second, and third trimesters for bisphenol exposure assessment, and neonatal heel prick blood samples for TSH measurement. Multiple informant model and quantile g-computation were used to evaluate the trimester-specific associations of bisphenols individually and mixture with TSH, respectively. RESULTS: The Each doubling concentration increase of maternal urinary BPA in the first trimester was significantly related to a 3.58 % (95% CI: 0.58 %, 6.72 %) increment in neonatal TSH. Each doubling concentration increase of BPS in the first, second and third trimesters were associated with 3.58 % (95% CI: 0.58 %, 6.72 %), 3.58 % (95% CI: 0.58 %, 6.72 %), and 3.58 % (95% CI: 0.58 %, 6.72 %) increment in neonatal TSH, respectively. The concentration and TSH was observed. The relationship between exposure to BPA/BPS and neonatal TSH were more evident in female infants. Quantile g-computation indicated that maternal co-exposure to bisphenols in the first trimester was significantly associated with neonatal TSH levels in a non-linear fashion. CONCLUSIONS: Maternal exposure to BPA and BPS were positively associated with neonatal TSH levels. The results indicated the endocrine disrupting effect of prenatal exposure to BPS and BPA, which should be of particular concern.	Sci Total Environ. 2023 Jul 1:880:163354.	10.1016/j.scitotenv.2023.163354	37023811	ヒト	甲状腺	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0073	C. Xiong, K. Chen, L. L. Xu, Y. M. Zhang, H. Liu, M. L. Gao, Z. Q. Xia, Y. L. Wang, X. Y. Ma, X. X. Fan, J. Q. Chen, Y. R. Liu, Y. Y. Li, W. Xia, Y. J. Wang and A. F. Zhou	2024	Associations of prenatal exposure to bisphenols with BMI growth trajectories in offspring within the first two years: evidence from a birth cohort study in China	BACKGROUND: Prenatal bisphenol exposure has been reported to be associated with lower birth weight and obesity-related indications in early childhood. These findings warrant an investigation of the relationship between prenatal bisphenol exposure and BMI growth trajectories in offspring within the first two years. METHODS: Maternal urine samples were collected during the first, second, and third trimesters. A total of 1,000 pairs of children aged up to two years and its identify the critical exposure periods. METHODS: A total of 850 mother-offspring pairs were recruited from Wuhan Children's Hospital between December 2013 and March 2016. Maternal urine samples collected during the first, second, and third trimesters were analyzed for bisphenol A (BPA), bisphenol S, and bisphenol F (BPF) concentrations. Measurements of height and weight were taken at 0, 1, 6, 8, 12, 18, or 24 months. Children's BMI was assessed according to the World Health Organization criteria, and group-based trajectory modeling was used to identify BMI growth trajectories. The associations between prenatal bisphenol exposure and BMI growth trajectory patterns were assessed using multinomial logistic regression models. RESULTS: The BMI growth trajectories of the 826 children were categorized into three groups: "Low-stable" (n = 413, 50.0%), "Medium-increasing" (n = 330, 40.0%), and "High-increasing" (n = 83, 10.0%). Children in the "High-increasing" group had the highest prenatal exposure to BPA during the second trimester (odds ratio (OR) = 2.38, 95% confidence interval (CI) = 1.09–5.22) and BPF during the third trimester (OR = 1.59, 95% CI: 1.03–2.47) of the children's quartile concentration were associated with an increased likelihood of the low-increasing BMI trajectory. Furthermore, in the subgroup analysis by infant sex, the positive association between the highest quartile of prenatal exposure to BPA and BPF concentration during the whole pregnancy and the low-increasing BMI trajectory was found only in girls (OR = 2.42, 95% CI = 1.02–5.68). CONCLUSIONS: Our study findings suggest that prenatal exposure to BPA and BPF is commonly and substitute for BPA is associated with BMI growth trajectories in offspring during the first two years, increasing the likelihood of the low-increasing pattern. Video Abstract (MP4 120000 kb).	World J Pediatr. 2024 Jun;20(7):701-711.	10.1007/s12519-023-00767-x	38019382	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0074	T. Xiao, Z. Huang, C. Zhang, B. Quach, Y. Zhu, F. Li, W. Liang, J. Baker, C. Reichetzeder, B. Hocher and Y. Yang	2024	Associations of bisphenol A exposure with metabolic syndrome and its components: A systematic review and meta-analysis	Mounting evidence shows that bisphenol A (BPA) is associated with metabolic risk factors. The aim of this study was to review related epidemiologic studies and conduct a meta-analysis to quantitatively estimate the association between BPA and metabolic syndrome. Four electronic databases were systematically searched to identify suitable articles. A total of 47 published studies were finally included. Two studies involved metabolic syndrome (N for 17, 11 16, and 13 studies on the relationship between BPA with abdominal obesity, blood pressure, fasting plasma glucose, and dyslipidemia, 31, 6, 5, and 6 studies were included in the meta-analysis, respectively. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using random-effects models. Higher BPA exposure was associated with MetS (OR = 1.46, 95%CI: 1.31–1.63; I2 = 0%), abdominal obesity (OR = 1.53, 95%CI: 1.33, 1.76; I2 = 0%), hypertension (OR = 1.16, 95%CI: 1.01, 1.33; I2 = 0%), fasting plasma glucose (OR = 1.22, 95%CI: 1.03–1.44; I2 = 0%), and dyslipidemia (OR = 1.16, 95%CI: 1.01, 1.33; I2 = 0%). However, there was no significant association between BPA exposure and metabolic syndrome components including hypertension, abnormal fasting plasma glucose, and dyslipidemia. The present study found that BPA exposure is significantly associated with a higher risk of abdominal obesity. However, the relationship between BPA with metabolic syndrome and its other components needs further longitudinal studies to verify.	Obes Rev. 2024 Jun;25(6):e13738.	10.1111/obr.13738	38491337	ヒト	代謝（メタアナリシス）	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0075	L. Xiao, X. Wen, L. Li and Y. Li	2024	Correlation of bisphenol A and bisphenol S exposure with the metabolic parameters on FDG PET/CT image	PURPOSE: Bisphenol A (BPA) and its analogs have been proved to be harmful to human health. This study aimed to assess the correlation of BPA and its major analog, Bisphenol S (BPS), with metabolic parameters within main organs using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) imaging. METHODS: A retrospective analysis was conducted on patients who had undergone FDG PET/CT imaging and urine was examined for BPA and BPS levels. Urine samples were collected for detection of BPA and BPS. Standardized uptake values (SUVmean) and SUV(mean) of main organ tissues including liver (SUVliver), fat (SUVfat), and muscle (SUVmuscle) were measured. Pearson correlation analysis was used to assess the correlation between BPA and BPS levels and SUVmean. RESULTS: A total of 100 patients were included. Urine samples revealed detectable BPA and BPS concentrations in 67.0 % (67/100) and 11.0 % (11/100), respectively. Urine BPA exhibited a moderate positive correlation with liver SUVmean (r = 0.381, p < 0.001) and SUVmuscle (r = 0.362, p < 0.001). Urine BPS showed a weak positive correlation with liver SUVmean (r = 0.222, p = 0.027). Conversely, urine BPS demonstrated a negative correlation with thyroid SUVmean (r = -0.413, p < 0.001) and SUVmuscle (r = -0.332, p < 0.001), while a positive correlation was observed between BPS and cerebral cortex SUV(mean) (r = 0.386, p < 0.001). CONCLUSIONS: Urinary levels of BPA and BPS exerted distinct influences on tissue metabolic parameters observed via FDG PET/CT imaging, particularly affecting the liver, thyroid, and cerebral cortex.	Front Public Health Vol.12 Pages 1433122	10.3389/fpubh.2024.1433122	39664558	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0076	Z. Xiang, H. Wang, K. Zhu, R. Liu, S. Zhao, H. Fan, Q. Chen, B. Zhu and R. Song	2025	Phenol exposure, polygenic risk score, and dyslexia in Chinese children: Gene-environment interaction	Phenols, widespread environmental chemicals, may influence neurodevelopment, but their association with dyslexia remains poorly understood. This case-control study, part of the Tongji Reading Environment and Dyslexia Research Project, included 1282 children. We measured urinary levels of three bisphenols, three benzophenones, and two antimicrobials, and constructed a dyslexia-specific polygenic risk score (PRS) using genome-wide association study data. Conditional logistic regression assessed the relationship between phenol exposure and dyslexia risk. Participants were stratified by low or high PRS, and multiplicative and additive models were used to examine the modifying role of genetic susceptibility. Phenol compounds were detected in most urine samples. Elevated urinary bisphenol A (BPA) levels were significantly associated with increased dyslexia risk (OR = 1.39, 95% CI: 1.03–1.87, p = 0.029), and this association was more pronounced among children with high genetic susceptibility (OR = 1.75, 95% CI: 1.22–2.51). Compared to those with low PRS and low BPA exposure, those with high PRS and high BPA exposure had a substantially higher dyslexia risk (OR = 1.75, 95% CI: 1.22–2.51). No significant interaction was observed between PRS and BPA exposure. These findings underscore the importance of reducing BPA exposure as a potential preventive measure and highlight the need for further research to elucidate causal pathways and mechanisms underlying these associations.	Environ Pollut. 2025 Aug 15:379:126536.	10.1016/j.envpol.2025.126536	40425062	ヒト	発達神経	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0077	Z. Xia, C. Lu, Y. Zhang, R. Shi, Q. Lu, Y. Tian, X. Lei and Y. Gao	2023	Associations of exposure to bisphenol A and its substitutes with neurodevelopmental outcomes among infants at 12 months of age: A cross-sectional study	BACKGROUND: Bisphenol A (BPA) exposure has been linked to adverse childhood neurodevelopment, but little is known about whether BPA substitutes exposures are also related to childhood neurodevelopment. OBJECTIVES: To investigate the associations of exposure to BPA and its substitutes with infant neurodevelopment at 12 months. METHODS: A total of 320 infants at 12 months were included from the Laizhou Wan Baseline Cohort Study. Urinary concentrations of BPA, bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF) were measured by ultra-performance liquid chromatography-tandem mass spectrometry. Infant neurodevelopment was measured by Ages and Stages Questionnaires, Third Edition (ASQ-3). Five domain scores measured: Developmental quotient (DQ) scores based on the Gesell Development Schedules (GDS) were used to evaluate infant neurodevelopment. The multivariable linear regression and weighted quantile sum (WQS) regression were applied to estimate the associations of exposure to individual bisphenols and their mixtures with DQ scores, respectively. Dose-stratified analyses were also performed. RESULTS: BPA was detected in 99.4% of urine samples, followed by BPS (93.8%), BPF (83.8%), and BPAF (58.1%). Urinary concentrations of BPA, BPS, BPF, and BPAF were 1.10 ng/mL, 0.14 ng/mL, 0.10 ng/mL, and 0.03 ng/mL, respectively. BPA was positively associated with social DQ scores among all infants (β = 0.59; 95% CI: 0.002, 0.09). After sex stratification, this inverse association was significant in girls (β = 0.085; 95% CI: -0.002, 0.180). Besides, BPA exposure was negatively related to gross motor DQ scores in boys (β = -0.065; 95% CI: -0.078, -0.005). WQS analyses confirmed these results. CONCLUSIONS: Our study suggests that bisphenol exposure during infancy may be associated with poor infant neurodevelopment, and BPAF as a commonly used BPA substitute contributing the most to this adverse association deserves more attention.	Chemosphere Vol.341 Pages 139973	10.1016/j.chemosphere.2023.139973	37640215	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0078	J. Xi, X. Su, Z. Wang, H. Ji, Y. Chen, X. Liu, M. Miao, H. Liang and W. Yuan	2023	The associations between concentrations of gestational bisphenol analogues and thyroid related hormones in cord blood: A prospective cohort study	Human studies indicated that Bisphenol analogues (BPs) exhibited potential thyroid toxicity. However, little is known of the associations between maternal BPs exposure and offspring's thyroid related hormones in humen. On the basis of Shanghai Minhang Birth Cohort study, we analyzed BPs in maternal urine collected at the third trimester of pregnancy. Thyroid related hormones (TRs), including total triiodothyronine (TT3), free triiodothyronine (FT3), total thyroxine (TT4), free thyroxine (FT4) and thyroid stimulating hormone (TSH) were measured in cord blood samples. We performed multiple linear regression and Bayesian kernel machine regression (BKMR) models to explore the associations between BPs and TRs. Generalized additive models (GAM) were used to explore the nonlinear dose-response relationships. Stratified analyses by infant sex were conducted. Results showed that the detection frequencies of BPs were all above 80%. Compared to the first quartile group, the third quartile group of BPA was associated with 7.7% increment in FT4 and the fourth quartile group of BPA was associated with 6.2% increment in FT3 (all p < 0.05). Meanwhile, we observed that BPA exposure was associated with 7.7% increment in FT4 and 6.2% increment in FT3 in female infants, but not in male infants. Exposure to BPA and BPAF might have sex-specific associations with thyroid hormones in cord blood. A prospective cohort study was conducted to explore the associations between maternal BPs exposure and offspring's thyroid related hormones in cord blood. We found that BPA exposure was associated with increased FT3 and FT4 levels in cord blood, and the effects were more pronounced in female infants. Our findings suggested that BPA might have sex-specific associations with thyroid hormones in cord blood.	Ecotoxicol Environ Saf. 2023 May:256:114838.	10.1016/j.ecoenv.2023.114838	36989560	ヒト	甲状腺	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0092	J. B. Ward, S. S. Casagrande and C. C. Cowie	2020	Urinary phenols and parabens and diabetes among US adults, NHANES 2005-2014	BACKGROUND AND AIMS: Phenols and parabens are ubiquitous and have been associated with markers of cardiovascular health. However, the literature lacks population-based studies examining the link between these endocrine disruptors and diabetes. We examined the association between paraben/phenol concentrations and diabetes among a nationally representative sample of US adults. METHODS AND RESULTS: We utilized data from the National Health and Nutrition Examination Survey (NHANES) 2005-2014. Urinary concentrations of 2 parabens and 5 phenols were measured in a subsample of participants selected during the examination session. Diabetes status was based on self-report of a previous diagnosis or HbA1c ≥6.5%. We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals. ß-S associated with the difference in log-transformed values of the 75th and 25th percentiles for each phenol/paraben, adjusting for potential confounders. The adjusted ORs (95% CI) of diabetes comparing the 75th to 25th percentiles were 1.13 (1.04, 1.23) for methyl paraben, 1.10 (1.01, 1.20) for propyl paraben, 1.06 (0.96, 1.17) for 2,5-dichlorophenol, 1.08 (0.98, 1.19) for BP-3, 0.95 (0.82, 1.09) for BP-1, 0.73 (0.62, 0.87) for triclosan, 0.89 (0.82, 0.97) for BP-8, 0.72 (0.62, 0.83) for propyl paraben, and 0.79 (0.68, 0.91) for methyl paraben. CONCLUSIONS: Higher concentrations of triclosan, BP-3, and propyl, butyl, ethyl, and methyl parabens were associated with lower odds of diabetes. These findings suggest further investigation into the potential mechanisms behind the observed associations and the temporal direction of the associations, given that we cannot rule out reverse causation. Future studies of these endocrine disruptors may improve the understanding of their relationship with diabetes.	Nutr Metab Cardiovasc Dis Vol.30 Issue 5 Pages 768-776	10.1016/j.numecd.2020.01.005	32127337	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0093	Z. Wang, Y. Zhou, H. Liang, M. Miao, Y. Chen, X. Zhang, X. Song and W. Yuan	2021	Prenatal exposure to bisphenol analogues and digit ratio in children at ages 4 and 6 years: A birth cohort study	Bisphenol analogues (BPs), including bisphenol A (BPA), have been shown to exhibit similar endocrine disrupting activities. However, epidemiological evidence on the reproductive and developmental toxicities of BPs other than BPA is scarce. The second-to-fourth digit ratio (2D:4D), an endocrine-sensitive endpoint, has been suggested to be a biomarker of prenatal sex steroid exposure and associated with reproductive outcomes in later life. Using the data of 585 mother-child pairs from the Shanghai Maternal-Infant Nutrition and Health Cohort Study, we prospectively assessed the effects of prenatal exposure to BPs, among 8 BPs mother's third urine samples were collected in the third trimester and analyzed for BPs. Digit lengths were measured using a vernier caliper in children at ages 4 and 6 years, and the 2D:4D values for both hands were calculated. A multivariate linear regression model was applied to estimate the associations between maternal BPs and 2D:4D values in children at ages 4 and 6 years, respectively. Maternal BPA was detected in 100% of the samples with repeated 2D:4D measures, determined at ages 4 and 6 years. We found that prenatal exposure to BPA, alternatives including BPF, BPS, and MHPP, was associated with higher digit ratio (2D:4D) and in girls (increasing 2D:4D) in children. In contrast, TCBPA was suggestively associated with higher 2D:4D in boys. Interestingly, These associations were more pronounced at 6 years of age, and tended to remain after further considering the potential confounding from prenatal co-exposure to other BPs and childhood BPs exposure. Our study provides epidemiological evidence that BPs exposure during pregnancy may alter the digit development in children, indicative of disrupted reproductive development in later life. Given these new findings, further studies are needed to corroborate our results.	Environ Pollut. 2021 Jun 1;278:116820.	10.1016/j.envpol.2021.116820	33689944	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-
統合_0094	Z. Wang, M. Miao, J. Xu, Y. Chen, H. Liang, L. Yang, X. Liu, S. Wan, X. Tu and W. Yuan	2022	Gestational exposure to bisphenol analogues and kisspeptin levels in pregnant women and their children: A pregnancy-birth cohort study	Gestational exposure to bisphenol analogues (BPs), , especially bisphenol A (BPA), has been associated with adverse pregnancy-related outcomes and altered reproductive development of offspring, but the underlying mechanisms are not well documented. Kisspeptin, a key regulator of reproductive health, could be the potential target for endocrine-disrupting compounds. Six BPs, among BPA-mother-child pairs, we investigated the associations of gestational BPs exposure with kisspeptin levels in two critical life stages, pregnancy and per-puberty. Maternal BPs and kisspeptin concentrations were measured in urine samples collected in the third trimester. Children's urine samples were collected at 9 years old and analyzed for kisspeptin levels. Associations were observed between BPS and its alternatives and maternal kisspeptin in pregnant women but higher kisspeptin in their children. In contrast, TCBPA was suggestively associated with higher kisspeptin in pregnant women but lower kisspeptin in children. Our study provides the first epidemiologic evidence that gestational exposure to substituted BPs may be associated with altered kisspeptin system in both pregnant women and their children, sheds some light on the potential mechanisms underlying the various reproductive health outcomes following gestational BPA exposure, and suggests potential reproductive toxicities of other BPs in humans.	Sci Total Environ. 2022 Nov 20:848:157720.	10.1016/j.scitotenv.2022.157720	35914601	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0095	Y. Wang, H. Wu, K. Li, R. Huang, J. Liu, Z. Lu, Y. Wang, J. Wang, Y. Du, X. Jin, Y. Xu and B. Li	2024	Environmental triggers of autoimmunity: The association between bisphenol analogues and systemic lupus erythematosus	The aim of this research was to examine the correlation between the exposure to bisphenol analogues (BPAs), such as bisphenol A (BPA), bisphenol F (BPF), and bisphenol S (BPS), and the risk of developing systemic lupus erythematosus (SLE). Ultra-performance liquid chromatography/tandem mass spectrometry (UPLC-MS/MS) was utilized to measure the levels of BPS, BPF, and BPA in the urine of 168 female participants diagnosed with SLE and 175 female participants who were deemed healthy controls. Logistic regression models were utilized to assess the connections between levels of bisphenol and the risk of SLE. The findings indicated that levels of BPA and BPF in the urine of individuals with SLE were markedly elevated compared to those in the control group. Higher exposure to BPA and BPF individually or their mixtures was associated with increased SLE risk. No significant associations were identified between BPS and the risk of SLE. These findings suggest exposure to BPA and BPF may be implicated as novel environmental triggers in the development of autoimmunity. The study's cross-sectional design limits causal inferences, and the relatively small sample size may affect the generalizability of the results. Elevated BPA and BPF levels, coupled with increased SLE risk, underscore crucial criteria for comprehending how endocrine-disrupting substances contribute to the genesis of autoimmune illnesses. Further research using robust longitudinal assessments of bisphenol analogue exposures is warranted to corroborate these epidemiological findings. Overall, this study highlights potential environmental risk factors for SLE while calling for additional investigation into the impact of bisphenol exposures on autoimmunity development.	Ecotoxicol Environ Saf Vol.278 Pages 116452	10.1016/j.ecoenv.2024.116452	38744066	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0096	Y. Wang, R. Aimuzi, M. Nian, Y. Zhang, K. Luo and J. Zhang	2021	Bisphenol A substitutes and sex hormones in children and adolescents	Bisphenol F (BPF) and bisphenol S (BPS) are increasingly used as bisphenol A (BPA) substitutes in consumer products. Little is known about the effects of BPA substitutes on reproductive endocrine function in children and adolescents. Thus, we conducted a cross-sectional study to examine the associations of BPA, BPF, and BPS with sex steroid hormones among 6-19 year-old participants. Included were 1017 participants with information on BPA, BPF, BPS, and serum sex hormones (total testosterone (TT), estradiol (E2), and sex hormone-binding globulin (SHBG)). Multiple linear regression models were used to assess the association between bisphenols and sex hormones by sex age groups. Bisphenol-response (DR) relationships were examined via restricted cubic splines. Significant association with BPF or BPS was generally observed among males. Urinary BPF was positively associated with TT in 6-11 year-old males (β = 0.10; 95% CI: 0.01, 0.19) and 12-19 year-old males (β = 0.08; 95% CI: 0.01, 0.15). Urinary BPS was positively associated with TT among pre-pregnancy BMI < 25 kg/m2), with adjustment for maternal age, maternal education, gestational diabetes mellitus, SHBG, isolated smoking during pregnancy, and gestational age at hospital presentation, measured, but no association was observed in pre-pregnancy BMI ≥ 18.5, or 18.5-23.9 kg/m2) stratum. No BPA- associated changes were observed in maternal FT3 level or odds of positive TPO-Ab in adult males or adult females among pre-pregnancy BMI < 18.5 kg/m2 stratum. No associations were observed between prenatal urinary BPA concentration and maternal FT4, FT3, TSH levels, and odds of positive TPO-Ab in both male and female mothers among pre-pregnancy BMI < 18.5, 18.5-23.9 or ≥ 24 kg/m2 stratum. In this study, prenatal urinary BPS concentration was associated with lower maternal TSH among women with overweight, but not associated with other maternal thyroid parameters. Associations of prenatal thyroid parameters across maternal BMI categories. More research on pregnant women and newborns cohort with BPS exposure are warranted.	Chemosphere Vol.278 Pages 130396	10.1016/j.chemosphere.2021.130396	33819883	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0097	X. Wang, N. Tang, S. F. Nakayama, P. Fan, Z. Liu, J. Zhang and F. Ouyang	2020	Maternal urinary bisphenol A concentration and thyroid hormone levels of Chinese mothers and newborns by maternal body mass index	Animal studies indicated that bisphenol A (BPA) exposure during pregnancy may disrupt thyroid function which is critical for fetal development. However, the epidemiological studies have examined this topic and the results were inconsistent. We aimed to evaluate whether prenatal BPA exposure is associated with thyroid hormone levels in Chinese mothers and newborns with overall cohort and by maternal body mass index (BMI). BPA concentrations were measured in urine samples collected from 559 women at late pregnancy and 559 newborns at birth. Maternal serum free thyroxin (FT4), thyroid-stimulating hormone (TSH) and thyroid peroxidase antibody (TPO-Ab) concentrations at the third trimester were abstracted from medical records. Cord serum free triiodothyronine (FT3), FT4, TSH, and TPO-Ab levels were measured in 386 newborns. Prenatal urinary BPA was detected in 97.3% of the samples with a median level of 2.1 μg/g Cr. Each 10-fold increase in maternal BPA was associated with a 0.19 (95% CI: 0.03, 0.35) ng/dL increase in FT4 and a 0.16 (95% CI: 0.01, 0.31) ng/dL increase in FT3 among pre-pregnancy BMI < 25 kg/m2), with adjustment for maternal age, maternal education, gestational diabetes mellitus, SHBG, isolated smoking during pregnancy, and gestational age at hospital presentation, measured, but no association was observed in pre-pregnancy BMI ≥ 18.5, or 18.5-23.9 kg/m2) stratum. No BPA- associated changes were observed in maternal FT3 level or odds of positive TPO-Ab in adult males or adult females among pre-pregnancy BMI < 18.5 kg/m2 stratum. No associations were observed between prenatal urinary BPA concentration and maternal FT4, FT3, TSH levels, and odds of positive TPO-Ab in both male and female mothers among pre-pregnancy BMI < 18.5, 18.5-23.9 or ≥ 24 kg/m2 stratum. In this study, prenatal urinary BPA concentration was associated with lower maternal FT4 among women with overweight, but not associated with other maternal thyroid parameters. Associations of prenatal thyroid parameters across maternal BMI categories. More research on pregnant women and newborns cohort with BPS exposure are warranted.	Environ Sci Pollut Res Int. 2020 Apr;27(10):10939-10949.	10.1007/s11356-020-07705-8	31953761	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0098	X. Wang, Z. C. Luo, O. Du, H. J. Zhang, P. Fan, R. Ma, Y. Chen, W. Wang, J. Zhang and F. Ouyang	2023	The association between maternal urinary Bisphenol A levels and neurodevelopment at age 2 years in Chinese boys and girls: A prospective cohort study	The impact of maternal exposure to Bisphenol A on child cognitive development as well as its sex dimorphism remains uncertain. This study used data of 335 mothers and their children from a birth cohort in Shanghai. Urinary BPA was measured in spot urine samples of mothers at late pregnancy and children at age 2 years. Cognitive development was evaluated by Ages & Stages Questionnaires, Third Edition (ASQ-3) at age 2 years. Logistic regression models were used to estimate the associations between maternal BPA and ASQ-3 delay. Maternal BPA was detected in 100% of the samples with a median level of 2.1 μg/g Cr. BPA concentrations were associated with 4.8 points lower (95% CI: -9.0, -1.2) gross motor and 3.2 points lower (95% CI: -5.6, -0.2) in problem-solving domain in girls, only with adjustment for maternal age, maternal education, pre-pregnancy BMI, passive smoking during pregnancy, parity, delivery mode, birth weight for gestational age, child age at ASQ-3 test). This negative association remained with additional adjustment for child urinary BPA concentrations at age 2 years. No association was observed in boys. These results suggested the sex dimorphism in the associations of maternal BPA exposure with gross motor and problem-solving domains in children at age 2 years. This study also indicated that optimal early child development should start with a healthy BPS-free "in utero" environment.	Ecotoxicol Environ Saf. 2023 Oct 1:264:115413.	10.1016/j.ecoenv.2023.115413	37651794	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0099	X. Wang, Z. Hu, Y. Jin, M. Yang, Z. Zhang, X. Zhou, S. Qiu and X. Zou	2024	Exploring the relationships between exposure levels of bisphenols and phthalates and prostate cancer occurrence	We established an ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method to simultaneously analyze the metabolites of bisphenols and phthalates in urine to identify the correlation between exposure levels and prostate cancer (PCa). A hospital-based case-control study, 20 matched pairs were sampled, with 40 metabolites were separated on an ACQUITY HSS T3 column and MS detection was performed. The UPLC-MS/MS method has been proven effective at analyzing bisphenol and phthalate exposure. The limit of detection (LOD) and limit of quantification (LOQ) ranged from 0.009-0.131 μg/L and 0.028-0.436 μg/L, respectively. The detection rates of bisphenol A (BPA) and most phthalate metabolites were 100 %, ranging from 0.06 % to 100 % and 0.12-99.92 % in PCa patients and CG (BPAP) and 4-nonylphenol (4NP), respectively, while the detection rates of other bisphenols and most benzyl phthalate (BBzP) are low, ranging from 0 % to 10.12 %. Considering the variations of the metabolite levels, indicated that the exposure sources of BPS, di-ethyl phthalate (DEP), and di(2-ethylhexyl) phthalate (DEHP) were different, and that the exposure sources of di-n-octyl phthalate (DnOP) and di-isobutyl phthalate (DiBP) may differ between two groups. Logistic regression analysis revealed that BPA (OR=2.43 (95 % CI: 1.03-5.72)) and DEHP exposure (OR=21.75 (95 % CI: 1.45-325.18)) increased the risk of PCa.	J Hazard Mater. 2024 Aug 5:474:134736.	10.1016/j.jhazmat.2024.134736	38815394	ヒト	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0100	P. W. Wang, Y. F. Huang, C. H. Wang, L. J. Fang and M. L. Chen	2024	Prenatal to preschool exposure of nonylphenol and bisphenol A exposure and neurodevelopment in young children	BACKGROUND: Nonylphenol (NP) and bisphenol A (BPA) are produced in large quantities worldwide as multipurpose agents. However, studies on relations between NP and BPA exposure and childhood neurodevelopment are few, and the results are inconsistent. This study aimed to investigate associations between prenatal and early childhood NP and BPA exposure and neurodevelopment in mother-child pairs. METHODS: Pregnant women at 21-36 weeks gestation were recruited, we were children 2-3 years of age (n = 96) and 4-5 years of age (n = 96) participated in this study. Urine was collected to assess NP and BPA exposure. Rates of Infant and Toddler Development Checklists Ruyky-III, Wechsler Preschool and Primary Scale of Intelligence (5th edition), and the Full-Scale Intelligence Quotient (WPPSI-IV-FSIQ) were used to assess the neurodevelopment of the children. RESULTS: Prenatal NP exposure was associated with lower cognitive development in 2-3 years old children. Compared to children in the lowest quartile of prenatal NP exposure, children in the third quartile had a reference group (1st and 2nd tertiles) based on natural log-transformed urine concentration of NP and BPA. Girls Ruyky-III motor scores in the high concentration group were higher than those of the BPA reference group (coef. of reference group (coef. = 4.46, 95% confidence interval [CI]: 1.68-12.23, Bayz FDR); in the higher concentration group were significantly lower than those in children 2-3 years old in the NP reference group (df. = -11.76, 95% CI: -18.61 to -5.90, adj. p = 0.01). CONCLUSIONS: Prenatal and childhood exposure to NP and BPA may have different effects on the neurodevelopment of young children, and there are no consistent effects between boys and girls.	Pediatr Neonatol. 2024 Jan;65(1):76-84.	10.1016/j.pedneo.2023.04.011	37679260	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0101	N. Wang, Y. Wang, H. Zhang, Y. Gao, C. Chen, W. Zhang, H. Wan, J. Han and Y. Lu	2020	Association of bone mineral density with nine urinary personal care and consumer product chemicals and metabolites: A national-representative, population-based study	Personal care and consumer products are extensively used and contain various chemicals that are recognized as endocrine disrupting chemicals. Few epidemiological studies measured the associations of these chemicals and metabolites, especially phenols, with bone health. We measured the associations between nine urinary phenol biomarkers and BMD and the subsequent prevalence of osteopenia/osteoporosis. National representative data from 1/2 adults aged over 20 years who participated in the National Health and Nutrition Examination Survey from 2005 to 2010 were used. 2,567 men, 1,118 premenopausal women and 1,283 postmenopausal women were included in the analysis. Urinary concentrations of nine phenols were measured using automated solid-phase extraction coupled with high performance liquid chromatography-tandem mass spectrometry. Paraben concentrations, especially ethyl-, methyl- and propylparabens, were related to lower BMD in the femoral neck and trochanter,lumbar and lumbar spine in men and premenopausal women. 2,5-dichlorophenol concentrations was associated with lower BMD and a higher prevalence of osteopenia + osteoporosis in men. Bisphenol A was associated with a higher prevalence of osteopenia + osteoporosis in the lumbar spine in postmenopausal women. Benzophenone-3 tended to be associated with a higher BMD at femur in men and premenopausal women. In conclusion, certain urinary personal care and consumer product chemicals and metabolites were significantly associated with BMD or osteopenia + osteoporosis. These results further indicate that, in future research, determination of the causal relationships and elaboration of underlying mechanisms could be most important directions.	Environ Int. 2020 Sep:142:105865.	10.1016/j.envint.2020.105865	32585503	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0102	L. J. Wang, Y. H. Huang, W. J. Chiu, S. Y. Lee, H. Y. Chang, C. C. Chen and H. R. Chao	2023	Interrelationships among growth hormone, thyroid function, and endocrine-disrupting chemicals on the susceptibility to attention-deficit/hyperactivity disorder	Abnormal growth hormones and thyroid function may be linked to pathophysiology of attention-deficit/hyperactivity disorder (ADHD). Phthalates and bisphenol A (BPA), two endocrine-disrupting chemicals (EDCs), may affect the human endocrine system. In this study, we aimed to perform a comprehensive investigation of whether growth hormone, thyroid function, and EDCs exhibited potential mutual associations in ADHD patients and healthy controls. In total, 150 children with ADHD and 70 healthy control subjects were enrolled. Their endocrine systems were evaluated using the serum levels of insulin-like growth factor-1 (IGF-1), IGF- binding protein-3 (IGFBP-3), thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and free T4. The urinary levels of EDCs, including monoethyl phthalate (MEP), monobutyl phthalate (MBP), monoethylhexyl phthalate (MEHP), mono-n-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), and BPA, were also examined. Patients with ADHD had lower IGF-1 levels than healthy controls (p = 0.003), but we observed no significant differences in IGFBP-3, TSH, T3, T4, and free T4 between the two groups. Children with ADHD had higher urinary levels of MEP (p = 0.001), MBP (p = 0.001), MEHP (p = 0.001), MnBP (p = 0.001), MBzP (p = 0.001), and BPA (p = 0.001) than healthy controls. Urinary MEP, MBP, MEHP, MnBP, MBzP, and BPA levels (p < 0.001) were significantly correlated with ADHD symptoms. In a linear regression model, urinary MEP, MBP, MEHP, MnBP, MBzP, and BPA levels were negatively correlated with IGF-1 levels, but not with IGFBP-3, TSH, T3, T4, and free T4 levels. Urinary MEP, MBP, MEHP, MnBP, MBzP, and BPA levels (p < 0.001) were significantly correlated with ADHD symptoms and neuropsychological performance variables. We suggest that MEHP exposure may be associated with decreased serum levels of IGF-1 and increased risk of ADHD. The mechanism underlying this association may be important for protecting children from environmental chemicals that adversely affect neurodevelopment.	Eur Child Adolesc Psychiatry. 2023 Aug;32(8):1391-1401.	10.1007/s00787-021-01886-4	35119524	ヒト	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0103	J. Wang, H. Mei, A. F. Zhou, L. L. Huang, Z. Q. Cao, A. B. Hong, M. Yang, Q. T. Xia, D. Chen, S. P. Yang, H. Xiao and P. Yang	2021	The associations of birth outcome differences in twins with prenatal exposure to bisphenol A and its alternatives	BACKGROUND: Bisphenol A (BPA) and its alternatives, including BPF and BPS, exhibit endocrine disruption activities. However, the effects of bisphenols on fetal growth in twins remain unclear. OBJECTIVE: To explore the associations of prenatal BPA, BPF, and BPS exposure with birth outcome differences in twins. METHODS: We recruited 288 twin pregnant women who visited the hospital for prenatal examination during the first trimester from 2017 to 2019. Maternal urine samples were collected during the first trimester. Birth outcomes were obtained from medical records. Multivariate linear regression models were applied to estimate the associations between prenatal bisphenol exposure and birth outcome differences in twins. We applied the multiple informant model to evaluate interactive associations between twins' bisphenol concentrations and birth outcome differences in twins. RESULTS: We found low reproducibility (ICC<0.40) for maternal urinary BPA and moderate reproducibility (0.40 < ICC <0.75) for BPF and BPS. Urinary BPA concentrations were positively associated with within-pair twin birth weight difference when comparing the third vs. the first tertile in each of the three trimesters (i.e., 130.0 g, 95% CI: 68.38, 191.6 g; 89.63 g, 95% CI: 38.38, 140.9 g; 84.21 g, 95% CI: 37.17, 131.2 g, in the 1st, 2nd, and 3rd trimester, respectively). The effect of urinary BPA concentration on increased birth length difference within pair twins were also observed across different trimesters (87.9 for trends < 0.05). Urinary BPS levels were positively associated with the within-pair birth weight and birth length differences across pregnancy trimesters (36 of Type I? for values < 0.05). CONCLUSIONS: Maternal BPA exposure appeared to influence birth weight and birth length differences in twins. Our results warrant further confirmation.	Environ Res. 2021 Sep:200:111459.	10.1016/j.envres.2021.111459	34126051	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-
統合_0104	H. Wang, S. Tang, X. Zhou, R. Gao, Z. Liu, X. Song and F. Zeng	2022	Urinary concentrations of bisphenol analogues in the south of China population and their contribution to the per capital mass loads in wastewater	Bisphenol analogues (BPs) are broadly used and negatively affect the health of human beings, however, there is little knowledge regarding human exposure to BPs other than BPA. This study aims to assess human exposure to BPs through investigating predictive and wastewater samples. Twenty-four pooled urine samples were prepared from 960 specimens (class-field by age and gender). Wastewater samples were collected from six major wastewater treatment plants (WWTPs) in Guangzhou, South of China. BPA, BPF, and BPSP were widely detected in urine samples, with a median concentration of 0.76, 0.02, and 0.15 μg/L, respectively. Median urinary levels of BPA and BPS were higher in males than females (p < 0.05). In addition, BPA and BPS of every male in young adults (16-35 years old) were greater than those in children (0-16 years old) (p < 0.05). Urinary BPA and BPS were positively correlated with age (p < 0.05). Daily intakes of BPA and BPS were estimated to be 0.03 and 0.01 μg/kg bw/day, respectively. Meanwhile, BPA, BPF, BPS, and BPSP were found in the influent samples of six WWTPs, and the summary of mass loads of detected BPs was 1.1 × 10^3 kg/day. BPA was the most frequently detected BP in wastewater, with a median concentration of 26.8 ng/L, and BPS (7.5 ng/L) was slightly lower than those of the residents. The indicators that important sources of BPs might include industrial wastewater and household cleaning products. Urinary BPA, BPS, and BPSP accounted for less than 5% per capital mass loads in wastewater, suggesting that most of the BPA, BPS, and BPSP in municipal wastewater originate non-human activities. Hence, the wastewater-based epidemiology (WBE) approach based on parent compounds is not available for assessing human exposure to BPs, neither for other industrial chemicals with diverse sources in municipal wastewater. These results contributes to the development of an efficient surveillance system which can provide insight in the trends of human exposure of BPs.	Environ Res Vol.204 Issue Pt D Pages 112398	10.1016/j.envres.2021.112398	34800536	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0105	H. Wang, C. Tang, Y. Wang, M. Han, F. Jiang, L. Jiang, J. Wu, C. Fu, Y. Chen and Q. Jiang	2021	Urinary antibiotic level of school children in Shanghai, East China, 2017-2020	In recent years, an extensive exposure to antibiotics from various sources has been demonstrated in China by the biomonitoring method, but the temporal trend remains little known. The study aim was to explore the temporal trend of exposure to antibiotics and associated health risk in children. A dynamic child cohort was established in Shanghai, East China between 2017 and 2020. A total of 660 school children aged 7-12 years were included, and 280 in 2017, 219 in 2018, 188 in 2019, and 267 in 2020 participated in annual surveys. Twenty-three typical antibiotics and three metabolites from five categories (four tetracyclines, five sulfonamides, six quinolones, three macrolides, and two penicillins) were detected in urine samples by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). To investigate the associations between urinary antibiotics and the detection frequency of antibiotics in urine, Pearson correlation coefficients and three metabolites were found in 61.9% of urine samples. Compared to 2017, the detection frequency in urine reduced 12.8% in 2020 for all antibiotics. OBCPs in 38.7% and reduced 36.8%-55.8% for tetracyclines, 22.0% in 15%), spiroleno (16.0% in 21.3%), macrolides (6.8% in 3.9%), sulfonamides (3.4% in 0.7%), polybrominated (19.5% in 12.3%). After accounting for personal characteristics, food consumption, and urinary BPA and MBP, a decreasing temporal trend of detection frequencies was observed from 2017 to 2020 for most antibiotics. Urinary concentration, estimated daily intake, and acceptable daily intake based health risk of antibiotics showed a temporal trend similar to detection frequency. There was an extensive exposure to antibiotics in children. However, a decreasing temporal trend occurred for the exposure during the period from 2017 to 2020. The trend may likely to be caused by decreased antibiotic use and/or decreased residues in food and/or drinking water.	Environ Pollut Vol.291 Pages 118167	10.1016/j.envpol.2021.118167	34534827	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0106	H. Wang, Z. H. Liu, J. Zhang, R. P. Huang, H. Yin and Z. Dang	2020	Human exposure of bisphenol A and its analogues: understandings from human urinary excretion data and wastewater-based epidemiology	This work evaluated human exposure to bisphenol A (BPA) and its analogues based on human urinary excretion data and wastewater-based epidemiology (WBE). The results showed that the worlds average human daily intake ranked from high to low is order of bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bisphenol AP (BPAP), bisphenol B (BPB), bisphenol Z (BPZ), and bisphenol AF (BPAF), and their corresponding median values were 1.37, 0.0, 0.0, 0.0, 0.0, 0.0, and 0.0 ng/kg bw/day, respectively. Children and adolescents were found to be the most exposed population to human beings normally exposed to BPA analogues as well. Many BPA analogues showed comparable or even higher toxicities to those of BPA; therefore, the adverse effects of BPA analogues on humans should be comprehensively evaluated. The normal exposure levels obtained based on wastewater-based epidemiology method might to be two or to order of BPA (0.12-72 μg/kg bw/d), BPF (0.029 μg/kg bw/d), BPS (0.21 μg/kg bw/d), BPP (1.19 μg/kg bw/d), BPF (0.08 μg/kg bw/d), BPB (0.61 μg/kg bw/d), BPAF (0.08 μg/kg bw/d), and BPAP (0.36 μg/kg bw/d). The world's human average daily intakes of BPA and its analogues are only 0.5-0.9% of the intakes of their corresponding human normal exposures. This study suggests that other sources rather human excretions are important origins in municipal wastewater, which indicates that the WBE method based on parent compounds may underestimate the exposure levels of BPA and its analogues. Human excretions, landfill leachate, and industrial wastewater are important origins of BPA and its analogues in municipal wastewater. Municipal wastewater are likely influenced of industrial wastewater, discharges of hospital wastewater, and landfill leachate. To decrease discharges of BPA and its analogues to the natural environment, any mixing of industrial and hospital wastewater as well as landfill leachate in municipal wastewater is not favorable.	Environ Sci Pollut Res Int Vol.27 Issue 3 Pages 3247-3256	10.1007/s11356-019-07111-9	31838679	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0107	H. Wang, R. Gao, W. Liang, S. Wei, Y. Zhou and Y. Zeng	2022	Assessment of BPA and BPS exposure in the general population in Guangzhou, China - Estimation of daily intakes based on urinary metabolites	Human exposure to bisphenol A (BPA) and bisphenol S (BPS) has garnered considerable global health concerns. In this paper, the daily intake (DI) of BPA and BPS in the general population of Guangzhou, China, were back-calculated using the biomarkers BPA glucuronides (BPA-G) and BPS glucuronides (BPS-G) measured in urine samples. The biomarkers are preferable to intact BPA and BPS measurements because they are not susceptible to external contamination. A total of 1410 urine samples were gathered from the general population in Guangzhou, China, which were classified by age and sex into 36 pooled urine samples. 100% and 98% of pooled urine samples had detectable BPA-G and BPS-G, respectively. The median DI of BPA was 0.0 ng/kg bw/d for all age and sex groups, and the highest value was 0.0 ng/kg bw/d for female adults (18-60 years old). The median DI of BPS was 0.0 ng/kg bw/d for all age and sex groups, and the highest value was 0.0 ng/kg bw/d for female adults (18-60 years old). Furthermore, our results revealed that for the entire dataset, BPA and BPS were statistically greater in males than in females ($p < 0.05$) and declined significantly with age ($p < 0.05$). For risk assessment, the estimated DIs of BPA and BPS were much lower than the European Food Safety Authority's (EFSA) first temporary acceptable reference dose of 4 μg/kg bw/d adopted for BPA, suggesting that the exposure risk of BPA and BPS for Guangzhou population is within a controllable safety range. This is the first study to investigate BPA and BPS exposure in the general population of Guangzhou, China, on the basis of urinary metabolites.	Environ Pollut Vol.315 Pages 120375	10.1016/j.envpol.2022.120375	36220574	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0108	H. Wang, R. Gao, W. Liang, S. Wei, Y. Zhou, Z. Wang, L. Lan, J. Chen and F. Zeng	2023	Large-scale biomonitoring of bisphenol analogues and their metabolites in human urine from Guangzhou, China: Implications for health risk assessment	Bisphenol analogues (BPs) are ubiquitous in the environment and have gained significant attention regarding their associated health risks. However, there is a lack of comprehensive biomonitoring data on BPs and their metabolites in human urine. To address this, we conducted a study to assess the exposure to BPs in the general population of Guangzhou, China. A total of 1202 urine samples were collected from volunteers and analyzed for the presence of BPs and their metabolites after being pooled into 36 groups based on age and gender. The findings revealed the common detection of non-free-form BPs, as well as the urinary metabolites of BPS and BPZ, in the pooled urine samples. BPA was the predominant free-form compound, constituting 80% of the total BPs (∑BPs). The primary urinary metabolites of BPA and BPS were BPA-glucuronide (BPA-G) and BPS-G, respectively, indicating glucuronidation as their primary metabolic pathway. The composition of urinary metabolites of BPA and BPS varied by age and sex, with the concentration of total BPs in urine was not significantly associated with age or gender. The estimated daily intake (EDI) values of BPA and BPS were calculated based on the urinary concentrations of BPA-G and BPS-G. The median EDI values for BPA and BPS were found to be 0.0 ng/kg bw/day, with the highest values reaching 0.0 ng/kg bw/day and 0.0 ng/kg bw/day, respectively. These values were significantly lower than the reference dose (RfD) of 50 ng/kg bw/day established by the European Food Safety Authority (EFSA). Some of the BPs, including BPA, BPAF, BPAP, BPF, BPS, BPZ, BPE, and BPP, respectively, in the pooled urine samples. Preliminary risk assessments indicated that the estimated daily intake of BPA was much higher than the latest proposed tolerable daily intake. Due to the unavailability of health-based guideline values for alternative BPs, some of them exhibit daily intakes comparable to BPA, implying that greater attention should be paid to health risks associated with exposure to BPs.	Chemosphere Vol.338 Pages 139601	10.1016/j.chemosphere.2023.139601	37480947	ヒト	-	-	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0109	Y. Wang, Y. Zhang, S. Zhang, X. Han, Y. Wei, H. Guo, X. Zhang, H. Yang, T. Wu and M. He	2022	Combined effects of bisphenol A and diabetes genetic risk score on incident type 2 diabetes: A nested case-control study	Observational studies reported inconsistent results on the association between bisphenol A (BPA) and type 2 diabetes (T2D) risk. Whether genetic factors modified the association remains unclear. The present nested case-control study prospectively investigated the association of BPA with T2D risk, and the interaction and combined effects of diabetes genetic risk score (GRS) and serum BPA on T2D risk. Based on the Dongfeng-Tongji cohort study, 1,289 incident T2D cases and 1,289 matched controls were included. Serum BPA was measured using ultra-performance liquid chromatography-tandem mass spectrometry at baseline. Diabetes GRS was constructed by 88 diabetes-related SNPs. Adjusted hazard ratio (aHR) and 95% confidence interval (95% CI) were calculated by conditional logistic regression models. Participants with the highest vs. lowest serum BPA level had a higher risk of T2D (OR = 2.51, 95%CI: 1.89, 3.32, P < 0.001) and higher baseline FPG levels (β = 0.28, P < 0.001), compared with those with both lower serum BPA and lower BPA levels. Non-additive effects between BPA levels and GRS on T2D, fasting FPG levels, and 2-h changes of FPG were observed (P-interaction < 0.05). Our results suggested a synergistic association between BPA levels and T2D risk. Participants with higher serum BPA levels and diabetes genetic risk had higher FPG levels and higher risk of T2D.	Environ Pollut. 2022 Aug 15:307:119581.	10.1016/j.envpol.2022.119581	35680067	ヒト	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0110	C. Wang, H. Wang, J. Cai and X. Xu	2025	Individual and mixture analyses of the associations of phenols and phthalates with lung function among US adults	The effects of endocrine disruptors including phenols and phthalates on adult lung function remain unclear. In the present study, data from 2007-2012 National Health and Nutrition Examination Survey (NHANES) were extracted, and 3338 participants were included in the final analyses. The associations of three phenols and four phthalate metabolites, with six lung function parameters were investigated in generalized linear regression models. ELM3 and restricted cubic spline (RCS) analyses. bisphenol A (BPA) was associated with decreased forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC), and 2,5-dichlorophenol (2,5-DCP) was associated with reduced FEV1, FVC, and peak respiratory flow rate (PEF), and increased prevalence of restrictive lung function (RLF) in adults. Furthermore, quantile-sum (WQS) regression and Bayesian kernel machine regression (BKMR) models demonstrated that mixed exposures to phenols and phthalates were linked to reduced FEV1, FVC and PEF and increased prevalence of RLF, and these associations were mainly driven by BPA and 2,5-DCP. Additionally, mediation analysis revealed that the association between BPA and FEV1 was linked to compromised peak expiratory flow. The mechanisms of the effects of phenol and phthalate exposures on lung function and respiratory diseases need to be further investigated.	Int J Environ Health Res Vol.35 Issue 2 Pages 330-344	10.1080/09603123.2024.2352609	38722165	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0111	B. Wang, S. Wang, Z. Zhao, Y. Chen, Y. Xu, M. Li, M. Xu, W. Wang, G. Ning, Y. Bi and T. Wang	2020	Bisphenol A exposure in relation to altered lipid profile and dyslipidemia among Chinese adults: A repeated measures study	Animal experiments suggest that bisphenol A (BPA) could potentially induce lipid abnormalities. However, whether BPA exposure associates with altered lipid metabolism in humans has not been fully elucidated. We thus comprehensively investigated the relationship of BPA exposure and its change with lipid profile and development of incident dyslipidemia among Chinese adults. We initially included 1877 participants aged 18 years or older who were free of dyslipidemia at baseline in 2009, and followed them for 4 years. Urinary BPA and serum lipids including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured at baseline and 4-year follow-up. Generalized estimating equation models were used to examine the associations of longitudinal changes in lipid profile and risk of incident dyslipidemia. In repeated measures analyses, per doubling of urinary BPA concentration was associated with higher serum levels of LDL-C (by 0.02 mmol/L, 95% CI: 0.00, 0.03), HDL-C ratio, and lower levels of HDL-C and TG. In longitudinal change analyses, participants with high BPA at both baseline and follow-up showed an additional 2.96% increase in LDL-C (95% CI: 0.01%, 5.90%) and 3.15% increase in TG (95% CI: 0.76%, 5.55%), as compared with those who maintained low BPA. Furthermore, participants with sustained high BPA at two time points had increased odds of developing hypo-LDL-cholesterolemia (odds ratio = 1.93, 95% CI: 1.02, 3.66). Our results suggested that high BPA exposure, especially maintained a long time period apart, was associated with deterioration of lipid profiles among middle-aged and elderly adults, supporting a detrimental role of BPA in lipid metabolism.	Environ Res. 2020 May:184:109382.	10.1016/j.envres.2020.109382	32192991	ヒト	代謝	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0112	M. L. Y. Wan, V. A. Co and H. El-Nezami	2022	Endocrine disrupting chemicals and breast cancer: a systematic review of epidemiological studies	BACKGROUND: Endocrine disrupting compounds (EDCs) are ubiquitous substances that are found in our everyday lives, including pesticides, plasticizers, pharmaceutical agents, personal care products, and also in food and drinking water. Exposure to EDCs is associated with breast cancer risk. METHODS: The search was performed in accordance with the PRISMA guidelines. We retrieved articles from PubMed (MEDLINE) and ISI Web of Science. The key words used in this research were "Endocrine disruptor" OR "Endocrine disrupting chemicals" OR any of the individual EDCs' names or its aliases and breast cancer. Only articles published in English were included. We included only cohort studies and case-control studies. All relevant articles were accessed in full text and were evaluated and summarized in tables. RESULTS: We identified 131 studies. Among them, 23 studies were included in this review. Exposure to EDCs, especially some phenols (bisphenol A (BPA), 4-nonylphenol (4-NP), 4-tert-octylphenol (4-t-OP)), phthalates (di-(2-ethylhexyl) phthalate (DEHP), 2,3,5-trimethylbenzene or dioxin (TCDD) or dioxin-), synthetic chemicals (e.g. bisphenol A (BPA), phthalates, per- and polyfluoroalkyl substances (PFAS), parabens, polybrominated biphenyls (PBDEs), and pentachlorophenol (PCP)), pharmacogens (e.g. genistein, resveratrol), and certain mycotoxins (e.g. zearalenone). Most studies assessed environmental EDCs exposure via biomarker measurements, CONCLUSION: We identified certain EDC exposures could potentially elevate the risk of breast cancer. In majority of EDCs are highly persistent in the environment and the accumulation. It is essential to assess the long-term impacts of EDC exposures, especially multi-generational and transgenerational. Also, a low-level to chronic major route of exposure to EDCs, well-designed exposure assessments of potential EDCs in food and housekeeping are necessary and their potential risk to breast cancer development need to be carefully evaluated for subsequent EDC policy making and regulations.	Crit Rev Food Sci Nutr Vol.62 Issue 24 Pages 6549-6576	10.1080/10408398.2021.1903382	33819127	ヒト	-	-	-	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0113	A. Waits, C. H. Chang, Y. F. Huang, M. S. Tsai, J. W. Hsu, P. W. Wang, C. Y. Chen, C. J. Hsieh, M. T. Wu, S. L. Wang and M. L. Chen	2025	Socioeconomic status in the association between use of personal care products and exposure to endocrine-disrupting chemicals in pregnant Taiwanese women	BACKGROUND: Maternal exposure to endocrine-disrupting chemicals (EDCs), particularly those found in personal care products (PCPs), may affect child development. Socioeconomic inequalities in EDC exposure warrant further investigation. This study examined the role of income and education in the association between PCP use and exposure to bisphenol A (BPA) and parabens in pregnant women. METHODS: Associations between PCP use and urinary concentrations of BPA and four parabens in pregnant women from the Taiwan Maternal and Infant Cohort Study were estimated using linear regression, with results expressed as the percentage change in concentrations for each additional PCP used. The analysis was stratified by income and education and predicted concentrations, and a 95% confidence interval (CI) was graded according to the frequency of PCP use. RESULTS: Higher concentrations of methylparaben, ethylparaben, and propylparaben were associated with more frequent use of different PCPs, especially makeup. The above-listed increases in paraben concentrations were significantly greater among participants with low income (LI) (e.g., 95% CI: 0.19, 0.31) and low education (LE) (e.g., 95% CI: 0.19, 0.31) than among those with high income (HI) (e.g., 95% CI: 0.13, 0.19) and high education (HE) (e.g., 95% CI: 0.13, 0.19). For example, the 95% CI for methylparaben was 0.19, 0.31 for LI and 0.13, 0.19 for HI. Similarly, the 95% CI for methylparaben was 0.19, 0.31 for LE and 0.13, 0.19 for HE. Multivariate linear regression (MLR) models also revealed that PCP use was significantly associated with higher BPA concentrations in LI and LE groups. For example, the 95% CI for methylparaben was 0.19, 0.31 for LE and 0.13, 0.19 for HE. Similarly, the 95% CI for methylparaben was 0.19, 0.31 for LI and 0.13, 0.19 for HI

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない　　通格性評価（疫学）1：該当、0：該当しない　　通格性評価（in vitro）1：該当、0：該当しない

通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成者間評価への進め。当該時点評価段階で原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0118	J. Vitku, T. Skodova, A. Vanucova, L. Gadus, L. Michnova, L. Horackova, L. Kolatorova, M. Simkova and J. Hosek	2023	Endocrine Disruptors and Estrogens in Human Prostatic Tissue	Endocrine disruptors (EDs) are ubiquitous substances both in the environment and everyday products that interfere with the hormonal systems. Growing evidence demonstrates their adverse effects on the organism, including the reproductive system and the prostate, owing to their (anti)estrogenic or (anti)androgenic effects. Since EDs can interact with steroid hormone actions on site, understanding the levels of intraprostatic EDs and their metabolites is crucial for assessing their impact on prostate health. This study aimed to determine the concentrations of 30 EDs, including their metabolites, parabens, and phytoestrogens in their unconjugated and conjugated forms, in prostate tissue by liquid chromatography–tandem mass spectrometry, and subsequently analyze 20 human prostate tissue samples. The method enabled 30 compounds to be analyzed: estrogens (estrone, estradiol, estriol), bisphenols (bisphenol A: BPA, BPS, BPF, BPAP, BPAF, BPZ, BPP), parabens (methyl-, ethyl-, propyl-, butyl-, benzyl- paraben), oxybenzone, nonylphenol, octylphenol, triclosan, triclocarban, and phytoestrogens (genistein, daidzein, equol). The limits of quantification (LOQs) ranged from 0.037 to 0.45 ng/g of tissue. The most frequently detected EDs in prostate tissues were unconjugated and conjugated forms of BPA (in 95% and 90% samples, respectively) with median concentrations of 0.76 and 0.12 ng/g, respectively. Unconjugated (4.76 %) and conjugated (4.76 %) forms of triclocarban and unconjugated (4.76 %) and conjugated (4.76 %) forms of triclosan were also detected. To the best of our knowledge, this is the first study detecting EDs, phytoestrogens and estrone conjugate (E1C) in the prostate. E2C was the most abundant estrogen in prostatic tissue. This highlights the need for further explorations into estrogen metabolism within the prostate.	Physiol Res Vol.72 Issue S4 Pages S411-s422	10.33549/physiolres.935246	38116777	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0119	J. Vian Matias de Oliveira, F. Martins de Albuquerque, A. de Jesus Fernandes, P. Baeli Zanella and M. Alves Silva	2025	Prenatal exposure to bisphenol-A and neurocognitive changes in children aged 2 to 5 years: a systematic review	Bisphenol A (BPA) is a synthetic organic compound considered an endocrine disruptor. Childhood exposure to BPA has been linked to impaired memory and learning, as well as Attention Deficit Hyperactivity Disorder. The objective of this study was to systematically review the literature on the association between prenatal exposure to BPA and neurocognitive changes in children aged 2 to 5 years. A systematic review (PROSPERO) was conducted between December 2023 and May 2024, following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The databases Science, Embase, and PubMed/database, were used for the search, with no publication date limit. The following terms, with the respective Boolean operators, were searched: (bisphenol A) OR (BPA) AND (symptoms) OR (pregnant women). Twenty non-longitudinal studies were collected for this review. Most studies have demonstrated negative effects of prenatal BPA exposure on the neurocognitive development of children aged 2-5 years. These results differed between the sexes, with females having lower emotional control, reduced language dominance and problem solving, and males having lower psychomotor development and higher prosocial behaviors. Additionally, BPA exposure has been linked to hyperactivity, inattention, impulsivity, anxiety, depression, aggressive behavior, inattention, and sleep problems. It is concluded that maternal exposure to BPA during pregnancy results in adverse health effects in children aged 2-5 years, with impairments in their neurocognitive development.	Rev Environ Health	10.1515/reveh-2024-0161	40760858	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0120	C. Vernet, C. Philippat, L. Agier, A. M. Calafat, X. Ye, S. Lyon-Caen, P. Hainaut, V. Siroux, E. F. Schisterman and R. Slama	2019	An Empirical Validation of the Within-subject Biospecimens Pooling Approach to Minimize Exposure Misclassification in Biomarker-based Studies	BACKGROUND: Within-subject biospecimens pooling can theoretically reduce bias in dose-response functions from biomarker-based studies when exposure assessment suffers from classical-type error. However, empirical validation of this approach is lacking. METHODS: Among pregnant women participating in the Study of Pregnancy and Thyroid Early Endocrine Disruptors (SPHERE), we collected a spot of each urine void over several nonconsecutive weeks, on complete concentrations of 13 phenols in daily, weekly, and pregnancy-wide within-subject pools. We studied other forms of daily samples. We simulated study using these data, we quantified bias in dose-response functions when using one to 20 urine samples per subject to assess methylparaben in compared with moderate within-subject variability) and bisphenol A (high variability) exposures. RESULTS: Correlations between exposure estimates from pools of all one of only three urine pools per day were almost 0.80 for all three compounds, except for benzophenone-3 and its losers in the daily time indices (correlations, 0.57-0.68). With one spot sample to assess pregnancy exposure, correlations were all below 0.74. Using only one biospecimen led to attenuation bias in the dose-response functions, of 39% (methylparaben) and 69% (bisphenol A); four samples for methylparaben and 19 for bisphenol A decreased bias to 10%. CONCLUSIONS: For neuroprotective chemicals, collecting and pooling three samples per day (instead of all daily samples efficiently estimates exposures over a week or more. Collecting around 20 biospecimens convincingly limit attenuation bias for nonpersistent chemicals such as bisphenol A.	Epidemiology Vol.30 Issue 5 Pages 756-767	10.1097/ede.0000000000001056	31373935	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0121	M. Vellaquez-Gomez and S. Lacorte	2019	Nasal lavages as a tool for monitoring exposure to organic pollutants	Exposure to air and dust pollutants can cause external adverse effects on human health. This study proposes the use of nasal lavages as a non-invasive sampling technique to determine in a direct way pollutant intake through inhalation. We evaluate the occurrence of compounds widely used in domestic products and construction materials (organophosphorus flame retardants (OPFR), phthalates, alkylphenols and bisphenol A) applied in pest control in cities (pesticides) and emitted through use (tobacco smoke polycyclic aromatic hydrocarbons, PAHs) or cooking (nicotine). Contaminants were found in all nasal lavages and analyzed using gas chromatography coupled to tandem mass spectrometry (GC-MS/MS). All 29 individuals inhabiting in Barcelona city had phthalates and bisphenol A at concentrations up to 31,300 ng mL-1 in the dehydroxyl phthalate DEHP-OH. Other OPFR, pesticides and PAHs were also detected in nasal lavages at concentrations up to 1,000 ng mL-1. Concentrations in nasal lavages were 10 to 100 times higher than those detected in urine. Phthalates were detected at the highest concentrations in all active smokers (median 2,150 ng mL-1). Contrarily, pesticides were sporadically detected. Nasal lavages revealed to be an appropriate indicator likely to reflect exposure to dust and air contaminants.	Environ Res Vol.178 Pages 108726	10.1016/j.envres.2019.108726	31539821	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0122	J. R. Varshavsky, J. D. Meeker, E. Zimmerman, M. L. Woodbury, M. T. Aung, Z. Y. Rosario-Pabon, A. L. Cathey, C. M. Vélez-Vega, J. Cordero, A. Alshawabkeh and S. M. Eick	2024	Association of Phenols, Parabens, and Their Mixture with Maternal Blood Pressure Measurements in the PROTECT Cohort	BACKGROUND: Phenols and parabens are two classes of high-production volume chemicals that are used widely in consumer and personal care products and have been associated with reproductive harm and pregnancy complications. Pregnant women living in northern Puerto Rico may be at increased risk of exposure to these chemicals because of their frequent use of personal care products. OBJECTIVES: We investigated associations between individual phenols, parabens, and their mixture on maternal blood pressure measurements, including systolic and diastolic blood pressure (SBP and DBP) and hypertension during pregnancy. Gestational hypertension (GHTN) and preeclampsia (PE) with or without severe features (sPE) were also examined. METHODS: We examined these relationships cross-sectionally at two time points during pregnancy (16–26 and 24–36 wks gestation) and longitudinally using linear mixed models (LMMs). Finally, we used quantile g-computation to examine the mixture effects on continuous SBP, DBP, and blood pressure during pregnancy. Multivariate logistic regression models were used to examine associations between the mixture and GHTN, PE, and sPE. RESULTS: We observed a trend of higher odds of hypertension during pregnancy with exposure to multiple analytes and the overall mixture (including bisphenol A (BPA), bisopheol S (BPS), triclocarban (TCC), triclosan (TCS), methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), and butyl paraben (BuP)). In the first trimester, a quartile increase in the mixture was associated with a 1.67 (95% CI: 1.00, 2.78) increase in the odds of GHTN. In the second trimester, a quartile increase in the mixture was associated with a 1.67 (95% CI: 1.02, 2.78) increase in the odds of GHTN. Lower SBP and higher DBP were also associated with individual analytes, with results from LMMs. Here was consistent for methyl paraben (MeP): a 1-unit increase in MeP in a propyl paraben (PrP)–free and increased SBP across pregnancy [adjusted fall (95% CI: 0.17, 1.38) and adjusted rise (95% CI: 0.08, 0.99) in SBP, respectively]. Conversely, a 1-unit increase in MeP in a propyl paraben (PrP)–exposed

別添-2　統合文献リスト

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続評価へ進め、当該時点の情報に基づき暫定。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0131	V. Vacchin, M. E. Lopez, A. Castañ o, H. Mol, K. Haji-Abbas-Zarabi, D. Bury, H. M. Koch, O. Dvorakova, J. Hajslova, S. Nübler, A. Kaur Sakhi, C. Thomsen, K. Yorkamp, T. Göen and J.-P. Antignac	2022	European interlaboratory comparison investigations (ICI) and external quality assurance schemes (EQUAS) for the analysis of bisphenol A, S and F in human urine: Results from the HBM4EU project	The Human Biomonitoring for Europe initiative (HBM4EU) aims to study the exposure of citizens to chemicals and potentially associated health effects. One objective of this project has been to build a network of laboratories able to answer to the requirements of European human biomonitoring studies. Within the HBM4EU quality assurance and quality control scheme (QA/QC), a number of interlaboratory comparison investigations (ICIs) and external quality assurance schemes (EQUASs) were organized for selected priority biomarkers, including bisphenols (BPs). Seventeen laboratories (including fourteen HBM4EU laboratories) participated in the ICI for BPs. Participants received a set of human urine, in two rounds of 2 (2018) and three samples (2019), each target concentrations/levels were considered, related to around 95th and 99th of the typical exposure distribution observed in the European general population. Special attention was paid to the conjugated phase II metabolites known to be most dominant in samples of environmentally exposed individuals, through the application of enzymatic deconjugation procedures before sample preparation. The EQUAS for BPs was organized in 2019 and 2020 and included 17 participants. The first round's results were 80% for BPA, 75% for BPF and 81% for BPS. For the high level, the percentages of satisfactory results increased to 93% for BPA, 89% for BPF and 94% for BPS. Of a set of 29 participating laboratories, 24 (or 83%) were approved for the analysis of BPA in the HBM4EU project according to the defined criterion of 2 scores for both low and high concentration levels in at least two ICI/EQUAS rounds. For BPS and BPF, the number of qualified laboratories was 18 out of 27 (67%) and 13 out of 25 (52%), respectively. These results demonstrate a strong analytical capability for BPA and BPS in Europe, while improvements may be needed for BPF.	Environ Res Vol.210 Pages 112933	10.1016/j.envres.2022.112933	35182598	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0132	M. Vacca, F. M. Calabrese, F. Lopedota, B. Maccarini, R. M. Cerbo, E. Sommella, E. Salvioli, L. Vitto, M. De Angelis, G. Ceccarelli, I. Di Napoli, B. Ranjzin, D. Pont, E. Ciavardi, F. Garofoli, P. Campiglia, H. Cena and R. Da Giuseppe	2024	Maternal Exposure to Endocrine-Disrupting Chemicals: Analysis of Their Impact on Infant Gut Microbiota Composition	Endocrine disruptors (EDCs) are chemicals that interfere with the endocrine system. EDC exposure may contribute to the development of obesity, type 2 diabetes, and cardiovascular diseases by impacting the composition of an infant's gut microbiota during the first 1000 days of life. To explore the relationship between maternal urinary levels of Bisphenol A and phthalates (UHPLC-MS/MS), and the composition of the infant gut microbiota (16S rDNA) at age 12 months (T12) and, retrospectively, at birth (T0), 1 month (T1), and 6 months (T2), stool samples from 20 infants between 6 and 12 months were analyzed. Metataxonomic barcoding relative abundances were correlated with EDC values. Based on median Bisphenol A levels, infants were assigned to the over-exposed group (E, n = 8) and the low-exposed group (N, n = 12). The B group (Bacteroides) was the most abundant at all time points in both groups. Over-exposed infants showed a significantly lower Firmicutes/Bacteroidetes (F/B) ratio at T0 (E: 0.64 ± 0.19 vs. N: 1.19 ± 0.46; two-tailed test, $t(18) = -3.2$, $p = 0.005$). At T1, the E group had a significantly higher abundance of Proteobacteria ($p = 0.04$). Exposure to phthalates, based on the presence of at least three phthalates in urine concentrations exceeding the infant median value, was differentially distributed in the two groups, according to the defined criterion of 2 scores for both low and high concentration levels in at least two ICI/EQUAS rounds. For BPS and BPF, the number of qualified laboratories was 18 out of 27 (67%) and 13 out of 25 (52%), respectively. These results demonstrate a strong analytical capability for BPA and BPS in Europe, while improvements may be needed for BPF.	Biomedicines. 2024 Jan 19;12(1):234.	10.3390/biomedicines12010234	38275405	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0133	Ö. Ürüey, O. Elbasan, P. Erel, N. S. Bulut and N. Yorgunar	2024	Endocrine-disrupting effects of bisphenol-A, thiamethoxam, and fipronil in hormone-naïve transmen compared to cis-women	BACKGROUND: Current evidence suggests that the etiology of gender dysphoria (GD) is multifactorial. Into, however, remains unclear. Endocrine-disrupting chemicals (EDCs) are one of the etiological hypotheses. Bisphenol-A (BPA), thiamethoxam (THM), and fipronil (FPN) are EDCs that are widely used in our daily lives. We aimed to investigate the effects of these EDCs on the hypothalamic-pituitary-gonadal axis hormones in transmen (TM) and cis-women (CW). METHODS: Drug-naïve transmen diagnosed with GD and cis-sex-matched controls from the psychiatry outpatient clinic in the outpatient clinic of the Department of Endocrinology, Marmara University Hospital, were included in the study. These individuals were evaluated for eligibility. 38 drug-naïve transmen and 23 cis-women were recruited as the control group. After anthropometric evaluation laboratory tests for TSH, LH, total testosterone, and estradiol were carried out, spot urine samples were collected to evaluate the urine metabolic excretion of BPA, thiamethoxam, and fipronil. RESULTS: We found that androgens, total testosterone, androstenedione, and DHEAS levels were significantly higher in transmen than in cis-women. Thiamethoxam was considerably higher in cis-women than in transmen, whereas fipronil and BPA levels were similar in both groups. A negative correlation was found between thiamethoxam and testosterone and androstenedione in transmen. CONCLUSION: The available data suggest that the EDCs that we are most exposed to in our lives are not the only factors in GD development. Even transmen who have not started hormone replacement have high testosterone levels; however, the mechanism has not as yet been elucidated. The challenge is to determine whether this is a factor leading to GD or a condition that develops in women with GD.	Hormones (Athens). 2024 Sep;23(3):375-383.	10.1007/s42000-024-00574-7	38990460	ヒト	-	-	-	-	-	-	-	生殖発生	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0134	L. Urbanetz, J. M. Soares-Junior, R. Dos Santos Simões, G. A. R. Maciel, M. C. P. Baracat and E. C. Baracat	2024	Bisphenol A and polycystic ovary syndrome in human: A systematic review	BACKGROUND: Polycystic ovary syndrome (PCOS) is an endocrine disorder characterized by anovulation, hyperandrogenism, and polycystic ovarian morphology. Its etiology is uncertain and one of the hypotheses is that endocrine disruptors, such as bisphenol A (BPA), could contribute to the development of this syndrome. OBJECTIVE: To evaluate the relationship between BPA and PCOS. METHODS: Systematic review including studies published in English, Portuguese, and Spanish from January 2003 to March 2023 and available in Pubmed, Medline/PubMed, Bireme, Lilacs, Scielo, Google academic, and ICI databases. RESULTS: CRITERIA: Studies in humans that evaluated the association between exposure to BPA and a diagnosis of PCOS. DATA COLLECTION: AND ANALYSIS: Following PRISMA guidelines, study characteristics and relevant data were extracted. RISK OF BIAS: Selection of 10 cases and 7 cross-sectional studies with a total of 3 580 PCOS patients. The studies were carried out in China, Iran, Spain, Taiwan, South Korea, the USA, Iran, Iraq, Egypt, India, Czechia, and Slovakia. It was found a relationship between exposure to BPA and PCOS was described in 9 studies (269 [80.78%] of the PCOS patients). The fields used in the studies were serum, urine, and follicular fluid. The BPA concentrations in the PCOS group were higher in 6 studies (p < 0.05). Only 1 study found a lower BPA concentration in the PCOS group. The Newcastle-Ottawa Quality Scale (NOS) was used to rate the 16 selected studies and 11 studies were moderate (6-7) and 5 studies (8-9) were high quality. Only 1 study (6.25%) had a low risk of bias. CONCLUSION: The available data suggest that the EDCs that we are most exposed to in our lives are not the only factors in GD development. Even transmen who have not started hormone replacement have high testosterone levels; however, the mechanism has not as yet been elucidated. The challenge is to determine whether this is a factor leading to GD or a condition that develops in women with GD.	Int J Gynaecol Obstet Vol.166 Issue 1 Pages 190-203	10.1002/ijgo.15349	38197560	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0135	C. S. Ublibjerg, Y. H. Lim, M. Kiraus, H. Frederiksen, A. M. Andersson and E. V. Bräuner	2022	Sex-specific associations between maternal exposure to parabens, phenols and phthalates during pregnancy and birth size outcomes in offspring	Current evidence on the effects of prenatal exposure to endocrine-disrupting chemicals on birth size remains largely inconclusive. We aimed to investigate sex-specific associations between maternal exposure to parabens, phenols, and phthalates during pregnancy and birth weight, height and head/abdominal circumference. We performed a prospective study of 88 pregnant women who underwent ambulatory ultrasound in the period 2012 to 2014. Maternal urine samples were collected during pregnancy in weeks 12 to 36 (median 18 weeks). The concentrations of parabens, phenols and individual phthalate diester metabolites were analyzed by isotope-diluted liquid chromatography-tandem mass spectrometry and creatinine adjusted. Linear regression models were used to estimate the associations between maternal urinary concentrations (T1) (first trimester), (T2) (second trimester), (T3) (third trimester) and (T1+T2+T3) (average) and birth size, stratified by offspring sex. A total of three parabens, two phenols, four individual phthalate metabolites and four sums of diester metabolites were detectable above limits of detection in ≥ 70% of the urine samples. The sum of di-2-ethylhexyl phthalate metabolites (ΣDEHP) was detected in all samples. Maternal urinary concentrations of ΣDEHP (T1) were associated with across-sex outcomes (birth weight: -128 g (95% CI: -256 to -0.1), birth length: -1.3 cm (95% CI: -2.5 to -0.2)) in adjusted cross-sectional analyses. Maternal urinary concentrations (T1) of ΣDEHP were associated with lower birth weight (-361 g, 95% CI: -591 to -131) and length (-3.1 cm, 95% CI: -5.7 to -0.6) compared to low exposure. None of these associations were statistically significant in female offspring. Across all compounds, individual exposures were associated with more negative estimates of birth weight for male than for female offspring. Our study indicates that prenatal exposure to BPA and DEHP may negatively affect birth size outcomes, with a possible sex effect. Given the small sample size, these findings need to be replicated in future large studies.	Sci Total Environ. 2022 Aug 25:836:155565.	10.1016/j.scitotenv.2022.155565	35508231	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0136	C. S. Ublibjerg, J. Leader, L. Mínguez-Alarcón, O. Chagnon, R. Dadd, J. Ford, E. Fleury, P. Williams, A. Jual, D. C. Bellinger, A. M. Calafat, R. Hauser and J. M. Braun	2024	Associations of maternal and paternal preconception and maternal pregnancy urinary phthalate biomarker and bisphenol A concentrations with offspring autistic behaviors: The PEACE study	BACKGROUND: Environmental chemical exposures in utero may play a role in autism development. While preconception risk factors for autism are increasingly being investigated, little is known about the influence of chemical exposures during the preconception period, particularly for paternal exposures. METHODS: In 196 children from the Preconception Environmental exposures And Childhood Health Effects (PEACE) cohort born to parents recruited from a fertility clinic in Boston, Massachusetts between 2006 and 2017, we quantified concentrations of 11 phthalate metabolites and bisphenol A (BPA) in urine samples collected from mothers and fathers before conception and mothers throughout pregnancy. When children were 6-9.5 years old, parents completed the Social Responsiveness Scale (SRS) questionnaire assessing autistic behaviors. We used linear mixed-effect models to estimate covariate-adjusted associations of phthalate biomarker and BPA concentrations, separately for maternal preconception (n = 173), paternal preconception (n = 121), and maternal pregnancy (n = 196) exposures, with SRS total raw scores. We also estimated associations with SRS subscales for social cognition, communication, social motivation, autistic mannerisms, and restricted interests. RESULTS: Across-sex outcomes (177 ≤ n ≤ 196), a two-fold increase in the summed molar sum of DEHP metabolites (ΣDEHP) was associated with a 1.2 point (95% CI: 0.0, 2.4) higher SRS total score. The observed associations of higher mono-isobutyl phthalate (MiBP) concentrations, measured in maternal preconception and paternal preconception periods with lower SRS T scores (2 points; 95% CI: -3.8, -0.2; n = 121 and 1.9 points; 95% CI: -3.6, -0.1; n = 173, respectively), were inverse. In a subset of participants with maternal preconception urine information, we primarily observed stronger inverse associations with higher folate and iron intake, particularly for folate intake and ΣDEHP concentrations. CONCLUSIONS: Urinary phthalate diester and BPA concentrations during preconception (maternal and paternal) and pregnancy (maternal) were not associated with adverse autistic behaviors in these children. Larger studies are needed to elucidate the observed associations, while considering interactions between maternal nutrition and chemical exposures.	Environ Res. 2024 Dec 15:263(Pt 3):120253.	10.1016/j.envres.2024.120253	39486680	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0137	J. Y. Uhm and H. R. Kim	2022	Cross-Sectional Association of Urinary Bisphenol A and Vaccine-Induced Immunity against Hepatitis B Virus: Data from the 2003-2014 National Health and Nutrition Examination Survey	Hepatitis B virus (HBV) infection poses a serious health burden; bisphenol A (BPA), a commonly used plasticizer for consumer products, is a potential immune disruptor. However, epidemiologic studies revealing the association between BPA exposure and immunity are limited. This study investigates the association between environmental BPA exposure and immune response following HBV vaccination in a nationally representative population. Data from 1,103 participants aged 12-19 years who participated in the National Health and Nutrition Examination Survey (NHANES) 2003-2014 were analyzed. The outcome was vaccine-induced immunity (n = 1068). Associations between BPA level and HBV vaccinability were assessed using multivariable logistic regression and expressed as odds ratios (ORs) of the pooled data and data for each cycle, separately. There was a significant association in the pooled data after adjusting for potential confounders (adjusted OR (aOR) 1.16; 95% confidence interval (CI) 1.04-1.29). However, the associations between BPA concentration and HBV vaccinability were inconsistent across the survey cycles, and tended to decrease in more recent cycles. Although this study preliminarily suggests that BPA attenuates the immune response to hepatitis B vaccination, further prospective studies are warranted to elucidate the discrepancies observed.	Int J Environ Res Public Health. 2022 Jan 19;19(3):1103.	10.3390/ijerph19031103	35162124	ヒト	-	-	-	-	-	-	-	免疫	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0138	P. Tyagi, T. James-Todd, L. Mínguez-Alarcón, J. B. Ford, M. Keller, J. Petrozza, A. M. Calafat, R. Hauser, P. L. Williams and A. Bellavia	2021	Identifying windows of susceptibility to endocrine disrupting chemicals in relation to gestational weight gain among pregnant women attending a fertility clinic	BACKGROUND: Exposure to endocrine disrupting chemicals (EDC), such as phthalates, and phenols, during pregnancy may be associated with excessive gestational weight gain (GWG), an important predictor of future obesity. OBJECTIVE: To identify windows of susceptibility to EDC exposure in relation to GWG among women undergoing fertility treatment. METHODS: We included 1,239 pregnancies conceived by 551 women in the LIFE Study (2005-2020). We examined the association between trimester-specific EDCs, mixtures and GWG in pregnant women attending a fertility clinic, to identify windows of susceptibility to EDC exposures, and assess the individual contribution of each chemical over pregnancy. METHODS: We included 252 pregnancy women from the Environment and Reproductive Health (ENVIRH) Study, who provided up to 3 urine samples (one per trimester), and with available data on GWG. Urinary concentrations of 7 phthalate metabolites, bisphenol A, and 2 parabens, corrected for specific gravity, were included in all models. The association between trimester-specific EDCs mixture and GWG was evaluated using multiple regression models - categorical g-computation. We used Bayesian Kernel Machine Regression (BKMR), while adjusting for potential confounders. RESULTS: During 1st trimester, higher EDC mixture was associated with lower GWG (-0.19 kg, 95% CI: -0.38, 0.00), with monobutyl phthalate (MBP) contributing the most to the negative association. During 2nd trimester, higher EDC mixture was associated with greater GWG (0.26 kg, 95% CI: 0.07, 0.45), with monoethyl phthalate (MEP) contributing the most to the positive association. RESULTS: During 3rd trimester, higher EDC was observed at higher sum of metabolites of di (2-ethylhexyl) phthalate (ΣDEHP) but not significantly associated with GWG (-0.12 kg, 95% CI: -0.32, 0.08). During 2nd and 3rd trimesters, positive associations with more or less significant phthalate and paraphenylene, and negative with 2 DEHP and methylparaben were observed. CONCLUSIONS: Exposure to EDC mixtures during 1st trimester was associated with lower GWG, while exposure during 2nd trimester was associated with greater GWG. In relation to GWG, within the 1st trimester, urinary 2-DEHP, mono-butoxyl phthalate and propylparaben had the highest contribution in the positive association between the mixture and GWG (0.03-0.05). All three ethylhexyl phthalate metabolites had similar contributions between urinary EDCs during pregnancy, especially DEHP metabolites, and GWG. Our results suggest the 1st trimester of pregnancy as the time window of highest susceptibility to the effects of EDCs on GWG, with potential indication for the design of public health interventions, informing preventive strategies for reducing sources of exposure at specific time points.	Environ Res. 2021 Mar:194:110638.	10.1016/j.envres.2020.110638	33359703	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0139	T. Tuzimski, S. Szubartowski, A. Słupek, W. Kaca, J. Grabek, M. Szałka-Mędlska, A. Kwaśniewska and B. Buszewski	2023	The Association between the Bisphenols Residues in Amniotic Fluid and Fetal Abnormalities in Polish Pregnant Women-Its Potential Clinical Application	The present study aimed to investigate the relationship between the concentrations of bisphenols residues in the amniotic fluid (AF) samples collected during aneuploidies and fetal chromosomal abnormalities in pregnant women. A total of 50 pregnant Polish women aged between 26 and 45 years, and scheduled to detect fetal risk for chromosomal defects in the first trimester, were included in this study. Samples were collected from three patients during routine diagnostics and treatment procedures at risk geneticist. The concentrations of various bisphenols residues in the samples were determined by liquid chromatography coupled with triple quadrupole tandem mass spectrometry (LC-ESI-QqQ-MS/MS). Recovery of eight analytes (BPS, BPF, BPA, BPAF, BADGE, BADGE·H2O, BADGE·2H2O and BADGE·H2O·HCl) was tested in amniotic fluid samples in the range 0.05 ng/mL to 5.38 ng/mL. Fetuses with chromosomal abnormalities showed a slightly higher frequency of occurrence of selected bisphenols residues in the AF samples collected between 15-36 weeks of pregnancy. Among the tested bisphenols, the highest concentrations in the AF samples were found for BPA and BPS. Statistically significant differences between the bisphenols concentrations in the healthy group (n = 30) and the group with fetal abnormalities (n = 20) were observed for BPA, BPS, BADGE·H2O and BADGE·2H2O. The AF samples taken from women after miscarriage in the second group. The number of detected compounds has been significant for the following analytes: BPS, BPAF, BADGE·H2O·HCl and BADGE. The proposed method may be an attractive alternative for application in large-scale human biomonitoring studies.	Int J Mol Sci. 2023 Jan 1;24(1):730.	10.3390/ijms24010730	36614173	ヒト	-	-	-	-	-	-	-	生殖発生	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0140	C. M. Tsen, J. H. Liu, D. P. Yang, H. R. Chau, J. L. Chen, W. C. Chou, Y. C. Ho and C. Y. Chiang	2021	Study on the correlation of bisphenol A exposure, pro-inflammatory gene expression, and C-reactive protein with potential cardiovascular disease symptoms in young adults	Bisphenol A (BPA) is a plasticizer used in the manufacture of polycarbonate and epoxy resins. It was found that higher urinary BPA levels are more likely to be associated with coronary artery disease (CAD). In recent years, the increasing incidence of CAD among young people is observed, which may be related with inflammation rather than the traditional triple-H risk factors. BPA is an endocrine disrupting chemical, and can induce inflammation. However, the correlation between BPA exposure and CAD development has not been established. Therefore, this study aimed to explore the association of BPA exposure with the gene expression of pro-inflammatory response (IL-6 and IL-8 mRNA), an inflammation biomarker of CAD (C-reactive protein, CRP), and symptoms of CAD development in young adults. The study divided BPA exposure levels into high and low groups based on the median plasma BPA level of 0.32 ng/mL, and found that the high BPA group obviously had higher BMI, blood pressure, CRP, IL-6 mRNA, and IL-8 mRNA levels than the low BPA group. Moreover, the BPA concentration was positively correlated with the above parameters. Furthermore, this study subjects who showed more CAD development symptoms had the highest levels of BPA (0.51 ng/mL), IL-6 mRNA (1.46), CRP (0.61 mg/L), IL-8 mRNA (1.46), BMI (21.68 kg/m2), and BP (SBP: 118.0 mm Hg; DBP: 74.0 mm Hg). These results indicated that exposure to BPA is potentially associated with expression of pro-inflammatory genes related to CRP secretion, which may promote the risk of CAD development symptoms in young adults. This study highlighted the possible connection between BPA exposure and CAD development but the mechanism between them needs to be further explored.	Environ Sci Pollut Res Int. 2021 Feb 24.	10.1007/s11356-021-12805-0	33625709	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0141	C. Tschersich, A. Murawski, G. Schwedler, E. Rucic, R. K. Moos, M. Kasper-Sonnenberg, H. M. Koch, T. Brüning and M. Kolossa-Gehring	2021	Bisphenol A and six other environmental phenols in urine of children and adolescents in Germany – human biomonitoring results of the German Environmental Survey 2014-2017 (GerES V)	Exposure to environmental phenols such as bisphenol A, benzophenone, 2-phenylphenol, triclosan, and triclocarbanis is of concern, because of their endocrine disrupting properties and broad application in consumer products. The current body burden of the 3-17-year-old population in Germany to these substances was assessed in first morning void urine samples (N = 510–512) collected within the population representative German Environmental Survey 2014–2017 (GerES V). Creatinine-corrected data were analysed for age and gender differences and compared to previous results from GerES IV (2003–2006). The limits of quantification (LOQ) for benzophenone-3 and bisphenol A (BPA) were 0.1 µg/L, 0.2 µg/L for triclosan, 0.4 µg/L for 2-phenylphenol, and 0.5 µg/L for triclocarbanis. Benzophenone-3, 2-phenylphenol and triclocarbanis were quantified in more than 50% of the samples. Benzophenone-3 and 2-phenylphenol concentrations were found to be associated with frequent application of personal care products. A comparison with the previous cycle of the survey, GerES IV (2003–2006), showed a decrease of urinary bisphenol A concentrations by 80% in children and by 70% in adolescents. Triclosan concentrations were found to be 50% lower in children and 70% lower in adolescents. BPA concentrations were still below the HBM-I value of 2 mg/L. To minimize environmental health risks, it is therefore necessary to maintain a further declining trend for bisphenol A and continue monitoring the exposure to environmental phenols, as well as to monitor substitutes such as bisphenol F and S.	Sci Total Environ Vol.763 Pages 144615	10.1016/j.scitotenv.2020.144615	33383503	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0142	C. S. Tsai, W. J. Chou, S. Y. Lee, M. J. Lee, M. C. Chia and L. J. Wang	2020	Phthalates, Para-Hydroxybenzoic Acids, Bisphenol-A, and Gonadal Hormones' Effects on Susceptibility to Attention-Deficit/Hyperactivity Disorder	This study aimed to examine whether endocrine-disrupting chemicals (EDCs), such as phthalates, para-hydroxybenzoic acids, and bisphenol-A (BPA), affect gonadal hormones and further link to the susceptibility to attention-deficit/hyperactivity disorder (ADHD). We recruited 98 boys with ADHD (7 girls with ADHD, 10 boys without ADHD) and any other psychiatric disorders, and 30 boys without ADHD and any other psychiatric disorders. Urine levels of EDCs, including mono-methyl phthalate (MMP), monoethyl phthalate (MEP), mono-n-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), monohydroxy phthalate (MHP), methylparaben (MeP), ethylparaben (EtP), propylparaben (PrP), butylparaben (BuP), and BPA, were measured. Serum levels of testosterone, estradiol, progesterone, sex hormone binding globulin (SHBG), and prolactin were also measured. Boys with ADHD had higher urinary levels of MnBP, but not other urinary EDCs, than control boys. There were no significant differences regarding EDCs between the females with ADHD and control groups. No significant differences in testosterone, free testosterone, FTRI, LH, estradiol, progesterone, or SHBG were found between the ADHD group and controls among either boys or girls. Among boys with ADHD, urine MBzP and MEHP levels were positively correlated with serum testosterone levels. Among girls, urine MEP levels were positively correlated with serum LH, testosterone, and free testosterone levels. The findings suggest that the possibility of an adverse impact of EDCs on gonadal hormones and neurodevelopment may exist. However, the results could be subject to potential selection bias, and the findings in this study should be interpreted with caution.	Toxics Vol.8 Issue 3	10.3390/toxics8030057	32823738	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0143	Z. Tkalec, T. Kosjek, J. Sirot Tratnik, A. Stajnko, A. A. Runkel, M. Sykiotou, D. Mazej and M. Horvat	2021	Exposure of Slovenian children and adolescents to bisphenols, parabens and triclosan: Urinary levels, exposure patterns, determinants of exposure and susceptibility	Chemicals such as bisphenols, parabens and triclosan are endocrine disrupting chemicals. They are used in a wide variety of consumer products, making human exposure to these chemicals widespread. In the present study, levels of three bisphenols: Bisphenol A, F and S ("analytes: trienfs)", ethyl-, isopropyl-, propyl-, isobutyl-, butyl- (sum) paraben) and triclosan were measured in first morning void from 196 Slovenian children and adolescents, aged 9-14 and 15-19 years and living in a rural region of Slovenia. Median levels of specific gravity-corrected levels for bisphenol A, bisphenol F, methyl paraben and ethyl paraben were 0.4, 0.089, 1.6 and 23 µg/L for children and 0.6, 0.11, 1.7 and 8.0 µg/L for adolescents, respectively. Median levels for all other endocrine disrupting chemicals were < LOQ. The levels are comparable with the levels reported in studies across Europe. Urinary concentrations of bisphenol A, methyl paraben and ethyl paraben were significantly higher in adolescents than in children. Exposure was found to be associated with several factors. Furthermore, individuals living in one of the sampling locations, Zavrč ka, were exposed to higher levels of bisphenol F and ethyl paraben than those in the remaining two sampling locations. Information about participants' dietary habits, use of food packaging and personal care products was obtained through questionnaires, and used to investigate associations between urinary levels of the biomarkers and potential exposure sources. High fat foods were associated with bisphenol A exposure, and cosmetics items such as lipstick and perfume with methyl paraben exposure. Significant correlation between methyl- and propyl paraben was observed in children's samples, suggesting similar exposure sources, while other compounds were not largely correlated, indicating independent sources. Furthermore, association between a single nucleotide polymorphism (SNP) in the estrogen receptor 1 gene and urinary bisphenol A concentrations was observed. Considering the endocrine disrupting properties of bisphenol A, this finding could indicate a potential genetic susceptibility to adverse effects caused by the exposure. The present study reports exposure of children and adolescents in Slovenia to a wide range of different endocrine disrupting chemicals for the first time, connecting it to exposure patterns and exposure sources. The study is to the authors' knowledge the first that investigates direct connection between levels of urinary endocrine disrupting chemical biomarkers and genetic polymorphism in ESTRR1.	Environ Int Vol.146 Pages 106172	10.1016/j.envint.2020.106172	33113465	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0144	Z. Tian, Z. He, Q. Zhang, L. Ding, L. Song, R. Ren, K. Tan, S. Cao, J. Wang and B. Pan	2024	The relationship between semen quality in male infertility clinic patients and bisphenol A : A Chinese cross-sectional study	Bisphenol A (BPA) is a growing concern as xenobiotic-disrupting chemical due to its adverse health effects. However, the association between BPA and sperm quality in adult human males remains unclear. The aim of this study was to assess the daily life exposure level of BPA and analyze its correlation with sperm quality in males. Patients who sought treatment in Chinese infertility clinics between May and October 2020 were recruited for this study. Urine samples were collected for BPA detection, and the concentrations were adjusted for creatinine. Semen samples were collected, and sperm morphology was analyzed using an improved Papanicolaou stain. A total of 656 participants, averaging 33.01 ± 5.42 years old, were included. We observed no sex-specific skewing participants in infertility clinics. Principal component analysis was performed for each semen quality index, and three principal components, reflecting sperm motility, count, and morphology were extracted. The participants' mean urine BPA level was 0.99 ng/mL. Negative correlations were observed between serum BPA content and total sperm count, sperm density, forward motility rate, and non-forward motility rate. A positive correlation was found between the non-motile sperm rate and the head deformity rate. Morphological abnormalities were the predominant adverse effects observed. Despite low daily life BPA exposure, long-term low-dose exposure in the general population may damage semen quality. This study provides a scientific basis for managing health risks associated with BPA exposure.	Heliyon Vol.10 Issue 16 Pages e35982	10.1016/j.heliyon.2024.e35982	39253254	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0145	Ö. Tezol, S. S. Yalçin, A. Yücin, A. Balcı Özyurt, Ç. Okçuoğlu and F. Erkekoğlu	2024	Plasma bisphenol a and phthalate levels in children with cerebral palsy: a case-control study	The case-control study aimed to evaluate potential sources of exposure and the plasma concentrations of bisphenol A (BPA) and phthalates in prepubertal children having cerebral palsy (CP) and healthy control. Blood samples of 68 CP and 70 controls were analyzed for BPA, di-(2-ethylhexyl) phthalate (DEHP), mono-(2-ethylhexyl) phthalate (MEHP), and alkyl phthalate (DBP, BPA and DEHP) levels were similar in groups. The median BPA level was 1.57 ng/mL. Significant correlations were observed between BPA and DEHP levels in the CP group. Gross motor function classification system, presence of spasticity, presence of dystonia, feeding difficulties, mixed/dual-type feeding, and oral-motor exercise were determined to increase odds of higher BPA and phthalate levels. In children with CP, in conclusion, potential exposure sources for BPA and phthalates differ in children with CP and healthy controls, and children with CP are not exposed to higher levels of BPA and phthalates.	Int J Environ Health Res. 2024 Jan;34(1):499-513.	10.1080/09603123.2022.2153811	36519276	ヒト	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0146	R. Tchoe, Y. Tan, D. Boyd Barr, P. Barry Ryan, Y. Tran, Z. Li, Y. Hu, A. K. Smith, D. P. Jones, A. L. Dunlop and D. Liang	2022	Use of high-resolution metabolomics to assess the biological perturbations associated with maternal exposure to Bisphenol A and Bisphenol F among pregnant African American women	BACKGROUND: Human and animal exposure to bisphenol A (BPA) has been associated with adverse developmental and reproductive effects. The molecular mechanisms by which BPA exposure exerts its effects are not well understood. Bisphenol F (BPF) is a replacement chemical for BPA in consumer products. OBJECTIVES: To characterize the metabolic perturbations in pregnant African American women associated with BPA/BPF exposure. In a pregnant African American cohort (METABOX). From a subset of study participants enrolled in the Atlanta African American Maternal-Child cohort, we collected both urine samples, for targeted exposure assessment of BPA (N = 218) and BPF (N = 18), and serum samples, for high-resolution metabolomics (HRM) profiling (N = 230), during early pregnancy (8-14 weeks' gestation). Using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method, we measured urinary concentrations of BPA and BPF. We used a multivariable linear regression model to estimate associations between early pregnancy urinary BPA/BPF concentrations, SEULTO. The geometric mean creatinine-adjusted concentrations of urinary BPA and BPF were 2.66 ± 2.7 ng/mL and 0.28 ± 1.3 ng/mL, respectively. BPA values were found to decrease non-correction at 20 % level, 262 and 730 unique metabolic features were significantly associated with urinary BPA and BPF concentrations, representing 16 and 12 metabolic pathways, respectively. Three metabolic pathways, including steroid hormones biosynthesis, lysine and leucine metabolism, were significantly associated with both BPA and BPF exposure. Using chemical standards, we have confirmed the chemical identity of 14 metabolites significantly associated with BPA or BPF exposure. CONCLUSIONS: Our findings support that exposure to BPA and BPF in pregnant women is associated with the perturbation of aromatic amino acid metabolism, xenobiotics metabolism, steroid biosynthesis, and other amino acid metabolism closely linked to stress response, inflammation, neural development, reproduction, and weight regulation.	Environ Int. 2022 Nov;169:107530.	10.1016/j.envint.2022.107530	36148711	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0147	E. M. Tanner, M. U. Hallerbäck, S. Wikström, C. Lindh, H. Kiviranta, C. Gennings and C. G. Bornehag	2020	Early prenatal exposure to suspected endocrine disruptor mixtures is associated with lower IQ at age seven	BACKGROUND: Endocrine disrupting chemicals (EDCs) are xenobiotics with the ability to interfere with hormone action, even at low levels. Prior environmental epidemiology studies link numerous suspected EDCs, including phthalates, bisphenols, and perfluoroalkyl substances (PFAS), to neurodevelopmental deficits. However, most studies have focused on single chemicals. OBJECTIVE: To assess the overall impact of prenatal exposure to an EDC mixture on neurodevelopment in school-aged children, and identify chemicals of concern while accounting for co-exposures. METHODS: Among 718 mother-child pairs from the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy study (SELMA) study, we used Weighted Quantile Sum (WQS) regression to assess the association between 29 EDCs, measured in late trimester urine or blood, with Wechsler Intelligence Scale for Children-IV) Intelligence Quotient (IQ) scores at age seven. Models were adjusted for child sex, gestational age, mother's education, maternal IQ, BMI/BMI, weight, and smoking status. To evaluate potential stability, we conducted repeated holdout validation, a machine learning technique. RESULTS: Using repeated holdout validation, IQ scores were 1.9 points (CI: -3.6, -0.2) lower per quartile increase in the EDC mixture. Maternal urinary concentrations of bisphenol A (BPA), bisphenol F (BPF), and PFAS had the strongest negative associations with IQ. BPA (-1.1 points; CI: -2.1, -0.1), BPF (-0.9 points; CI: -1.8, -0.1), MEHP (NA), MBuP (NA), MiBuP (NA), PFHxS (NA), PFHpA (NA), PFOA (-0.6 points; CI: -1.5, 0.3), PFNA (NA), PFDA (NA), PFUnDA (NA), and PFOS (-0.5; CI: -1.5, 0.5) were identified as chemicals of concern. Maternal urinary BPA and BPF concentrations were correlated (Spearman's rho = 0.7). Among all children whose testing and testing (at age 7), this identified bisphenol F as the primary chemical of concern, suggesting that the BPA replacement compound may not be any safer for children. Future studies are needed to confirm the potential neurotoxicity of replacement analogues.	Environ Int. 2020 Jan;134:105185.	10.1016/j.envint.2019.105185	31668669	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0148	S. Tang, C. He, P. K. Thai, A. Heffernan, S. Vijayasarathy, L. Toms, K. Thompson, P. Hobson, B. L. Tscharke, J. W. O'Brien, K. V. Thomas and J. F. Mueller	2020	Urinary Concentrations of Bisphenols in the Australian Population and Their Association with the Per Capita Mass Loads in Wastewater	Health concerns and related regulation of bisphenol A (BPA) in some countries have led to an increase in the production and use of unregulated and poorly understood BPA analogues, including bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF). Biomonitoring data for these analogues in the general population are limited. This study investigated the occurrence of nine bisphenols in urine samples collected between 2012 and 2017 and analyzed for 5-hydroxytryptophol, a key untargeted human biomarker found in wastewater-based epidemiology studies. BPA and BPS were the most frequently detected bisphenols in both urine and wastewater samples, with median concentrations of 2.0 and 0.8 μg/L in urine and 0.92 and 1.1 μg/L in wastewater, respectively. BPA, BPF, and BPAF had low detection frequencies in both urine and wastewater samples. Concentrations of BPA in urine declined from 2012 to 2017, while BPS increased, with a significant (p < 0.05) increase in BPS and a significant decrease in BPA concentrations observed between 2015 and 2017 (Mann-Whitney U test). Urinary concentrations of BPA and BPS were significantly correlated with their per capita mass loads in wastewater (R^2 = 0.71 and 0.72, respectively). The quantile g-computation revealed a statistically significant and negative joint effect of the five bisphenols on the risk of GDM (OR: 0.67; 95% CI: 0.48, 0.72) with BPA (35.2%), TBBPA (21.3%), and BPB (9.9%) had positive contribution to the overall effect. These findings suggested that BPS had a positive effect on the risk of GDM, while BPA and TBBPA had negative effect on the risk of GDM. Moreover, exposure to the mixture of the five bisphenols was negatively associated with the risk of GDM.	Environ Sci Technol Vol.54 Issue 16 Pages 10141-10148	10.1021/acs.est.0c00921	32806918	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0149	P. Tang, J. Liang, Q. Liao, H. Huang, X. Gao, M. Lin, B. Liu, B. Wei, X. Zeng, S. Liu, D. Huang and X. Qu	2023	Associations of bisphenol exposure with the risk of gestational diabetes mellitus: a nested case-control study in Guangxi, China	A growing number of epidemiologic studies have estimated the associations between endocrine disrupting chemicals and gestational diabetes mellitus (GDM). However, reports on the association between bisphenol A (BPA) substitutes and GDM are limited. This investigation aimed to explore the associations of maternal serum BPA, bisphenol B (BPB), bisphenol F (BPF), bisphenol S (BPS), and bisphenol AF (BPAF) with the risk of GDM. A nested case-control study was performed among 600 pregnant women. In unconditional logistic regression models, the OR for BPS was significantly increased in the medium exposure group: OR = 1.77, 95% CI: 1.02, 3.08 and the high exposure group: OR = 1.83, 95% CI: 1.05, 3.19 compared with the low exposure group. Restricted cubic spline (RCS) models revealed a linear dose-response relationship between BPS exposure and GDM risk ($P_{overall}$ = 0.027, $P_{nonlinear}$ = 0.102). In the stratified analysis, the joint effect of bisphenols was associated with the risk of GDM. BPS showed positively additive effects with BPA and TBBPA in multiple models, respectively. The quantile g-computation revealed a statistically significant and negative joint effect of the five bisphenols on the risk of GDM (OR: 0.67; 95% CI: 0.48, 0.72) with BPA (35.2%), TBBPA (21.3%), and BPB (9.9%) had positive contribution to the overall effect. These findings suggested that BPS had a positive effect on the risk of GDM, while BPA and TBBPA had negative effect on the risk of GDM. Moreover, exposure to the mixture of the five bisphenols was negatively associated with the risk of GDM.	Environ Sci Pollut Res Int. 2023 Feb;30(10):25170-25180.	10.1007/s11356-021-17794-8	34837624	ヒト	生殖発生	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0150	N. Tang, D. Wang, K. Chen, M. Zhang, W. Lv and X. Wang	2022	Maternal bisphenol A and triclosan exposure and allergic diseases in childhood: a meta-analysis of cohort studies	Bisphenol A (BPA) and triclosan (TCS) are both endocrine-disrupting chemicals (EDCs), and pregnant women are usually exposed to them through daily consumption. This study aimed to explore the relationship between prenatal BPA and TCS exposure and allergic diseases in childhood by systematic review and meta-analysis. We searched the topic of prenatal BPA and TCS exposure and allergic diseases in childhood published before December 2021 in PubMed, Embase, Web of Science, Cochrane Library, and Google Scholar databases. Cohort studies with data on prenatal BPA and TCS exposure and allergic diseases in childhood were included in this meta-analysis. The cross-sectional between prenatal exposure to BPA and total allergic diseases in childhood showed a pooled effect estimate of 1.21 (95% CI: 1.03, 1.39; I^2 = 0%; P_h = 0.674). The effect estimates between BPA exposure and each allergic disease were 1.38 (95% CI: 1.02, 1.58) for wheezing, 1.23 (95% CI: 1.01, 1.50) for asthma, 1.08 (95% CI: 0.99, 1.18) for eczema/rashes or itches, and 1.19 (95% CI: 1.01, 1.39) for aeroallergens. Prenatal exposure to TCS had no association with the four types of allergic diseases in childhood. BPA exposure during the prenatal period was positively associated with allergic diseases in childhood. Strengthening prenatal EDC exposure control is necessary for child health.	Environ Sci Pollut Res Int. 2022 Nov;29(55):83389-83403.	10.1007/s11356-022-21575-2	35764729	ヒト	免疫(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0151	S. Tait, F. Carli, L. Busani, D. Ciscato, V. Della Latta, A. Daudati, E. Fabbrizzi, A. P. Pala, F. Marangh, R. Tassinari, G. Trifirò, S. Ciarfaglia, A. Garofalidi, C. La Rocca and G. Life Persuaded Project	2021	Italian Children Exposure to Bisphenol A: Biomonitoring Data from the LIFE PERSUADED Project	A human biomonitoring (HBM) study on bisphenol A (BPA) in Italian children and adolescents was performed within the LIFE PERSUADED project, considering the resulting mass, sex and age. The median urinary BPA level was 1.32 μg/L, with children living in the South of Italy or in Sardinia having higher levels than those living in the North or in rural areas. Children aged 9–11 years had the highest BPA levels, more than those aged 7–8 and 12–14 years, but no differences were detected between sexes. The exposure in Italian children was higher compared to children from other countries, but lower than the HBM guidance value (130 μg/L). The estimated daily intake was 8.37 μg/kg body weight (bw) per day, about 20-fold below the temporary Tolerable Daily Intake of 4 μg/kg bw set by the established by the European Food Safety Authority. However, this threshold was exceeded in 1.46% of the enrolled children, raising concern about the normal exposure of Italian young population.	Int J Environ Res Public Health Vol.18 Issue 22	10.3390/ijerph182211846	34831602	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0152	E. Taheri, R. Riahi, N. Rafiei, A. Fatehizadeh, H. M. N. Iqbal and S. M. Hosseini	2021	Bisphenol A exposure and abnormal glucose tolerance during pregnancy: systematic review and meta-analysis	In the present work, a systematic review and meta-analysis were performed to examine the probable relation between maternal exposure to bisphenol A (BPA), as estrogen-disrupting compounds, and gestational diabetes mellitus (GDM), and impaired glucose tolerance (IGT). We comprehensively searched three electronic databases to retrieve published studies on maternal exposure to BPA and GDM/IGT through February 2021. Cochran's Q test and I2 statistics were employed for testing heterogeneity across studies. DerSimonian and Laird random effects model was used to determine the pooled estimates. Ethanol, the fixed effects model with Mantel–Haenszel method was applied. Publication bias was assessed by Egger's regression asymmetry test and Begg's adjusted rank correlation test. Sensitivity analysis was performed to evaluate the effect of individual studies on the overall estimate by omitting one study in each turn. Weight and Egger's tests. The pooled odds ratio did not show BPA exposure to be a significant risk factor for GDM (OR = 0.98; 95% CI = 0.60–1.35; I2 = 0%; P_h = 0.96). Also, no significant association was observed between BPA exposure and risk of IGT (OR = 0.93; 95% CI = 0.60–1.38; I2 = 11.5%). Based on the findings of this study, no association was found between exposure to BPA during pregnancy and the risk of GDM/IGT. Albeit no heterogeneity was found between studies.	Environ Sci Pollut Res Int. 2021 Nov;28(44):62105-62115.	10.1007/s11356-021-16691-4	34590231	ヒト	代謝(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0153	R. Tagne-Fotso, M. Risa, A. Saoudi, A. Zeghnoun, H. Fréderiksen, T. Bjerman, P. Montazeri, A. M. Andersson, L. Rodriguez-Martin, A. Akesson, M. Berglund, P. Bist, A. Castaño, M. A. Cirtiles, E. Cocco, E. Der Hovsepian, M. C. Dewolf, M. Esteban-Lopez, L. Gilles, E. Govarts, C. Gutleb, A. C. Gutleb, C. Hartmann, T. Kold Jensen, G. Koppen, T. Kosjek, N. Lambrechts, R. McEachran, A. K. Sakhi, J. Sioen, Trine K. M. Uhl, J. Urquiza, M. Vafeiadi, A. Van Nieuwenhuyse, M. Vrijheid, T. Weber, C. Zaros, E. Tarrijo-Aulina, L. E. Knudsen, A. Covaci, R. Barouki, M. Kolossa-Gehring, G. Schoeters, S. Dwyer, C. Filist and L. Rambaud	2024	Exposure to bisphenol A in European women from 2007 to 2014 using human biomonitoring data - The European Joint Programme HBM4EU	BACKGROUND: Bisphenol A (BPA) or 4,4′-isopropylidenediphenol) is an endocrine disrupting chemical. It was widely used in a variety of plastic-based manufactured products for several years. The European Food Safety Authority (EFSA) recently reduced the Tolerable Daily Intake (TDI) for BPA by 20,000 times due to concerns about immune toxicity. OBJECTIVE: We used human biomonitoring (HBM) data to investigate the general level of BPA exposure from 2007 to 2014 of European women aged 18–75 years (n = 1,236) and its determinants. METHODS: Fifteen studies from 12 countries (Austria, Belgium, Denmark, France, Germany, Greece, Israel, Luxembourg, Slovenia, Spain, Sweden, and the United Kingdom) were included in the BPA Study protocol developed within the European Joint Programme HBM4EU. Seventy variables related to the BPA exposure were harmonized and analyzed. Descriptive statistics, univariate and multivariate analyses were performed. RESULTS: The geometric mean (GM) of urinary BPA concentrations was 0.40 μg/L (95% CI: 0.38, 0.42) and the 95th percentile was 3.0 μg/L (95% CI: 2.7, 3.3). BPA was detected in 80–98% of women in 13 out of 15 contributing studies. Only the Austrian FRIDA study (Advanced Europe), which had a limit of quantification (LOQ) of 0.16 μg/L, and the Spanish INMA-Valencia study (Early Iberia) had a LOQ of 0.4 μg/L. The geometric mean (GM) of total urine BPA ranged from 0.77 to 2.37 μg/L among the contributing studies. The lowest GM of total BPA was observed in France (Western Europe) from the ELFE subset (GM = 0.77 μg/L, 0.68 μg/g creatinine), n = 1701), and the highest levels were found in Belgium (Western Europe) and Greece (Southern Europe), from ESTEBAN (GM = 2.37 μg/L, 2.12 μg/g creatinine), n = 139) and MOLI-SANI (GM = 2.27 μg/L, 2.13 μg/g creatinine), n = 190) subsets, respectively. One hundred percent of women in 13 out of 15 data collections in this study exceeded the health-based guidance value (HBGV) of 0.2 ng/kg bw/day established by EFSA in 2015. Only 1.5% of women in the Austrian FRIDA subset and 3.5% of women in the Spanish INMA-Valencia subset exceeded the HBGV. Several factors related to the socio-demographic characteristics (age, height, weight, education, smoking status) were collected in almost all studies, while several variables related to BPA exposure factors were not gathered in most of the original studies (consumption of beverages, contained in plastic bottles, consumption of canned food or beverages, consumption of food in contact with plastic packaging, use of plastic films or containers in the kitchen, frequency of use of plastic bottles). Univariate and multivariate analyses revealed that the socio-demographic characteristics among European women were found. A broader range of data planned for collection in the original questionnaires of the contributing studies would have enabled a more thorough investigation of the determinants of BPA exposure in European women. CONCLUSION: This study highlights the urgent need for action to further reduce exposure to BPA to protect the population, as is already the case in the European Union. The case study also underscores the importance of and harmonizing HBM design and data for producing comparable data and interpretable results at a European scale level, and to increase HBM uptake by regulatory agencies.	Environ Int Vol.190 Pages 108912	10.1016/j.envint.2024.108912	39116556	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0154	Y. P. Tabanli, S. S. Yalçin, S. Remziİş, Ş. Kılıaç Altınbaş, A. Yücin, A. Balcı Özyurt, F. Gürçel, F. Erkekoğlu and K. Yurdakök	2023	Association of bisphenol A with 25(OH)D, 1,25(OH)2D and 25(OH)D ratio in cord blood	The aim was to investigate the association between bisphenol A (BPA), 25-hydroxy vitamin D (25(OH)D), and 1α,25-dihydroxy vitamin D (1,25(OH)2D) levels in the cord blood of newborn babies. BPA was measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) and 25(OH)D and 1,25(OH)2D by chemiluminescence immunoassay (CLIA) in 100 cord blood samples. The median BPA level was 1.0 ng/mL (IQR: 0.6–2.0) and median 1,25(OH)2D level was 51.5 pg/mL (IQR: 42.3–66.3). 25(OH)D levels were < 20 ng/mL in 74.0% of the babies. BPA was detectable in 72.4% of the cord blood samples; median BPA level was 1.57 ng/mL (IQR = [16.–0.05 ng/mL). Frequencies of vitamin D deficiency and frequencies of cases having the highest tertile active vitamin D levels were similar in groups of BPA tertiles in both univariate and multivariate analysis. In conclusion, both BPA exposure and insufficient vitamin D (mainly) or low cord blood are common in newborns. Bisphenol A levels were not correlated with vitamin D levels in cord blood of healthy mother–fetus pairs.	Environ Sci Pollut Res Int. 2023 Sep;30(45):100391-100402.	10.1007/s11356-023-29288-w	37626198	ヒト	その他(ビタミンDレベル)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0155	C. Symeonides, K. Vacy, S. Thomson, S. Tanver, H. K. Chua, S. Dixit, T. Mansell, M. O'Hely, B. Nowakowski, J. B. Harbertson, S. Wang, J. Gao, J. Chia, N. T. Tran, S. E. Hwang, K. Britz, F. Chan, T. H. Kim, C. A. Reid, A. El-Bitar, G. B. Bennetsen, L. M. D. Delbridge, V. R. Harley, Y. W. Yap, D. Dewey, C. J. Love, D. Burgner, M. L. K. Tang, P. D. Sly, K. Saffery, J. F. Mueller, N. Kinahan, B. Tonpa, P. Vuillermin, A. L. Ponsonby and M. C. Boon	2024	Male autism spectrum disorder is linked to brain aromatase disruption by prenatal BPA in multimodal investigations and 19HDA ameliorates the related mouse phenotype	Male sex, early life chemical exposure and the brain aromatase enzyme have been implicated in autism spectrum disorder (ASD). In the Barwon Infant Study birth cohort (n = 3270), higher prenatal maternal bisphenol A (BPA) levels are associated with higher ASD symptoms at age 2 and diagnosis at age 8 only in males with low aromatase genetic pathway activity scores. Higher prenatal BPA levels are predictive of higher cord blood methylation across the CYP19A1 brain promoter (1 region [P < 0.005] and aromatase gene methylation mediates (P = 0.02) the link between higher prenatal BPA and brain-derived neurotrophic factor methylation, with independent cohort replication. BPA suppressed aromatase expression in vitro and in vivo. Male mice exposed to mid-gestation BPA or with aromatase knockout have ASD-like behaviors with structural and functional brain changes. 3D-histology-7 discovers and 12HNEK, an estrogenic fatty acid alleviated these features and reversed detrimental neurodevelopmental gene expression. First we demonstrate that prenatal BPA exposure is associated with impaired brain aromatase function and ASD-related behaviors, and brain abnormalities. In males that may be reversible through postnatal 19HDA intervention.	Nat Commun. 2024 Aug 7;15(1):6367.	10.1038/s41467-024-48897-8	39112449	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0156	C. Symeonides, E. Aromataris, Y. Mulders, J. Dizon, C. Stern, T. H. Barker, A. Whitehorn, D. Pollock, T. Marin and S. Dunlop	2024	An Umbrella Review of Meta-Analyses Evaluating Associations between Human Health and Exposure to Major Classes of Plastic-Associated Chemicals	Background: Epidemiological research investigating the impact of exposure to plastics, and plastic-associated chemicals, on human health is critical, especially given exponentially increasing plastic production. In parallel with increasing production, academic research has also increased exponentially both in terms of the primary literature and ensuing systematic reviews with meta-analysis. However, there are few overviews that capture a broad range of chemical classes to present a scale of play regarding impacts on human health. Methods: We undertook an umbrella review to review this systematic reviews with meta-analysis. Given the complex composition of plastic and the large number of identified plastic-associated chemicals, it was not possible to capture all chemicals that may be present in, and migrate from, plastic materials. We therefore focussed on a subset of chemicals that are commonly detected in humans and/or the environment, and/or are known to be used in the manufacture of plastics. These included bisphenols and their analogues, phthalates and flame retardants as the two classes of functional additive with the highest concentration ranges in plastics. In addition, we included bisphenols and per- and polyfluoroalkyl substances (PFAS) as two other major plastic-associated chemicals with significant known exposure through food contact materials. Epidemiology and PubMed were searched for systematic reviews with meta-analyses, meta-analyses, and pooled analyses evaluating the association of plastic polymers, particles (microplastics) or any of the selected groups of high volume plastic-associated chemicals above, measured directly in human biospecimens, with human health outcomes. Results: Fifty-two systematic reviews were included, with data contributing 178 meta-analyses. Most meta-analyses (78%) were from reviews of moderate methodological quality. Across all the publications, evidence was identified for 38 associations between exposure to plastics and plastic-associated chemicals and 20 unique health outcomes, including cancer, cardiometabolic, reproductive, and neurodevelopmental. Synthesized estimates of the effects of plastic-associated chemical exposure were identified for the following health outcome categories in humans: birth, childhood adult reproductive, endocrine, child neurodevelopment, nutritional, circulatory, respiratory, skin related and cancers. Bisphenol A (BPA) is associated with decreased positional distance in infants, type 2 diabetes (T2D) in adults, insulin resistance in children and adults, and increased body mass index (BMI) and overweight in children, attention deficit hyperactivity disorder (ADHD) in girls and allergic rhinitis. Potential protective associations were found, namely observed pubertal timing in boys being less common with higher phthalate exposure. Increased high-density lipoprotein (HDL) with exposure to mono(2-ethyl-5-oxohexyl) phthalate (MEHHP) and reduced incidence of chronic lymphocytic leukaemia in a subset of TAG 1 with PCB exposure. Conclusions: Exposure to plastic-associated chemicals is associated with adverse outcomes across a wide range of human health domains, and many plastic-associated chemical group is associated in at least one adverse health outcome. Large gaps remain for many plastic-associated chemicals. Given the complexity of plastic composition and the ubiquity of exposure, we recommend that regulation of plastic and plastic-associated chemicals should not be based solely on systematic reviews, could introduce minor- and investigative as well as emerging plastic-associated chemicals of concern such as bisphenol analogues and replacement phthalates and flame retardants. With respect to chemical regulation, we propose that safety for plastic-associated chemicals in humans cannot be assumed at market entry. We therefore recommend that improved independent, systematic based testing for all plastic-associated chemicals is undertaken before market release of products. In addition because of the limitations of laboratory-based testing for predicting harm from plastic in humans, independent and systematic post-market bio-monitoring and epidemiological studies are essential to detect potential unforeseen harms.	Ann Glob Health Vol.90 Issue 1 Pages 52	10.5334/aogh.4459	39183960	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0157	N. Suwannarin, Y. Nishihama, T. Isobe and S. F. Nakayama	2024	Urinary concentrations of environmental phenol among pregnant women in the Japan Environment and Children's Study	Humans are exposed to various bisphenols, alkylphenols and nitrophenols through dietary intake, food packaging and container materials, indoor and outdoor air/dust. This study aimed to evaluate exposure of Japanese pregnant women to environmental phenols, by measuring target compounds in urine samples. From a cohort of the Japan Environment and Children's Study, JECS program, we randomly selected and sent 40 questionnaires to pregnant women. Bisphenol A (BPA), bisphenol F (BPF), bisphenol AF (BPAF), para-nitrophenol (PNP), 3-methyl-4-nitrophenol (MNP), 2-sec-butyl-4,6-dinitrophenol (DNBP), and 2-cyclohexyl-4,6-dinitrophenol (DCHP) were analyzed in urine samples collected in the second trimester. Urinary BPA was detected in 99.8% of samples, and the geometric mean (GM) was 1.1 μg/L. Urinary BPF was detected in 97.6% of samples, and the GM was 0.4 μg/L. Urinary BPAF was detected in 1.2% of samples. Urinary PNP, MNP, DNBP, and DCHP were not detected in any samples. Urinary BPA concentrations were positively correlated with urinary BPF concentrations. Urinary BPA concentrations were higher in participants who were younger, had lower household income, and had lower educational attainment. Urinary BPA concentrations were lower in participants who had a history of allergic rhinitis. Potential protective associations were found, namely observed pubertal timing in boys being less common with higher phthalate exposure. Increased high-density lipoprotein (HDL) with exposure to mono(2-ethyl-5-oxohexyl) phthalate (MEHHP) and reduced incidence of chronic lymphocytic leukaemia in a subset of TAG 1 with PCB exposure. Conclusions: Exposure to plastic-associated chemicals is associated with adverse outcomes across a wide range of human health domains, and many plastic-associated chemical group is associated in at least one adverse health outcome. Large gaps remain for many plastic-associated chemicals. Given the complexity of plastic composition and the ubiquity of exposure, we recommend that regulation of plastic and plastic-associated chemicals should not be based solely on systematic reviews, could introduce minor- and investigative as well as emerging plastic-associated chemicals of concern such as bisphenol analogues and replacement phthalates and flame retardants. With respect to chemical regulation, we propose that safety for plastic-associated chemicals in humans cannot be assumed at market entry. We therefore recommend that improved independent, systematic based testing for all plastic-associated chemicals is undertaken before market release of products. In addition because of the limitations of laboratory-based testing for predicting harm from plastic in humans, independent and systematic post-market bio-monitoring and epidemiological studies are essential to detect potential unforeseen harms.	Environ Int Vol.183 Pages 108373	10.1016/j.envint.2023.108373	38088018	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0158	S. Suresh, S. A. Singh and C. Vellapandian	2022	Bisphenol A exposure links to exacerbation of memory and cognitive impairment: A systematic review of the literature	This systematic review probes the deleterious outcome of Bisphenol A (BPA) exposure on cognitive/memory by scrutinizing the extent pre-clinical studies on this focus, to promote apprehension about this environmental issue among the general population with a long-term goal to tackle plastic (BPA) free manufacturing practices. Methods: Bibliographic databases, including Scopus, ProQuest, PubMed Central, Science Direct, and ScienceDirect were searched for preclinical reports assessing the impact of BPA exposure on memory/cognition. The review protocol has been published in PROSPERO with the registration number CRD42021233966. The ETHICUS, PuBrowser, SYRCLE's RoB tool was employed to assess the quality of the studies. Results: Out of 1,256 records identified, 20 studies were included in the review. Most studies confirmed the likelihood of the latent neurodevelopmental dysfunction, which may manifest as memory/cognitive decline. BPA impairs memory and cognition by binding to estrogen receptors, inducing ROS/RNS/MDA signaling pathway, altering the expression of synaptic proteins, impacting the morphology of pyramidal neurons in the hippocampus, dysregulation of thyroid hormones, and altering the neurotransmitter levels.	Neurosci Biobehav Rev Vol.143 Pages 104939	10.1016/j.neubiorev.2022.104939	36328120	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0159	U. Sur, P. Erkekoglu, A. D. Bulut, N. Andiran and B. Kocer-Gumusel	2019	Oxidative stress markers, trace elements, and endocrine disrupting chemicals in children with Hashimoto's thyroiditis	In this study, we aimed to investigate whether bisphenol A (BPA) and di (2-ethylhexyl) phthalate (DEHP) exposure have any association with Hashimoto's thyroiditis (HT) and its biomarkers, and to determine whether oxidative stress biomarkers and trace element levels showed any alterations in children with HT. We found that superoxide dismutase and glutathione peroxidase activities are lower in HT group from control (39% and 48%, respectively, p < 0.05). Zinc levels were significantly lower in HT group vs. control. In addition, the levels of mono (2-ethylhexyl) phthalate (MEHP) which is the primary metabolite for DEHP, were markedly higher in HT group compared to control (p < 0.05). A negative correlation was observed between urinary BPA levels and FT3. In children with HT, redox/antioxidant balance is changed and these differences may be related to EDC exposure, the importance of which should be evaluated with further studies.	Toxicol Mech Methods Vol.29 Issue 9 Pages 633-643	10.1080/15376516.2019.1646367	31354016	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0160	V. Supornkhchal, L. Suttiloet, I. Kaewkamnerdpong, C. Jantarat, N. Sakoon, W. Nossangkaew, T. Chalkiopoplek, L. Samarnsaeng, S. Wachsmanit-hs and T. Piantaweetus	2025	Bisphenol A Biomonitoring after Sealant Placement: A Prospective Cohort Study in Schoolchildren	INTRODUCTION: Bisphenol A (BPA), known for its endocrine-disrupting properties, is a concern when leaching from dental sealants. This study investigates the systemic BPA exposure following the placement of Bis-GMA-based dental sealants in Thai primary school students. OBJECTIVES: The main objective was to evaluate the changes in urinary BPA concentrations after the application of Bis-GMA dental sealants in a cohort of Thai students. METHODS: In a prospective cohort of Thai primary school students participating in a voluntary sealant placement program, urinary BPA concentrations were measured. Urine samples (immediately before and on days 1, 7, and 14 after sealant application) BPA levels were measured using high-performance liquid chromatography. Repeated measures analysis using generalized estimating equations was performed to assess changes in BPA concentrations over time. Creatinine levels were also measured to account for urine dilution. Estimated daily intake (EDI) values were calculated using the formula: EDI = (BPA concentration × urine volume)/body weight, considering the mean urine volume for children aged 6–12 years. RESULTS: Data were collected from 50 Thai students (mean age of 8.9 ± 1.3 years; 60% female). The mean body mass index (BMI) was 17.7 ± 3.0 kg/m2, and the average volume was 0.4 ± 0.3 mL. Urinary BPA concentrations were 1.1–122 ng/mL with 0.66 creatinine. The median adjusted BPA levels before sealant placement and on days 1, 7, and 14 were 0.02, 0.03, 0.19, and 0.23 μg/g creatinine, respectively. The analysis revealed a significant association between the number of sealed teeth and increased BPA levels at all visits (GEE2) (0.0019). The application of Bis-GMA-based dental sealants, in children results in low-level BPA exposure due to chemical leaching. Despite such a low level of BPA exposure, approved by international health authorities, it could be considered a silent, chronic, and persistent systemic event, the long-term implications of which are yet to be fully understood. Our findings underscore the importance of monitoring BPA exposure from dental materials, aligning with international limits. However, the long-term effects are unknown. This information should inform dental care practices and guide policymakers in assessing the chronic impacts of BPA exposure from dental materials.	JDR Clin Trans Res Pages 23800844251320009	10.1177/23800844251320009	40077867	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0161	B. Sa-man, K. Yurdakök, B. Kocer-Gumusel, Ö. Özgünci, F. Akkuyik, A. Batcı, G. Oskamallı, P. Erkekoğlu and M. Yurdakök	2019	Prenatal bisphenol a and phthalate exposure are risk factors for male reproductive system development and cord blood sex hormone levels	Bisphenol A (BPA) and phthalates can adversely affect the fetal development. However, observational studies on the effects of these chemicals on fetal male reproductive system are still limited. A hundred of umbilical cord blood samples were analyzed for the levels of BPA, di-2-ethylhexyl phthalate (DEHP), mono-(2-ethylhexyl) phthalate (MEHP), and sex hormones. After birth, male newborns underwent a physical examination that included measurements of anogenital distance, stretched penile length (SPL), and penile width. BPA, DEHP and MEHP levels were detectable in >99% of cord blood samples. In univariate adjusted models, cord blood BPA levels were inversely associated with SPL, of newborns and positively associated with cord blood estradiol levels. In addition, there was a significant inverse relationship between cord blood DEHP levels and anogenital distance index of newborn males. Our results suggest that in vitro BPA and DEHP exposure exerted adverse effects on fetal male reproductive development and cord blood estradiol levels.	Reprod Toxicol. 2019 Aug;87:146-155.	10.1016/j.reprotox.2019.05.005	31170452	ヒト	生殖発生	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0162	M. Sung, H. M. Jee, J. H. Kim, E. K. Ha, Y. H. Shin, J. H. Kim, D. H. Lim and M. Y. Han	2022	Serum vitamin D level mitigates fractional exhaled nitric oxide linked to bisphenol-A in school-aged children	OBJECTIVE: Previous studies on the relationship of bisphenol A (BPA) with fractional exhaled nitric oxide (FeNO) had conflicting results, suggesting that other factors may modulate this relationship. Thus, we investigated the modifying effect of vitamin D on the relationship of BPA with FeNO in children. PATIENTS AND METHODS: This study recruited 1,130 children (6 to 12 years old) from 2 metropolitan areas of Korea between June and July 2017. We conducted measurements of urinary BPA, serum vitamin D, specific serum IgE, FeNO, and data from inactive oscillometry (resistance and [Xrs]), airway resistance at 5 Hz ([Rrs5]) and 20 Hz ([Rrs20]), and reactance area ([AX]). RESULTS: Urinary BPA was detected in 1,129 children (99.9%). Urinary BPA concentrations were significantly associated with FeNO in children with low vitamin D levels (1.25 ng/mL < d < 3.66 ng/mL, n = 282), but not in children with high vitamin D levels (≥ 3.75 ng/mL). The interaction of vitamin D and BPA had a significant effect on FeNO (p(int) = 0.005). There was no relationship with the airway lung function (Rrs5, Rrs20, and Rrs5–20) in serum vitamin D and urinary BPA level. Vitamin D ameliorated the BPA-mediated increase of FeNO in children. CONCLUSIONS: These results suggest that children with low vitamin D levels may be more susceptible to airway inflammation due to BPA.	Eur Rev Med Pharmacol Sci. 2022 Mar;26(5):1640-1647.	10.26355/eurrev_202203_28232	35302211	ヒト	呼吸器系	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0163	A. A. Sukuroglu, D. Battal, K. Kocadal, M. A. Saygun, İ. Cok and I. Ustuoglu	2022	Biomonitoring of bisphenol A, 4-nonylphenol, and 4-t-octylphenol in Turkish population: exposure and risk assessment	Biomonitoring studies are important tools to understand the effects of endocrine-disrupting compounds on human health. Up to now, there have been no biomonitoring and risk assessment studies conducted in Turkish population in which urinary bisphenol A (BPA), 4-nonylphenol (4-NP), and 4-t-octylphenol (4-t-OP) levels were measured simultaneously. The aim of this study is to measure urinary BPA, 4-NP, and 4-t-OP on Turkish population and to estimate exposure and risk assessment. Urine samples were collected from 100 adults (50 males and 50 females) in Izmir, Turkey. Urinary BPA, 4-NP, and 4-t-OP were analyzed by using mentioned methods, and human biomonitoring was used as a risk assessment tool in EDI estimations. Using a Monte Carlo, Turkey, Izmir BPA, 4-NP, and 4-t-OP medians were 0.0019, 0.0 μg/g creatinine, 0.027, 0.0 μg/g creatinine, and 0.016 μg/g creatinine, respectively. The obtained environmentally intakes (EDIs) were calculated as 0.098 μg/kg bw/day, 0.061 μg/kg bw/day, and 0.092 μg/kg bw/day for BPA, 4-NP, and 4-t-OP, respectively. In conclusion, although no potential health risk due to BPA and 4-NP exposure was observed, there might be health risks associated with 4-t-OP exposure in the Turkish population.	Environ Sci Pollut Res Int Vol.29 Issue 18 Pages 26250-26262	10.1007/s11356-021-17796-6	34850348	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0164	M. Sugiura-Ogasawara, N. Suwannarin, H. Tamada, T. Ebara, Y. Ito, S. F. Nakayama, M. Takagi, S. Saitoh and M. Kamijima	2025	Effect of maternal bisphenol exposure on adverse pregnancy and neonatal outcomes: The Japan Environment and Children's study	Maternal exposure to bisphenols, including bisphenol A (BPA), reportedly results in adverse pregnancy and offspring health outcomes. However, large birth cohort studies on the risk of BPA exposure during pregnancy remain limited. Here, we examined bisphenol effects on adverse pregnancy and neonatal outcomes using data from the Japan Environment and Children's Study, a nationwide birth cohort study. We selected 2013 women with pregnancies resulting in singleton live births. First trimester urine concentrations of bisphenols A, F, S, and AF were determined via high-performance liquid chromatography–tandem mass spectrometry. We analyzed the association between BPA exposure and preterm birth, hypertensive disorders of pregnancy, gestational hypertension, preeclampsia, small- and large-for-gestational-age infants, low birth weight, shortening physiological chromosome aberrations using Bayesian logistic regression analysis after applying the 50 limp imputation method for concentrations within the minimum reporting limit. Bisphenol detection rates were generally low (0.2–4.2%), except for BPA (96.2%). The median BPA concentration was 1.1 ng/mL, and the 95th percentile was 6.4 ng/mL. Only 0.2% of participants (4 individuals) exceeded the European Food Safety Authority's tolerable daily intake (0.0002 μg/kg/day). However, BPA intake was not significantly associated with any outcome. These findings suggest that BPA's current exposure levels do not affect measured pregnancy and neonate outcomes in Japan. Here, although BPA levels reflect only recent exposure, the potential health risks associated with BPA underscore the need for further research to investigate the long-term effects of low-level exposure on maternal and child health.	Environ Int. 2025 Aug;202:109663.	10.1016/j.envint.2025.109663	40651277	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0165	H. Su, J. Xi, M. Miao, H. Liang, Y. Chen, Z. Wang, Y. Zhou, Y. Jin, H. Ji and W. Yuan	2025	Bisphenol analogs exposure in 4-year-old children and their intelligence quotient at 6 years: A prospective cohort study	Prenatal exposure to bisphenol A (BPA) has been shown to impact offspring cognition, behavior, and intelligence. However, whether co-exposure to bisphenol analogs (BPs) during childhood affects children's intelligence remains unclear. We included 681 mother-child pairs from the Shanghai Minhang Birth Cohort Study to examine the impact of children's exposure to BPs at 4 years of age on the intelligence quotient (IQ) measured at 6 years. BPs concentrations were measured in single-void urine samples collected from 4-year-old children. We used the Wechsler Intelligence Scale for Children-revised edition to assess children's IQ. Multiple linear regression models were used to examine the associations between BPs and IQ. Bayesian kernel machine regression (BKMR) models were used to evaluate the joint and single-exposure effects of BPs. Within 14 girls, exposure to BPA was positively associated with full-scale IQ (FSIQ) (β = 3.92, 95% CI: 0.01, 7.83), verbal IQ (VIQ) (β = 4.08, 95% CI: 0.01, 8.15), and performance IQ (PIQ) (β = 4.08, 95% CI: 0.01, 8.15). BPA contributed the most to the joint effect of BPs in girls. The associations remained robust after adjusting for children IQ. In boys, exposure to bisphenol analogs (BPA + bisphenol S + bisphenol F) was positively associated with an increase in FSIQ and PIQ; however, the number of exposed boys was small. Our study suggests that BPs exposure at 4 years of age may be associated with a boost IQ at 6 years. In girls, BPF may not be a safe substitute for BPA. Further epidemiological studies are required to confirm these findings.	Environ Res. 2025 Jul 1:276:121528.	10.1016/j.envres.2025.121528	40185270	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0166	S. M. Skurka Hoarty, A. L. Cathey, Z. Y. Rosado Pabón, C. M. Vélez Vega, A. N. Alshawabkeh, J. F. Cordero, D. J. Watkins and J. D. Meeker	2024	Urinary phenol and paraben concentrations in association with markers of inflammation during pregnancy in Puerto Rico	Exposure to phenols and parabens may contribute to increased maternal inflammation and adverse birth outcomes, but these effects are not well-studied in humans. This study aimed to investigate relationships between concentrations of 8 phenols and 3 parabens with 4 inflammatory biomarkers (C-reactive protein (CRP), matrix metalloproteinase-9 (MMP-9, 2, and 9), intercellular adhesion molecule-1 (ICAM-1)) and vascular cell adhesion molecule-1 (VCAM-1)) measured at two time points in pregnancy in the PROTECT birth cohort in Puerto Rico. Linear mixed models were used, adjusting for covariates of interest. Results are expressed as the percent change (95% confidence interval (CI)) in inflammatory biomarkers per interquartile range increase in urinary chemical concentrations. Bisphenol A (BPA) was associated with increases in CRP (% change = 11.2; CI: −0.92, 24.0) and intercellular adhesion molecule-1 (ICAM-1; % change = 3.26; CI: 0.26, 6.35). However, significant positive associations were also detected for metabolites of BPA (MMP-9 (17.1%; 95 % CI: 5.67, 29.48) and methyl paraben and MMP-2 (10.76%; 95 % CI: 2.27, 20.11)). Significant interactions with female fetal sex and the later study visit (at 26–28 weeks gestation) showed more positive associations compared to male fetal sex and the earlier study visit (12–16 weeks gestation). Our results suggest that phenols and parabens may disrupt inflammatory processes pertaining to uterine remodeling and endothelial function, with important implications for pregnancy outcomes. More research is needed to further understand maternal inflammatory status in an effort to improve reproductive and developmental outcomes.	Sci Total Environ. 2024 Apr 15:921:170889.	10.1016/j.scitotenv.2024.170889	38360311	ヒト	免疫	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0167	K. Strammer, J. L. Lycke, S. J. Motta, M. H. B. M. Uller, E. M. Blakstad, K. Boeke, A. E. Sakhi, C. Thomsen, B. Nakstad, A. E. Rønnestad, C. A. Drevon and P. O. Iversen	2022	Estimated daily intake of phthalates, parabens, and bisphenol A in hospitalised very low birth weight infants	Very low birth weight infants (VLBW, birth weight (BW) < 1500 g) are exposed to phthalates, parabens, and bisphenol A (BPA) early in life. We estimated daily intake (EDI) of these exposants in 60 VLBW infants the first and fifth week of life while hospitalised. Repeat urinary samples collected in 2015, EDI were calculated and compared to the tolerable daily intake (TDI) with hazard quotients (HQs) evaluated. A HQ > 1 indicates that EDI exceeded TDI with increased risk of adverse health effects. EDI was higher in VLBW infants compared to term infants and older children. VLBW infants born at mat gestational age (GA), or with lower BW, had higher EDI of DEHP, DBP, DiBP, BPA, and propylparaben (PrPa). EDI of DEHP, DBP, DiBP, BPA, and PrPa were higher in week 1 than week 5. HQ > 1 was found for DEHP and DiBP. DEHP + DiBP + DnBP, or a dual phthalate (DnBP, DiBP and di-iso-octyl phthalate (DiNP)) > 2.58xDiBP+DnBP+DEHP+DiNP, and in 50% of infants for propylparaben (PrPa), indicating increased risk of adverse effects. If this week EDI remained higher than TDI in all infants for BPA, in 75% for DEHP and 2.58xDiBP+DnBP+DEHP+DiNP, and 25% of infants for PrPa, indicating prolonged risk. Maximum EDI for di- iso-butyl phthalate was higher than TDI suggesting risk of adverse effects at maximum exposure. VLBW infants born earlier than 28 weeks GA had higher EDI, above TDI, for PrPa compared to infants born later than 28 weeks GA. Infants with low serum oxyphenisatrin (LOS) had higher EDI for DEHP, 2.58xDnBP+DiBP+DEHP+DiNP and BPA, above TDI, compared to infants achieving LOS. More 75% of the infants' EDI for DEHP and 2.58xDnBP+DiBP+DEHP+DiNP, 25% for PrPa, and 100% of infants' EDI for BPA, were above TDI resulting in HQs > 1, indicating increased risk of adverse health effects.	Chemosphere. 2022 Dec;309(Pt 1):136687.	10.1016/j.chemosphere.2022.136687	36206919	ヒト	生殖発生	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で排除に基づく排除。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については1100mM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0168	K. Stanmore, J. L. Lycha, S. J. Motta, M. H. B. M Ulhe, E. W. Blakstad, A. N. Alinaas, A. K. Satri, C. Thomsen, B. Nakstad, A. E. Rønnestad, C. A. Drevon and P. O. Iversen	2021	High urinary concentrations of parabens and bisphenol A in very low birth weight infants	Very low birth weight infants (VLBW; birth weight < 1500 g) are treated with pharmaceuticals and medical equipment containing parabens and bisphenol A (BPA). Parabens are used in pharmaceuticals, whereas BPA is medical equipment where concentrations are rarely reported in hospitalized VLBW infants. We measured urinary concentrations of parabens and BPA and hypothesized high and increasing concentrations in infants born extremely preterm (EPT; gestational age (GA) < 28 weeks) compared to infants born moderately preterm (MPT; GA 28–32 weeks) and near-term (NT; GA 33–36 weeks). Urine samples were collected during the first (n = 38) and 4th (n = 36) week of life. Methylparaben, ethylparaben, propylparaben, butylparaben, and BPA concentrations were measured using ultra high-performance liquid chromatography coupled to tandem mass spectrometry. VLBW infants had very high urinary concentrations of parabens and BPA compared to term infants and older children. The 3 paraben concentrations are higher than detected in previous studies on premature infants. Lower GA at birth was associated with higher concentrations of parabens and BPA. Infants born below 28 weeks GA had higher first week concentrations of propylparaben (38.6 % (95 % CI: 9.59 ng/mL, p = 0.007), butylparaben (52.8 % (95 % CI: 10.9 ng/mL, p = 0.06) and fifth week concentrations of BPA (19.1 % (95 % CI: 4.02 ng/mL, p = 0.02) than infants born after 28 weeks GA. Infants with LOS and BPD had higher fifth week concentrations of BPA than infants without LOS and BPD (0.05 (0.2 to -8.77 ng/mL, p = 0.07) BPD (8.6 to -7.02 ng/mL, p = 0.05).	Chemosphere Vol.271 Pages 129570	10.1016/j.chemosphere.2021.129570	33453489	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0169	T. P. Stein, M. D. Schluter, R. A. Steer and X. Ming	2023	Bisphenol-A and phthalate metabolism in children with neurodevelopmental disorders	BACKGROUND: The etiology of autism spectrum (ASD) and Attention Deficit Hyperactivity (ADHD) disorders are multifactorial. Epidemiological studies have shown associations with environmental pollutants, such as plasticizers. This study focused on two of these compounds, the Bisphenol A (BPA) and Diethylhexyl Phthalate (DEHP). The major pathway for BPA and DEHP excretion is via glucuronidation. Glucuronidation makes insoluble substances more water-soluble allowing for their subsequent elimination via urine. PTPRT/PTK7/SLITRK5 Glucuronidation of these two plasticizers is compromised in children with ASD and ADHD. Consequently, their tissues are more exposed to these two plasticizers. METHODS: We measured the efficiency of glucuronidation in three groups of children, ASD (n = 66), ADHD (n = 38) and healthy controls. (CTRL n = 37). The children were between the ages of 3 and 16 years old. Glucuronidation efficiencies for BPA and DEHP were calculated by measuring the ratio between the parent plasticizer and its glucuronide derivative. We used these ratio values for the efficiency of glucuronidation for 12 varied glucuronidation pathways including those for BPA and MEHP. RESULTS: (1) Both BPA and MEHP glucuronidation showed that the three groups of children were statistically different from each other. (2) Of the 12 pathways examined, only the BPA and MEHP pathways discriminated between the three groups. (3) Glucuronidation efficiencies for BPA were reduced by 13.1% in ASD (p < 0.025) and 17% for ADHD (p<0.001) compared to controls. DEHP-glucuronidation, but not significant levels. CONCLUSION: ASD and ADHD are clinically and metabolically different but share a reduction in the efficiency of detoxification for both BPA and DEHP with the reductions for BPA being statistically significant.	PLoS One Vol.18 Issue 9 Pages e0289841	10.1371/journal.pone.0289841	37703261	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0170	L. Stecca, I. Moscoso-Ruiz, Y. Gálvez-Ontiveros and A. Rivas	2022	Association between dietary exposure to bisphenols and body mass index in Spanish schoolchildren	The increase in children obesity worldwide has been of particular concern in recent decades. Environmental factors have been proposed as contributors to obesity, and there is a growing concern over obesogens, environmental chemicals with potential obesity-related endocrine disrupting properties. In this regard, bisphenol A (BPA) and its analogues are suspected to have obesogenic properties. Current document report on the activities of the latest, undertaken during the fourth, 2020-2021 cycle of the EU-COSI programme at the University of Granada, Institute of Nutrition and Food Science, in Spain. The work programme offered by the hosting site was related to the extrapolation of bisphenols exposure following the determination of these compounds in food frequently consumed by children and in the diet of children. The follow- ups were planned for the recruitment of the study population in the health centres. In addition, she has participated in the collection of the children biological samples, anthropometric measurements and dietary surveys and in the optimization of the laboratory methodology for the extraction of bisphenols, in biological samples. All these activities also provided the fellow an opportunity to develop her data science-related skills, which will benefit her professional development. In addition, the fellow gained an overview of various topics related to food safety risk assessment by attending the EU-FORA dedicated training modules.	EFSA J. 2022 May 25;20(Suppl 1):e200421.	10.2903/j.efsa.2022.e200421	35634546	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0171	A. Soundararajan, P. Prabu, V. Mohan, Y. Gibert and M. Balasubramanyam	2019	Novel insights of elevated systemic levels of bisphenol-A (BPA) linked to poor glycemic control, accelerated cellular senescence and insulin resistance in patients with type 2 diabetes	There is a striking interaction of genes and environment in the etiology of type 2 diabetes mellitus (T2DM). While endocrine disrupting chemicals (EDCs) like bisphenol-A (BPA) have received special attention for their mechanistic role in metabolic dysregulation, there is a lack of clinically relevant data on BPA levels in Asian Indians, a population which is more susceptible to type 2 diabetes mellitus (T2DM) and cardiovascular diseases. Therefore, we measured systemic levels of BPA in patients with T2DM compared to individuals with normal glucose tolerance (n = 50 each). Serum BPA levels were estimated using ELISA kit, and biochemical determinations were done by standard protocols. Peripheral blood mononuclear cells (PBMCs) were used to profile the gene expression alterations, with special reference to inflammation, estrogen receptors, and cellular senescence in these subjects. Serum levels of BPA were significantly higher in patients with T2DM compared to control individuals and positively correlated to poor glycemic control and insulin resistance. Patients with T2DM showed significantly higher expression of pro-inflammatory genes (TNF-α, IL-6, and MCP-1) in PBMCs, which positively correlated with BPA levels. Interestingly, the expression of estrogen receptor gamma (ERR-γ), a recently identified receptor for BPA, BPA levels were positively correlated to senescence indicators, inflammatory markers and ERR-γ and negatively correlated to telomere length. Our study is the first data in the clinical diabetic setting to demonstrate an association of increased BPA levels with cellular senescence, proinflammation, poor glycemic control, insulin resistance, and shortened telomeres in patients with T2DM.	Mol Cell Biochem. 2019 Aug;458(1-2):171-183.	10.1007/s11010-019-03540-9	31004310	ヒト	代謝	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0172	A. M. Soto, C. M. Schaeberle and C. Sonnenschein	2025	Development gone awry: Fetal exposure to bisphenol A and cancer		Ann Endocrinol (Paris). 2025 Jun;86(3):101786.	10.1016/j.ando.2025.101786	40446628	ヒト	発がん	-	-	-	-	-	-	-	Editorial	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0173	M. H. Saxena, G. England-Mason, A. J. F. Reardon, J. Liu, A. M. MacDonald, D. M. Kinniburgh, J. W. Martin and D. Dewey	2024	Maternal exposure to bisphenols, phthalates, perfluoroalkyl acids, and trace elements and their associations with gestational diabetes mellitus in the APrON cohort	The increasing global prevalence of gestational diabetes mellitus (GDM) has been hypothesized to be associated with maternal exposure to environmental chemicals. Here, among 526 women participating in the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort study, we examined associations between GDM and urine concentrations of endocrine disrupting chemicals (EDCs): bisphenol A (BPA), bisphenol S (BPS), twelve phthalate metabolites, eight perfluoroalkyl acids (PFAAs), and eleven trace elements. Fifteen (3.0%) of the women were diagnosed with GDM, and associations between the environmental chemicals and GDM were investigated using multivariable logistic regression models. Urine samples were collected in the second trimester (median = 26.1 weeks gestation) and first morning voids were analyzed. Women with GDM had higher urinary concentrations of BPA (GDM: 1.3 ng/mL, IQR: 0.6, 2.1; CONTROL: 0.8 ng/mL, IQR: 0.4, 1.5; p = 0.009), BPS (GDM: 0.2 ng/mL, IQR: 0.1, 0.4; CONTROL: 0.1 ng/mL, IQR: 0.0, 0.2; p = 0.008), and perfluorooctanoic acid (PFOA) (GDM: 1.1 ng/mL, IQR: 0.7, 1.6; CONTROL: 0.8 ng/mL, IQR: 0.5, 1.2; p = 0.04). The combined risk for the Canadian cohort suggest that second trimester blood mercury was a robust predictor of GDM diagnosis, whereas blood zinc and PFOA risk were protective factors. Research into mechanisms that underlie the associations between mercury, zinc, PFOA, and the development of GDM is needed.	Reprod Toxicol Vol.127 Pages 108612	10.1016/j.reprotox.2024.108612	38782143	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0174	X. Song, X. Zhou, F. Yang, H. Liang, Z. Wang, R. Li, M. Miao and W. Yuan	2020	Association between prenatal bisphenol a exposure and promoter hypermethylation of CAPS2, TNFRSF25, and HKR1 genes in cord blood	In utero exposure to bisphenol A (BPA) in early stages of development has been reported to exert adverse health effects as offspring later in life. Epigenetic alterations, particularly DNA methylation, may be one plausible biological mechanism involved. We examined the association between maternal BPA exposure and DNA methylation in cord blood. We randomly selected 96 paired samples of maternal urine and infant cord blood collected from the Shanghai Minhang Birth Cohort. BPA levels in maternal urine were measured using high-performance liquid chromatography (HPLC). Three cord blood samples with maternal BPA levels <2.0 μg/g Cr and three samples with undetected BPA were combined to generate wide methylation analysis using methylated DNA binding domain sequencing (MBD-Seq). Thirty genes with hypermethylated promoter regions were chosen for validation using quantitative methylation-specific polymerase chain reaction (Q-MSP). Based on MBD-seq results, we observed that maternal BPA exposure was primarily associated with hypermethylation of genes in cord blood. Validation of 30 genes revealed that CAPS2, TNFRSF25, and HKR1 were significantly hypermethylated in the high-BPA group. Hypermethylation of these genes was confirmed in an additional 90 paired samples. Multiple regression models using each increase in BPA was associated with 0.26% (95%CI: 7.1%, 17.1%), 19% (95%CI: 3.1%, 37.6%), and 14.5% (95% CI: 0.1%, 31.6%) increase in promoter of CAPS2, TNFRSF25, and HKR1 methylation, respectively. Our findings provide evidence that in utero exposure to BPA could alter the offspring's epigenome by altering DNA methylation pattern.	Environ Res. 2020 Nov;190:109996.	10.1016/j.envres.2020.109996	32763279	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0175	X. Song, Z. Wang, Z. Zhang, M. Miao, J. Liu, M. Luan, J. Du, H. Liang and W. Yuan	2021	Differential methylation of genes in the human placenta associated with bisphenol A exposure	Prenatal exposure to bisphenol A (BPA) is associated with numerous adverse health outcomes among offspring. Although DNA methylation is considered one of the underlying causes of these associations, few studies have focused on the association between prenatal BPA exposure and DNA methylation in the human placenta. In this study, we examined the association between prenatal BPA exposure and DNA methylation in the placenta of 116 mother–infant pairs from the Shanghai Minhang Birth Cohort Study. BPA concentrations in maternal urine samples were measured using high-performance liquid chromatography. The placenta samples were selected for whole-genome methylation analysis using Infinium HumanMethylation 850K BeadChip, followed by pyrosequencing-based methylation analysis of three selected genes in 116 placentas. Among 392 differentially methylated CpG sites (DMCs) identified between the high- and low-BPA groups, 382 DMCs were hypermethylated in the high-BPA group. Pyrosequencing validated the DMRs in individuals as determined using pyrosequencing, which was consistent with the whole-genome methylation analysis results. Compared with their subjects with low BPA exposure, the methylation level (re-transformed) of HLA-DRB6 in placentas from those with high BPA exposure increased by 0.29% (95% confidence interval [CI]: 0.07%, 0.50%) at the CpG site, and the average methylation level (re-transformed) of the three CpG sites increased by 0.26% (95%CI: -0.05%, 0.55%). Our findings provide evidence that prenatal BPA exposure might alter DNA methylation levels in the placenta.	Environ Health. 2021 Sep;20(1):60.	10.1186/s12940-021-00747-6	34089743	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0176	C. M. Sol, C. van Zeel-Janssen, E. M. Philips, A. G. Asimakopoulos, M. P. Martinez-Moral, K. Kannan, V. W. V. Jaddoe, L. Trasande and S. Santos	2021	Maternal bisphenol urine concentrations, fetal growth and adiverse birth outcomes: A population-based prospective cohort	BACKGROUND: Exposure to bisphenols may affect fetal growth and development. The trimester-specific effects of bisphenols on repeated measures of fetal growth remain unknown. Our objective was to examine the associations of maternal bisphenol urine concentrations with fetal growth measures and birth outcomes and identify potential critical exposure periods. METHODS: In a population-based prospective cohort study among 1279 pregnant women, we measured maternal bisphenol A, S and F urine concentrations in the first, second and third trimester. Fetal head circumference, length and weight were measured in the second and third trimester by ultrasound and at birth. RESULTS: An interquartile range increase in maternal pregnancy averaged bisphenol S concentrations was associated with larger fetal head circumference (difference 0.20 SD; 95% confidence interval (CI) 0.04, 0.36), length (0.19 SD; 95% CI 0.03, 0.35) and weight (0.19 SD; 95% CI 0.03, 0.35) at birth. Bisphenol S concentrations in the second trimester were associated with larger fetal head circumference (difference 0.14 SD; 95% CI 0.01, 0.27) and length (0.14 SD; 95% CI 0.01, 0.27) at birth. Bisphenol S concentrations in the third trimester were associated with larger second and third trimester fetal head circumference (difference 0.14 (95% CI 0.01 to 0.26 and 0.13 (95% CI 0.01 to 0.25) SDS, respectively) and fetal weight (difference 0.12 (95% CI 0.01 to 0.23) and 0.13 (95% CI 0.01 to 0.25) SDS, respectively). The other bisphenols were not consistently associated with fetal growth outcomes. Any detection of bisphenol S and bisphenol F in first trimester was also associated with a lower risk of being born small size for gestational age (Odds Ratio 0.58 (95% CI 0.38 to 0.72) and 0.53 (95% CI 0.34 to 0.80), respectively). Bisphenols were not associated with risk of preterm birth. CONCLUSIONS: Higher maternal bisphenol S urine concentrations, especially in the first trimester, seem to be related with larger fetal head circumference, higher weight and a lower risk of being small size for gestational age at birth.	33992119	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0177	C. M. Sol, S. Santos, L. Duijts, A. G. Asimakopoulos, M. P. Martinez-Moral, K. Kannan, E. M. Philips, L. Trasande and V. W. V. Jaddoe	2020	Fetal exposure to phthalates and bisphenols and childhood general and organ fat. A population-based prospective cohort study	OBJECTIVES: Fetal exposure to phthalates and bisphenols might have long-lasting effects on growth and fat development. We could to know about the effects on general and organ fat development in childhood. We examined associations of maternal phthalate and bisphenol urine concentrations during pregnancy with childhood general and organ fat measures. METHODS: In a population-based prospective cohort study among 1,279 pregnant women, we measured maternal urinary phthalate metabolites and bisphenol concentrations in first, second, and third trimester. Offspring body mass index, fat mass, total body lean mass, total body bone mass, total body fat mass (dual-energy X-ray absorptiometry), and visceral and pericardial fat indices and liver fat fraction were measured by magnetic resonance imaging at 10 years. RESULTS: After adjustment for confounders and correction for multiple testing, an interquartile range increase in first trimester urinary concentrations of mono-(3-carboxypropyl) phthalate (MCPP) was associated with lower childhood visceral fat index (-0.12 SD; 95% confidence interval (CI) -0.21, -0.03). Associations of higher maternal low-molecular-weight phthalate urinary concentrations in second trimester with childhood pericardial fat index, but these were not significant after adjustment for multiple testing. High molecular-weight phthalate, di-2-ethylhexyl phthalate, and di-n-octyl phthalate concentrations were not associated with childhood outcomes. Maternal urinary bisphenol concentrations were not associated with childhood adiposity. CONCLUSIONS: Maternal first trimester phthalic acid concentrations are associated with increased childhood pericardial fat index at 10 years of age, whereas maternal bisphenol concentrations are not associated with childhood adiposity. We did not find significant sex-specific effects. These findings should be considered as hypothesis-generating and need further replication and identification of underlying mechanisms.	Int J Obes (Lond). 2020 Nov;44(11):2225-2235.	10.1038/s41366-020-00672-7	32920592	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0178	C. M. Sol, S. Santos, A. G. Asimakopoulos, M. P. Martinez-Moral, L. Duijts, K. Kannan, L. Trasande and V. W. V. Jaddoe	2020	Associations of maternal phthalate and bisphenol urine concentrations during pregnancy with childhood blood pressure in a population-based prospective cohort study	OBJECTIVES: Fetal exposure to phthalates and bisphenols may lead to vascular developmental adaptations, which program later cardiovascular disease. We examined the associations of fetal exposure to phthalates and bisphenols with childhood blood pressure. METHODS: In a population-based prospective cohort study among 1,063 mother-child pairs, we measured maternal urine phthalate and bisphenol concentrations in first, second, and third trimester. Systolic and diastolic blood pressure were measured at the age of 6 years. We used multivariable linear regression models. RESULTS: Maternal urinary concentrations of mono-(3-carboxypropyl) phthalate (MCPP) were associated with lower systolic blood pressure at 6 years (-0.22 SD; 95% confidence interval (CI) -0.39, -0.05) and diastolic blood pressure (-0.21 SD; 95% CI -0.38, -0.04). Higher maternal second trimester urinary concentrations of mono-(2-ethylhexyl) phthalate (MEHP) were associated with lower systolic and diastolic blood pressure among girls (p-values < 0.05). Also, higher second trimester maternal urine total bisphenol and bisphenol S concentrations were associated with higher systolic blood pressure among boys (p-values < 0.01), but tended to be associated with a lower diastolic blood pressure among girls. CONCLUSIONS: Our results suggest sex-dependent associations of maternal urine phthalate and bisphenol concentrations during pregnancy with childhood blood pressure. Further studies are needed to explore the underlying mechanisms and long-term consequences.	Environ Int. 2020 May;138:105677.	10.1016/j.envint.2020.105677	32220816	ヒト	心血管	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0179	C. M. Sol, A. Gaylord, S. Santos, V. W. V. Jaddoe, J. F. Felix and L. Trasande	2022	Fetal exposure to phthalates and bisphenols and DNA methylation at birth: the Generation R Study	BACKGROUND: Phthalates and bisphenols are non-persistent endocrine disrupting chemicals that are ubiquitously present in our environment and may have long-lasting health effects following fetal exposure. A potential mechanism underlying these exposure-outcome relationships is differential DNA methylation. Our objective was to examine the associations of maternal phthalate and bisphenol concentrations during pregnancy with DNA methylation at birth. METHODS: In a population-based prospective cohort study among 1,279 pregnant women, we measured maternal urinary phthalate and bisphenol concentrations in first, second and third trimester. We measured DNA methylation in cord blood at birth using the Illumina Infinium HumanMethylation450 BeadChip and pre-engineered multi-associative approach. Using assembly computation, we examined the association of increasing all mixture components by one quartile with controlled DNA methylation. RESULTS: We did not find evidence for statistically significant associations of a maternal mixture of phthalates and bisphenols during any of the trimesters of pregnancy with DNA methylation in cord blood (all p-values > 0.01 * 10-4). However, we identified one suggestive association (p-value = 1.3 * 10-4) of the first trimester maternal mixture of phthalates and bisphenols and three suggestive associations of the second trimester maternal mixture of phthalates and bisphenols with DNA methylation in cord blood. CONCLUSIONS: Although we did not identify genome-wide significant results, we identified some suggestive associations of exposure to a maternal mixture of phthalates and bisphenols in the first and second trimester with DNA methylation in cord blood that need further exploration in larger study samples.	Clin Epigenetics. 2022 Oct 10;14(1):125.	10.1186/s13148-022-01345-0	36217170	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0180	A. R. Smith, K. R. Kogut, K. Parra, A. Bradman, N. Holland and K. G. Harley	2022	Dietary intake and household exposures as predictors of urinary concentrations of high molecular weight phthalates and bisphenol A in a cohort of adolescents	BACKGROUND: Phthalates and bisphenol A (BPA) are endocrine disrupting chemicals used in consumer products, building materials, and food processing and packaging materials. They are associated with adverse health outcomes, especially when exposure occurs during heightened windows of vulnerability. OBJECTIVE: We evaluated the relationship between housing and dietary characteristics and the concentrations of several high molecular weight (HMW) phthalate metabolites and BPA in a cohort of Latina adolescents. METHODS: We collected information on recent food consumption and housing characteristics and quantified the concentration of HMW phthalate and BPA metabolites in urine collected at two different time points. We used generalized estimating equations (GEE) to assess predictors of each metabolite. RESULTS: In significant associations were observed between housing and dietary characteristics and metabolites of di(2-ethylhexyl) phthalate (DEHP) or BPA. In contrast, higher urinary monobenzyl phthalate (MBzP) concentration was associated with consuming fast food (β = 0.26; 95% CI: 0.03, 0.49) and canned soup (β = 0.23; 95% CI: 0.01, 0.45) in the previous 24 hours. Higher concentration of sulfur (ΔS.CR; change: p-value <0.01), and had lead (Δ0.1b; change: p-value <0.05). DISCUSSION/CONCLUSION: These findings may be useful in targeting interventions that reduce phthalate uptake in young adults.	J Expo Sci Environ Epidemiol Vol.32 Issue 1 Pages 37-47	10.1038/s41370-021-00305-9	33619365	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0181	M. Sladić, S. Smrkulj, G. Kavšek, S. Imamović-Kumalić, I. Vierdenk and I. Vivanti-Klun	2025	Bisphenol A in the Urine: Association with Urinary Creatinine, Impaired Kidney Function, Use of Plastic Food and Beverage Storage Products but Not with Serum Anti-Müllerian Hormone in Ovarian Malignancies	Bisphenol A (BPA) is a high-production-volume industrial chemical and component of commonly used plastic products. However, it is also an endocrine-disrupting chemical that can negatively affect human health. It is not yet known whether it is associated with the development of epithelial ovarian cancer (EOC), a severe and highly fatal human disease. Therefore, the purpose of this study was to determine the concentrations of BPA in the urine of patients with EOC and to investigate the relationship between BPA and the clinicopathological characteristics of EOC. Urine samples were collected from 100 patients with EOC and 100 healthy control subjects. Using a questionnaire, we collected sociodemographic, lifestyle, and clinical data, including information on BPA exposure sources. Urinary BPA concentrations were measured by high-performance liquid chromatography with fluorescence detection (HPLC-FLD). Creatinine (CRE) was measured using a colorimetric assay, and urinary BPA concentrations were normalized to CRE levels to account for variations in urine dilution. Serum anti-Müllerian hormone (AMH) levels were measured using an enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed to assess differences in BPA concentrations between EOC patients and healthy controls, as well as associations between BPA exposure and clinicopathological characteristics of EOC. Urinary BPA concentrations were significantly higher in EOC patients than in healthy controls ($p < 0.001$). Multivariate logistic regression analysis revealed that urinary BPA concentration was significantly associated with EOC risk (OR = 1.003, 95% CI: 1.001–1.005, $p = 0.001$). Additionally, urinary BPA concentrations were significantly correlated with serum AMH levels ($p = 0.001$), suggesting a potential relationship between BPA exposure and ovarian reserve. However, no significant associations were observed between urinary BPA concentrations and clinicopathological characteristics, including tumor stage, histological grade, or lymph node metastasis. These findings suggest that BPA exposure may be associated with EOC risk and ovarian reserve, but its role in disease progression remains unclear. Further prospective studies with larger cohorts are needed to validate these findings and explore potential mechanisms underlying the observed associations.	Int J Mol Sci Vol.26 Issue 10	10.3390/ijms26104811	40429952	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0182	J. Skarha, C. Messerlian, D. Ballinger, L. Miguez-Alarcón, M. E. Romano, J. B. Ford, P. L. Williams, A. M. Calafat, R. Hauser and J. M. Braun	2020	Parental preconception and prenatal urinary bisphenol A and paraben concentrations and child behavior	Epidemiologic studies suggest that prenatal urinary bisphenol A (BPA) concentrations are associated with childhood behavior problems, but there is limited research on prenatal paraben concentrations. In rodent offspring, preconception maternal BPA exposure caused behavioral problems, and paraben exposure impacted sperm quality. However, the effects of parental preconception and prenatal BPA and paraben exposure on neurobehavioral outcomes in children are unknown. We measured urinary concentrations of BPA, methyl paraben (MeP), and butyl paraben (BuP) in 2,000 pregnant women in the Centers for Disease Control and Prevention (CDC)-supported BPA, Exposures, Lifestyles, and Kids (BEAK) 3 study and preconception concentrations in multiple urine samples collected before conception and during pregnancy. From the eligible parents (N = 226), we enrolled 136 children between 2 and 5 years of age. The parents completed the Behavior Assessment System for Children-3 (BASC-3); this estimated covariate-adjusted associations between average parental preconception and prenatal (a-transformed) urinary BPA and sum of paraben concentrations (1-parabens) with BASC-3 scores using linear regression and generalized estimating equations. RESULTS: Median urinary BPA and 2 paraben concentrations were 2.2 and 288 μg/L in mothers preconception and 1.7 and 29 μg/L in fathers preconception, respectively. Among all children, parental BPA and 2 paraben concentrations were not associated with BASC-3 scores. However, among children whose mothers had urinary BPA concentrations above the median, a 10% increase in maternal BPA was associated with a 0.2 unit (95% CI: 0.1, 0.3) increase in the hyperactivity subscale. Among children whose mothers had urinary BPA concentrations below the median, a 10% increase in maternal BPA was associated with a 0.1 unit (95% CI: −0.2, 0.3) decrease in the hyperactivity subscale. CONCLUSIONS: In this healthy clinic cohort, parental preconception and maternal prenatal BPA and paraben concentrations were not associated with problem behaviors among children. However, our small sample sizes reduced the precision of our results.	Environ Epidemiol Vol.4 Issue 1 Pages e082	10.1097/ee9.0000000000000082	33778347	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0183	D. Sirohi, R. Al-Ramadhani and L. D. Kridits	2021	Environmental exposures to endocrine disrupting chemicals (EDCs) and their role in endometriosis: a systematic literature review	PURPOSE: Endocrine related diseases and disorders are on the rise globally. Synthetically produced environmental chemicals (endocrine disrupting chemicals (EDCs)) mimic hormones like oestrogen and alter signalling pathways. Endometriosis is an oestrogen dependent condition, affecting 10-15% of women of the reproductive age, and has substantial impacts on the quality of life. The aetiology of endometriosis is believed to be multifactorial, and the role of environmental factors is unclear. The purpose of this review is to systematically review the literature on the association between exposure to EDCs and the development of endometriosis. We also aimed to assess a public on the relationship between body concentrations of EDCs and the severity of endometriosis. METHOD: Following PRISMA guidelines, a structured search of PubMed, Embase and Scopus was conducted for July 2020. The included studies analysed the association between one or more EDCs and the prevalence of endometriosis. The types of EDCs, association and outcome, participant characteristics and confounding variables were extracted and analysed. Quality assessment was performed using standard tools. RESULTS: A total of 29 studies were included. Phthalate esters were positively associated with the prevalence of endometriosis. The majority (72%) of studies revealed a significant association between bisphenol A, organochlorinated environmental pollutants and the prevalence of endometriosis. Dioxin/polychlorinated biphenyls (PCB) exposure was found to be associated with endometriosis in 50% of the studies. Polybrominated biphenyls was demonstrated in one study only. Cadmium, lead and mercury were not associated with the prevalence of endometriosis. There were conflicting results for the association between retinol and endometriosis. The relationship of EDCs and severity of endometriosis was not established in the studies. CONCLUSION: We found some evidence to suggest an association between phthalate esters, bisphenol A, organochlorinated environmental pollutants and the prevalence of endometriosis. Disentangling these exposures from various other factors that affect endometriosis is complex, but an important topic for further research.	Rev Environ Health Vol.36 Issue 1 Pages 101-115	10.1515/reveh-2020-0046	32903210	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0184	M. Šimková, J. Vítků, L. Kolátorová, J. Vrbíková, M. Vosáhlová, J. Vítník and M. Duškov	2020	Endocrine disruptors, obesity, and cytokines - how relevant are they to PCOS?	As environmental and genetic components contribute to the PCOS expression, we compared levels of endocrine disruptors, steroid hormones, cytokines, and metabolic parameters. In lovely healthy, nine-normal weight PCOS women, and ten obese PCOS women. Steroid hormones, bisphenols (BPA, BPS, BPF, BPAF) and parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-paraben) were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Cytokines were measured by Luminex multiplex assay. Metabolic parameters were measured by standard methods. Results: Free androgen index, testosterone, DHEA-S, BPA, and Aldosterone hormone, Estradiol, Estrone and Estriol were significantly higher in obese PCOS women than in lean PCOS women. BPS

別添-2　統合文献リスト

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別添-2 統合文献リスト

通格性評価（動物）1：該当、0：該当しない

通格性評価（疫学）1：該当、0：該当しない

通格性評価（in vitro）1：該当、0：該当しない

通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で排除に基づき排除。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0207	S. Schmidt	2022	Bisphenol A and Child Vascular Health: A Preview of Future Heart Disease Risk?		Environ Health Perspect. 2022 Jun;130(6):64003.	10.1289/ehp11498	35727643	ヒト	心血管	-	-	-	-	-	-	Editorial	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0208	A. F. Sanoo, R. Pirow, S. S. Andra, R. Church, R. M. Nachman, S. Linke, D. F. Kapraun, S. H. Schurman, M. Arora, K. A. Thayer, J. K. Bucher and L. S. Birnbaum	2020	Pharmacokinetics of bisphenol A in humans following dermal administration	BACKGROUND: Human exposure to bisphenol A (BPA) are widespread. The current study addresses uncertainties regarding human pharmacokinetics of BPA following dermal exposure. OBJECTIVE: To examine the absorption, distribution, metabolism and excretion of BPA in humans following dermal administration. METHODS: We dermally administered duplicate 0.5 mg BPA/cm 2 to 20 adults (5 men and 5 women) at a dose of 150 cm 2 (75 mg BPA) and 1000 cm 2 (500 mg BPA) on separate occasions. Serial blood and urine samples were collected for 24 h after the start of dosing. Total BPA ("free" + all BPA-conjugates) and unconjugated ("free") all BPA and available information to calculate terminal half-life and area under the curve. RESULTS: AT 1000 CONCLUSIONS: Detectable serum levels of total all BPA were observed at 1.5 h after the start of dosing and a maximum serum concentration (Cmax) of 3.26 nM was observed. Free all BPA was detectable in serum 2.8 h after start of dermal administration, with Cmax of 0.272 nM. Beginning at approximately serum levels and continuing to 12 h (which corresponds to cessation of exposure), the concentration of free and total bisphenol all BPA plateaued. The terminal half-lives of total all BPA and free all BPA in the body were 21.1 ± 10.5 h and 21.8 ± 7.8 h, respectively. Elimination from the body was rate-limited by kinetics in the dermal compartment. Free all BPA was a greater percentage of the area under the curve of total serum BPA (8.26%) compared to oral exposure (0.3%). Urinary excretion accounted for approximately 10% of the dermal dose. CONCLUSIONS: Dermal absorption of BPA is relatively slow and incomplete. Approximately 10% of the dermal dose became systemically available. These data are in line with prior studies indicating how pharmacokinetics of BPA differ following oral and dermal exposures. Dermal exposure resulted in a longer apparent half-life and higher fractional all BPA ratio compared to oral.	Environ Int Vol.144 Pages 106031	10.1016/j.envint.2020.106031	32798798	ヒト	-	-	-	-	-	-	-	臨床暴露試験	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0209	B. Sarco, R. Aburahmah, N. Mavis, S. Llop, A. Iberoula, I. Lopez-Flores, N. Fernes, A. K. Sakki, F. Ballester and M. J. Lopez-Espinosa	2022	Association between phenols and thyroid hormones: The role of iodothyronine deiodinase genes	Previous literature on prenatal phenol exposure and thyroid hormone (TH) alterations is conflicting, and the possible mechanisms of action involved remain unclear. We aimed to examine the association between prenatal exposure to bisphenol A (BPA), bisphenol S (BPS), triclosan (TCS), and benzophenone-3 (BP-3) and TH levels in pregnant women and to explore the role of iodothyronine deiodinase genes. We measurements of maternal phenols, total triiodothyronine (TT3) and free thyroxine (FT4), maternal and neonatal thyroid-stimulating hormone (TSH), and maternal genotypes for single nucleotide polymorphisms. In the GG(rs2235544) and GG(rs2268383) genes. We implemented multivariate linear and weighted quantile sum (WQS) regressions to examine the association between phenols and TH. Including sex-stratified models. BPA was detected in 100% of the samples, BPS in 98%, TCS in 97%, and BP-3 in 94%. Maternal BPA concentrations were associated with lower FT4 levels in the whole population (β = -0.04; 95% CI: -0.08, TH. In sex-stratified models, BPA was associated with lower FT4 levels in boys (WQS: -1.84; 0.05, -0.12) and suicidal phenol increased - stronger for girls - and less clearly for maternal triiodothyronine (FT4) and TSH (-2.27 (-4.56, 0.02). In sex-stratified models, only found an association with TSH. In the genetic interaction models, we found some evidence of effect modification of GG gene polymorphisms with stronger negative associations between methylparaben (MPB), propylparaben (PPB), butylparaben (BPB) and TT3 as well as bisphenol A (BPA) and FT4 for GG(rs12255612). CC. Stronger inverse associations for genotype GG(rs12885300) CC and GG(rs12885300) CT and positive ones for GG(rs12885300) TT were also reported for BPA and FT3. In conclusion, we found some evidence of an association between phenols and TSH during pregnancy and at birth. In single exposure models, the latter being stronger for girls. Since no sexual action was observed between maternal levels of phenols and TT3 or FT4, the possible role of the genetic background in these associations warrants further investigation.	Environ Pollut. 2022 Oct 15;311:119926.	10.1016/j.envpol.2022.119926	35964788	ヒト	生体影響（ヒト・ げっ歯類OHG）	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0210	D. Sarink, A. A. Franke, K. K. White, A. H. Wu, I. Cheng, B. Quon, L. Le Marchand, L. R. Wilkens, H. Yu and M. A. Merritt	2021	BPA, Parabens, and Phthalates in Relation to Endometrial Cancer Risk: A Case-Control Study Nested in the Multiethnic Cohort		Environ Health Perspect. 2021 May;129(5):57702.	10.1289/ehp8998	33950701	ヒト	発がん	-	-	-	-	-	-	nested case-control	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0211	Y. Sanchis, C. Coscollà, F. Copas-Burgos, M. Vento, M. Gormaz and Y. Yusà	2020	Biomonitoring of bisphenols A, F, S and parabens in urine of breastfeeding mothers: Exposure and risk assessment	In the present study we used human biomonitoring to assess the internal exposure and the risk to two parabens, and three bisphenols in 150 Spanish breastfeeding mothers participating in the BETTERMILK project. Samples were collected in 2017 and analysed by UPLC-MS/MS. Bisphenol A (BPA) was detected in 100% of the samples, bisphenol F (BPF) in 97% and bisphenol S (BPS) in 93%. Methylparaben (MPB) and propylparaben (PPB) were found in 99% and 95% of the samples, respectively. Geometric mean concentrations (GM) were 0.61 ng/mL for BPA, 0.39 ng/mL for BPF, 0.09 ng/mL for BPS, 2.2 ng/mL for MPB and 0.37 ng/mL for PPB. Estimated daily intakes (EDI) were calculated in order to interpret urinary levels in a risk assessment context. The obtained EDIs ranged from 0.0003 ng/kg bw/d for PPB to 0.830 ng/kg bw/d for BPF and BPA. Exposure to BPA, the estimated daily intakes (EDI) were calculated in order to interpret urinary levels in a risk assessment context. The obtained EDIs ranged from 0.0003 ng/kg bw/d for PPB to 0.830 ng/kg bw/d for BPF and BPA. A hazard quotient (HQ) was calculated for BPA (0.0008) and parabens (0.002-0.005), showing no risk to the studied population. Sociodemographic characteristics, food consumption, and usage patterns of personal care products (PCPs) were investigated as possible determinants of exposure. Use of makeup and skincare products were associated with higher concentrations of BP and PP, respectively. Regarding dietary habits, BPF was also associated with the consumption of packaged and bakery products.	Environ Res Vol.185 Pages 109481	10.1016/j.envres.2020.109481	32278926	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0212	E. Salamanca-Fernández, F. Vela-Soria, M. Rodríguez-Barranco, A. Arrebola-Moreno, L. M. Iribarne-Durán, N. Olea, M. J. Sánchez and J. P. Arrebola	2021	Serum levels of non-persistent environmental pollutants and risk of incident hypertension in a sub-cohort from the EPIC study	BACKGROUND: The prevalence of arterial hypertension (HYT), a well-known risk factor for cardiovascular disease, has considerably increased over last decades. Non-persistent environmental pollutants (nsPYs) are a group of ubiquitous chemicals, widely used in consumer products such as food packaging and cosmetics, which have been identified as endocrine disrupting chemicals and oestrogens. The aim of this study was to assess the potential associations of serum levels of three groups of nsPYs with the risk of incident HYT. METHODS: Cohort study within a sub-cohort of Granada EPIC-Spain center (n = 476). We quantified serum concentrations of 2 phenols (BPA and BP-3), 4 parabens (MeP, EtP, PrP and BuP) and 3 phthalate metabolites (MEP, MBP and MBzP) in 476 participants (cases = 238; controls = 238), matched by sex, age (± 1 year), menopause (in women) and recruitment date (± 1 year). A complete collection of anthropometric, lifestyle and dietary information was performed by means of Cox Proportional Hazard Models. RESULTS: The Median follow-up time was 20 years. BPA and MeP were found in >80% of the study population. Individuals within the 4th PP quartile (5.03-52.5 ng/ml) showed a statistically significant increased risk of HYT (HR = 1.45, p = 0.015). No associations were found for the rest of pollutants. CONCLUSIONS: Overall, our evidenced no associations of most nsPYs with HYT risk, with the exception of an increased risk in the highest PP percentiles. Considering the limitations of using non-spot serum samples for exposure characterization, further research on the potential contribution of nsPYs on the development of HYT risk is warranted.	Environ Res. 2021 Feb;193:110491.	10.1016/j.envres.2020.110491	33227247	ヒト	心血管	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0213	E. Salamanca-Fernández, M. Rodríguez-Barranco, D. Petrova, N. Larrañaga, M. Guevara, C. Moreno-Iribas, M. D. Chirlaque, S. Colorado-Yohar, J. P. Arrebola, F. Vela, N. Olea, A. Agudo and M. J. Sánchez	2020	Bisphenol A exposure and risk of ischemic heart disease in the Spanish European Prospective Investigation into cancer and nutrition study	BACKGROUND: Cardiovascular disease, particularly ischemic heart disease (IHD), is the leading cause of mortality worldwide. Bisphenol A (BPA) is considered an endocrine disruptor and obesogen, present in numerous products of daily use. The aim of this study was to assess the potential association of serum BPA concentrations and the risk of incident IHD in a sub-cohort of the Spanish European Prospective Investigation into Cancer and Nutrition (EPIC). METHODS: We designed a case-cohort study within the EPIC-Spain cohort. The population consisted of 2008 participants from 3 EPIC-Spain centers (369 IHD cases and 1646 sub-cohort participants). BPA exposure was assessed by means of chemical analyses of serum samples collected at recruitment. Cox Proportional Hazards Models were used for the statistical analyses. RESULTS: Median follow-up time was 18 years and 75% of the participants showed detectable BPA values (>0.2 ng/ml). Clinical records. Cox Proportional Hazards Models were used for the statistical analyses. RESULTS: Median follow-up time was 18 years and 75% of the participants showed detectable BPA values (>0.2 ng/ml). BPA concentrations were not associated with IHD risk (HR = 1.00; 95% CI: 0.99, 1.01 per 1 ng/ml increase). Stratified analyses by sex, smoking status, and presence of diabetes, showed no significant association of BPA serum levels with IHD, with the exception of obese/overweight participants (HR = 1.02; 95% CI: 1.00, 1.04 per 1 ng/ml increase). CONCLUSIONS: Our findings do not support an association between BPA exposure and IHD risk, with the exception of an obese/overweight subpopulation. We evidenced a similar percentage of detection of BPA among cases and sub-cohort participants from our population, and no dose-association with IHD risk was observed. However, further investigation is needed to understand the influence of BPA on IHD risk.	Chemosphere. 2020 Dec;261:127697.	10.1016/j.chemosphere.2020.127697	32731019	ヒト	心血管	-	-	-	-	-	-	case-cohort	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0214	E. Salamanca-Fernández, M. Rodríguez-Barranco, J. P. Arrebola, F. Vela, C. Díaz, M. D. Chirlaque, S. Colorado-Yohar, A. Jiménez-Zabala, A. Irizar, M. Guevara, E. Ardanaz, L. M. Iribarne-Durán, J. Pérez Del Palacio, N. Olea, A. Agudo and M. J. Sánchez	2020	Bisphenol-A in the European Prospective Investigation into Cancer and Nutrition cohort in Spain: Levels at recruitment and associated dietary factors	Bisphenol A (BPA) is considered an endocrine disruptor and is present in numerous products of daily use. The aim of this study was to analyze serum BPA concentrations in a subcohort of the Spanish European Prospective Investigation into Cancer and Nutrition (EPIC), so as to identify potential predictors of its exposure. The population consisted on 1863 subjects recruited in the EPIC-Spain centers. BPA levels were measured in serum samples by UHPLC-MS/MS. Almost 75% of the participants showed detectable BPA values (>0.2 ng/ml), with a geometric mean of 1.29 ng/ml (95% CI: 1.17-1.24). By sex, detectable percentages were similar in men (74.5%) and women (75.5%). Mean BPA levels were 1.29 ng/ml (95% CI: 1.17-1.24) and 1.29 ng/ml (95% CI: 1.17-1.24) in men and women, respectively. Multivariate linear regression models showed significant associations of BPA serum levels with BMI, and with menopausal status in premenopausal women, but not with educational level or anthropometric risk. CONCLUSIONS: We evidenced a similar percentage of detection of BPA among cases and sub-cohort participants from our population, and no dose-association with IHD risk was observed. However, further investigation is needed to understand the influence of BPA on IHD risk.	Environ Res Vol.182 Pages 109012	10.1016/j.envres.2019.109012	31837551	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0215	E. Salamanca-Fernández, M. Rodríguez-Barranco, P. Amiano, L. Dañobeitia, M. D. Chirlaque, S. Colorado, M. Guevara, A. Jiménez, J. P. Arrebola, F. Vela, N. Olea, A. Agudo and M. J. Sánchez	2021	Bisphenol-A exposure and risk of breast and prostate cancer in the Spanish European Prospective Investigation into Cancer and Nutrition study	BACKGROUND: Bisphenol A (BPA) is an endocrine disruptor that is present in numerous products of daily use. The aim of this study was to assess the potential association of serum BPA concentrations and the risk of breast and prostate cancer in the Spanish European Prospective Investigation into Cancer and Nutrition (EPIC). METHODS: We designed a case-cohort study within the EPIC-Spain cohort. The population consisted on 863 participants from 3 EPIC-Spain centers (321 breast cancer cases, 175 prostate cancer cases and 1896 sub-cohort participants). BPA exposure was assessed by means of chemical analyses of serum samples collected at recruitment. Barged Lowphat Cox regression was used to test breast cancer risk. RESULTS: Median follow-up time was 16 years. BPA geometric mean serum values of cases and sub-cohort were 1.12 ng/ml vs. 1.13 ng/ml respectively for breast cancer and 1.20 ng/ml vs 1.19 ng/ml respectively for prostate cancer. When categorizing BPA into tertiles, a 66% increase in risk of prostate cancer for tertile 3 (p = 0.023), 31% increase for tertile 2 (p = 0.036) and 31% increase for tertile 3 (p = 0.072) was observed with respect to values bellow the limit of detection. No significant association was observed between BPA levels and breast cancer risk. CONCLUSIONS: We found a similar percentage of detection of BPA among cases and sub-cohort from our population, and no association with breast cancer risk was observed. However, we found a higher risk of prostate cancer for the increase in serum BPA levels. Further investigation is needed to understand the influence of BPA in prostate cancer risk.	Environ Health. 2021 Aug 16;20(1):88.	10.1186/s12940-021-00779-y	34399780	ヒト	発がん	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0216	K. Sachs- Stoermoen, H. Thorstensboltz, A. K. Sakki, C. Thomsen, A. Lia, A. Bjøre and J. L. Lyche	2025	Urinary levels and estimated daily intake of phthalates and phenols in kidney transplanted Norwegian children	Kidney transplanted children are exposed to phthalates and phenols, potentially harmful environmental endocrine disrupting chemicals. Urinary levels of phthalates and phenols in 52 Norwegian kidney transplanted children were compared with levels in healthy children. In children with chronic kidney disease, evaluated against other selected variables, and urine estimated daily intakes (EDI) were back-calculated and examined as part of a risk assessment. Urine samples were collected at a mean age of 11.6 (range 2.2-18) years, after a median of 7 (range 1.0-13.5) years after the transplant. Kidney transplanted Norwegian children's urinary levels of the sum of DEHP metabolites (ΣDEHP), monoethyl phthalate (MEP), monobenzyl phthalate (MBzP), monobutyl phthalate (MBP), and monoisobutyl phthalate (MiBP) were 2-fold higher, however 3-fold higher for the sum of ΣDEHP and MEP. Urinary levels of bisphenol A (BPA) and triclosan, compared to other Norwegian children with chronic kidney disease and normal kidney function. EDIs had higher concentrations of monoethyl phthalate, with no differences observed among children with or without overweight or hypertension. The risk assessment showed that at least 30 % of children were at risk of adverse health effects due to PFA exposure, as well as a few children at maximum exposure to metabolites of ΣDEHP, and to ΣDEHP, and to ΣDEHP, and to

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については≤100mM以下の濃度設定の試験	透明性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0220	J. Rovira, M. Martínez, M. Mari, S. C. Cunha, J. O. Fernandes, I. Marmelo, A. Marques, L. S. Haug, C. Thomsen, M. Nadal, J. L. Domingo and M. Schuhmacher	2022	Mixture of environmental pollutants in breast milk from a Spanish cohort of nursing mothers	Breastfeeding is one of the most effective ways to ensure child health and survival, with several benefits for both the infants and their mothers. However, breast milk can contain environmental pollutants with endocrine disruption capacity, neurotoxicity and/or potential to alter microbiota. Monitoring breast milk provides information on the current chemical exposure of breastfed infants and, in addition, on the current and historical exposure of nursing mothers. The aim of the present study was to assess the presence of a wide range of pollutants in breast milk from nursing mothers living in Catalonia (Spain). Target analysis of 36 chemicals including polychlorinated dibenzo-p-dioxins/dibenzofurans (2,3,7,8-substituted congeners) (PCDD/Fs), dioxin-like polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), per- and poly-fluoroalkyl substances (PFASs) (including perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA)), chlorpyrifos, bisphenol A (BPA), tetrabromobisphenol A (TBBPA), and a number of toxic and essential elements. Traces of most chemicals were found, and correlations between the levels of some persistent organic pollutants (POPs) and maternal characteristics (age and body mass index) were observed, while smoking was associated to higher concentrations of some trace elements. Higher levels of PCBs were detected in samples from Spanish primiparous mothers compared to non-Spanish multiparous women. Breast milk from low-income mothers showed higher contents of DDT and DDE than that from high-income mothers. Although breastfeeding is clearly beneficial for babies, the exposure to this mixture of hazardous substances, as well as their interaction and combined effects must not be disregarded.	Environ Int Vol.166 Pages 107375	10.1016/j.envint.2022.107375	35777115	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0221	J. M. Ratchell, C. Austin, E. Chapman, C. A. Attwell, C. R. Liddle, T. S. Dunstan, B. Blackburn, A. Mead, K. Filani, E. Beeby, K. Cunningham, J. Allen, H. Draper and B. A. Guinn	2024	Microplastics in human urine: Characterisation using μ-FTIR and sampling challenges using healthy donors and endometriosis participants	Microplastics (MPs) are found in all environments, within the human food chain, and have been recently detected in several human tissues. The objective herein was to undertake an analysis of MP contamination in human urine samples, from healthy individuals and participants with endometriosis, with respect to their presence, levels, and the characteristics of any particles identified. A total of 38 human urine samples and 15 procedural blanks were analysed using μ-FTIR spectroscopy. Microplastics were identified in 24 of the 38 urine samples (63.2 %) and 5 of the 15 procedural blanks (33.3 %). The median value of the healthy donor (30 of) urine samples, compared with 23 MP particles at differing 10 MP polymer types in 12 of the samples from participants with endometriosis. Healthy donors presented an unadjusted average of 3589 ± 2631 MP/L and participants with endometriosis presented 4726 ± 4150 MP/L. Polyethylene (PE) (27%), polystyrene (PS) (18%), resin and polypropylene (PP) (both 12%) polymer types were most abundant in healthy donor samples, compared with polytetrafluoroethylene (PTFE) (39%), and PE (26%) in samples from endometriosis participants. The MP levels within healthy and endometriosis participant samples were not significantly different. However, the predominant polymer types varied, and the MPs from the endometriosis participant samples and healthy donors were significantly smaller than those observed in the procedural blanks. Fragments were the most abundant MP morphology observed (≥ 50 %), with fibres (≥ 30 %) and films (≥ 10 %) also identified. This is the first contamination inherent in measurement of MPs from donors. This is the first evidence of MP contamination in human urine with polymer characterisation and accounting for procedural blanks. These results support the phenomenon of transport of MPs within humans, specifically to the bladder, and their characterisation of types, shapes, and size ranges identified therein.	Ecotoxicol Environ Saf Vol.274 Pages 116208	10.1016/j.ecoenv.2024.116208	38489903	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0222	J. M. Rosin, N. Tretiakov, E. Hanriman, K. Hampton and D. M. Kurrasch	2022	Gestational Bisphenol A Exposure Impacts Embryonic Hypothalamic Microglia Numbers, Ramification, and Phagocytic Cups	Microglia are a resident population of phagocytic immune cells that reside within the central nervous system (CNS). During gestation, they are highly sensitive to their surrounding environment and can alter their function in response to maternal exposures. Bisphenol A (BPA) is a ubiquitous endocrine disrupting chemical (EDC) that can cross the placenta and has been detected in fetal tissues. Although microglia are a critical BPA-sensitive cell type, here we tested whether fetal microglia are exposed to gestational BPA exposure. Accordingly, we exposed pregnant dams to vehicle or 50 mg/kg BPA per day by oral gavage (equivalent to investigate the impact of maternal BPA on embryonic hypothalamic microglia. Gestational BPA exposure from embryonic day (E) 0.5 to E15.5 resulted in a significant increase in the number of microglia present in the hypothalamus of both male and female embryos. Staining for microglial activation using CD68 revealed no change between control and prenatal BPA-exposed microglia, regardless of sex. Similarly, analysis of cultured embryonic brains demonstrated that gestational BPA exposure failed to change the secretion of cytokines or chemokines, regardless of embryo sex at the dose 30 μg of BPA per kg or 50 mg of BPA per kg maternal diet of BPA treatment. In contrast, live cell imaging of microglia dynamics in E15.5 control and gestationally exposed BPA hypothalamic slices revealed increased ramification of microglia exposed to BPA. Moreover, live cell imaging also revealed a significant increase in the number of microglial phagocytic cups visible following exposure to gestational BPA. Together, these results suggest that gestational BPA exposure impacts embryonic hypothalamic microglia, perhaps leading them to alter their interactions with developing neural progenies.	Front Neurosci Vol.16 Pages 830399	10.3389/fnins.2022.830399	35250464	動物	-	-	0	1	1	不明	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0223	M. Rolland, S. Lyon-Caen, A. K. Sakhi, I. Pin, A. Sabaredzovic, C. Thomsen, R. Slama and C. Philippat	2020	Exposure to phenols during pregnancy and the first year of life in a new type of couple-child cohort relying on repeated urine biospecimens	BACKGROUND: Parabens, bisphenol A and triclosan have been forbidden or restricted in specific types of consumer goods in Europe and France. Limited biomonitoring data are available in France since the implementation of these regulations.METHODS: We measured urinary concentrations of parabens, bisphenol A and triclosan in 1,240 pregnant women and 1,150 of their children from the EDEN mother-child cohort. We described levels, variability and predictors of exposure in 2 cohorts: 1) pregnant women and infants recruited between 2003 and 2011 in 2 French couple-child cohort. METHODS: Among 279 pregnant women and 150 of their infants, we studied phenol urinary concentrations in within-subject, within-period pools of repeated urine samples collected during the second and third trimesters of pregnancy (up to 12 samples per women), at 2 weeks and 12 months (up to 12 samples per infant). Time trends and associations with demographic, protocol, sociodemographic and behavioral factors were studied using multivariate linear mixed models.RESULTS: Detection rates were above 90% for bisphenol A, ethylparaben, methylparaben, benzophenone-3 and triclosan and below 5% for bisphenol AF, 2,4,7 and 12-parabens. Median urinary concentrations of bisphenol A, methylparaben and triclosan were 1.1, 1.6 and 0.9 μg/L, respectively. Between 2003 and 2011, urinary concentrations of bisphenol A and triclosan showed a linear decrease between 2003 and 2011 (p-values < 0.02). Women with the shortest education (primary and secondary school) had higher urinary concentrations of triclosan (F = 3.38 (95% confidence interval (CI): -0.66; 1.20), ethyl (F = 6.63 (95%CI: 0.65; 0.82) and propyl paraben (F = 1.39 (95%CI: 0.98; 2.02) than those with the longest education. Cashiers had higher concentrations of bisphenol A (F = 0.99 (95%CI: 0.11; 2.09) than non-employed women. Bisphenol A, triclosan and paraben detection rates were high in women and young infants. High bisphenol and paraben median levels at 12 months, require further investigation as early infancy is a sensitive period for exposure to environmental contaminants.	Environ Int Vol.139 Pages 105678	10.1016/j.envint.2020.105678	32248023	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0224	A. Rodríguez-Carrillo, S. Reny, S. C. D'Cruz, E. Salamanca-Fernandez, F. Gil, P. Olmedo, V. Mustieles, F. Vela-Soria, K. Baken, N. Olea, F. Smagulova, M. F. Fernandez and C. Freire	2023	Kisspeptin as potential biomarker of environmental chemical mixture effect on reproductive hormone profile: A pilot study in adolescent males	BACKGROUND: Kisspeptin has been proposed as an effective biomarker to understand the mechanisms by which some environmental chemicals adversely affect the human reproductive system. OBJECTIVE: To ascertain whether kisspeptin is associated with exposure to a mixture of environmental chemicals and reproductive hormones in adolescent males.METHODS: We measured urinary concentrations of 11 phenols, including bisphenol A (BPA), methyl paraben (MPB), and benzophenone-3 (BP3), four toxic metals (arsenic and cadmium) and four metabolites of non-persistent pesticides, including pyrethroids (3-phenoxybenzoic acid (3-PBA), cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (DCCA) and fungicides (ethylenethiourea (ETU)) were measured in first morning urine samples of 110 adolescent male males aged 15-17 years from the INMA (Environment and Childhood) cohort. In blood samples collected in the same visit, kisspeptin, FSH, LH, testosterone, SHBG, and free T4, as well as several levels of thyroid protein, total testosterone (T), estradiol (E2), sex hormone binding globulin, dehydroepiandrosterone sulfate, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Multiple linear regression and Bayesian kernel machine regression (BKMR) models were used to assess associations between kisspeptin and the mixture of chemicals.RESULTS: Median (P25; P75) urinary concentrations (ng/mL) were 2.0 (0.9;3.6) and 1.9 (0.8;3.8) creatinine-adjusted MPB, with lower DNA methylation percentage at CpG1 and total CpGs (% change (95%CI): -1.2 (-1.9to-0.5); -0.89 (-1.7to-0.0), respectively) and MPB and DCCA (sum lower total CpGs methylation (-0.51 (-1.0; -0.02) and -0.49 (-1.0; -0.01), respectively). The pesticide mixture and the whole chemical mixture were associated with higher kisspeptin (% change (95%CI): + 9.89 (0.29;20.2) and 12.0 (1.9;24.0)), respectively) and lower methylation levels at several CpGs. Additionally, serum kisspeptin in the third tertile was associated with higher LH levels (% change (95%CI): + 29.8 (3.79; 65.62), and third tertile CpG1, CpG2, and total CpG methylation percentages were associated with lower FSH and E2.DISCUSSION: The findings of the present study and the negative correlation between serum kisspeptin levels and DNA methylation percentages suggested that kisspeptin may be a promising effect biomarker.	Sci Total Environ Vol.888 Pages 161668	10.1016/j.scitotenv.2023.161668	36657687	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0225	A. S. Rodríguez-Báez, S. E. Medellín-Garibay, M. Rodríguez-Aguilar, J. Sagahón-Azúa, R. D. C. Milán-Segovia and R. Flores-Ramírez	2022	Environmental endocrine disruptor concentrations in urine samples from Mexican Indigenous women	The Indigenous communities in Mexico show significant degrees of vulnerability to pollution due to the lack of knowledge of health risks, traditions, low levels of support, and restricted access to healthcare. As a result, they are disproportionately exposed to endocrine disruptors. Therefore, the objective of this study was to determine the urinary concentrations of bisphenol A (BPA), benzophenone-3 (BP3), triclosan (TCS), 2,4-dichlorophenol (2,4-DCP), and 2,5-dichlorophenol (2,5-DCP) in Indigenous women from Hidalgo, Mexico, and bisphenol A through biomonitoring data from Indigenous Mexican women. A total of 30 women from the Tenek community in San Luis Potosí, Mexico, were included. Urine samples were analyzed for bisphenol A and 4 phthalate metabolites by ultra-performance liquid chromatography couples to tandem mass spectrometry; additionally, the 1-hydroxypyrene concentrations were evaluated by high-performance liquid chromatography coupled to a fluorescence detector. Among the non-persistent pesticides sources were the use of plastic containers and bunting garbage (98-100%). Indigenous women presented exposure of 100% to mono-2-ethyl phthalate, mono-n-butyl phthalate, and 2-hydroxypyrene, with a median (25th-75th percentiles) of 17.078 (11.262-27.200), 1118 (81.7-283.6), and 1.2 (0.9-1.7) μg/g creatinine, respectively. The major findings show that the Indigenous women presented exposure to endocrine disruptors, and the concentrations were higher than those reported in the general population. The lack of knowledge of risks and restricted access to healthcare reflects the absence of regulatory policies in marginalized populations. It highlights the need to design strategies that mitigate exposure and the importance of biological monitoring to evaluate and prevent health risk associated with exposure to environmental endocrine disruptors.	Environ Sci Pollut Res Int Vol.29 Issue 25 Pages 38645-38656	10.1007/s11356-021-18197-5	35088728	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0226	[redacted] Iakovleva, J. Ericson, J. Tlgt, A. Covaci, A. K. Sakhi, A. Van Nieuwenhuyse, A. Kattonouri, A. M. Andersson, A. C. Gutleb, B. Janasik, B. Appenzeller, C. Gabriel, C. Thomsen, D. Mazej, D. Sarigiannis, E. Anastasi, F. Barbone, H. Tolonen, H. Frederiksen, J. Kranova, J. Kopparen, J. S. Trabnik, K. Peck, K. Gurban, K. Ghafoldtbi, L. E. Knudsen, L. Rambaud, L. Strumylaite, L. P. Mukinova, L. Fabelova, M. Kiss, M. Berglund, M. Szabados, M. Imbraim, M. Lawrensens, M. Eliši kovi, N. Jones-Hilton, N. Probst-Hensch, N. Vrolwijkova, N. Vogel, P. Pilar, P. Schmidt, R. Lange, S. Namorado, S. Koppany, T. Szigeti, T. I. Halldorsson, T. Weber, T. K. Jørser, V. Rousler, V. Puklova, W. Wasowicz, O. Sepai, L. Stewart, M. Kolarova-Gehring, M. Esteban-Lopez, A. Castaño, J. Bessems, G. Schoeters and E. Govarts	2023	Time Patterns in Internal Human Exposure Data to Bisphenols, Phthalates, DINCH, Organophosphate Flame Retardants, Cadmium and Polyaromatic Hydrocarbons in Europe	Human biomonitoring (HBM) data in Europe are often fragmented and collected in different EU countries and sampling periods. Exposure levels for children and adult women in Europe were evaluated over time. For the period 2000-2020, literature and aggregated data were collected in a harmonized way across studies. Between 2011-2012, biobanked samples from the ESTEEM/DEMOCOPHES project were used. For 2014-2021, HBM data were collected in the HBM4EU Aligned Studies. Time patterns were investigated for bisphenols, phthalates, DINCH, organophosphate flame retardants, cadmium, and polycyclic aromatic hydrocarbons (PAHs). Exposure trends were evaluated using Tobit models. Human exposure: DPHP(s) in children (5-17 years), and urinary bisphenols and polycyclic aromatic hydrocarbons (PAHs) in women (20-39 years). Restricted phthalate metabolites show decreasing patterns for children. Phthalate substitutes: DINCH, shows a non-significant increasing pattern. For DPHPs, no trends were statistically significant. For women, BPA shows a clear decreasing pattern, while substitutes BPF and BPS show an increasing pattern coinciding with the BPA restrictions introduced. No clear patterns are observed for PAHs or cadmium. Although the unusual relations were not studied as such, exposure levels to chemicals restricted at EU level sharply decreased, while the levels for some of their substitutes increased. The results support policy efficacy monitoring and the policy-supportive role played by HBM.	Toxics Vol.11 Issue 10	10.3390/toxics11100819	37888670	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0227	P. R. S. Rocha, H. Moura, N. G. Silva, F. A. R. Neves, F. F. Sudré and A. A. Amato	2024	Exposure of elementary school-aged Brazilian children to bisphenol A: association with demographic, social, and behavioral factors, and a worldwide comparison	Bisphenol A (BPA) is a plasticizer used to synthesize polycarbonate plastics and epoxy resins and is well known for its endocrine disrupting action. BPA occurrence in the environment is widespread, and there is a growing concern regarding exposure to this chemical during childhood, given the high vulnerability indicating the long-lasting lesions associated with exposure during early life.To investigate childhood BPA exposure and its concentrations from 324 elementary school-aged Brazilian children, using high-performance liquid chromatography coupled to high-resolution mass spectrometry. We found that urinary BPA was detectable in the majority of the children (81.2%), with a median concentration of 0.4 μg/L. Exposure was associated with demographic, social, and behavioral factors, and the results were compared with worldwide regulatory policies concerning exposure to BPA. They were similar to those reported from studies conducted in Egypt and Australia. Despite more protective regulatory policies in the European Union, they were similar to, lower than those reported in European studies. Our findings indicate that exposure of Brazilian children to BPA is widespread and comparable to or even lower than that of countries with stricter regulatory policies.	Sci Rep Vol.14 Issue 1 Pages 24355	10.1038/s41598-024-67267-4	39420023	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0228	V. Robles-Aguilera, Y. Gálvez-Ontiveros, L. Rodrigo, I. Salcedo-Bellido, M. Aguilera, A. Zafra-Gómez, C. Monteagudo and A. Rivas	2021	Factors Associated with Exposure to Dietary Bisphenols in Adolescents	Disruptor endocrine disrupting chemicals, such as bisphenol S (BPS) and its analogue bisphenol S (BPS), seem to play an important role in the development of obesity, although contradictory results have been reported. The aim of the present study was to conduct a gender analysis of the factors associated with exposure to dietary bisphenols in 988 Spanish adolescents. Dietary BPA and BPS exposure was assessed using a food frequency questionnaire. Foods and monounsaturated, accounting for more than 50% of energy intake were selected for analysis. Stepwise regression was used to maximize the foods that most contributed to dietary bisphenol exposure. Logistic regression was performed to evaluate the association between dietary bisphenol exposure and overweight/obesity. Dietary exposure to BPA and BPS in both adolescent boys and girls. Overweight/obese girls showed a higher risk of high dietary exposure to BPA (odds ratio (OR): 1.58; 95% confidence interval (CI): 1.01-2.47) and total bisphenols (OR: 2.66; 95% CI: 1.63-7.67) in comparison with girls with a BMI lower than 25 kg/m2. Present results indicate a positive association of dietary exposure to both total bisphenols and BPA with being overweight/obese in adolescent girls.	Nutrients. 2021 May 5;13(5):1553.	10.3390/nu13051553	34062990	ヒト	代謝	-	-	-	-	-	横断研究	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0229	J. Robin, M. Albouy, B. Jourdain, G. Binson, A. Sauvaget, P. Fierle-Eaglins, L. Wu, V. Migeot, A. Dupuis and N. Venisse	2024	Assessment of Endocrine Disruptor Exposure in Hospital Professionals Using Hair and Urine Analyses: An Awareness Campaign	BACKGROUND: In 2021, French public authorities initiated the fourth National Environmental Health Plan to prevent environment related health risks. This plan primarily focuses on the sensitization of health professionals and health care institutions. Endocrine disruptors (EDCs) are environmental factors associated with several adverse health effects, such as reproductive disorders, obesity, and cancer. This study aimed to conduct an awareness campaign among professionals at a general hospital center on the risks related to EDs.METHODS: Hospital professionals were directly involved in this study and urine and hair samples were collected. Urine samples were analyzed for bisphenol A, parabens, benzophenone-3, triclosan, and phthalate metabolites. Hair samples were analyzed for bisphenol A, parabens, and pesticides. A questionnaire on lifestyle habits was distributed to assess its relationship with the exposure profiles. Nineteen professionals were recruited for the study.RESULTS: Bisphenol A was detected in 95% of the urine samples, and the chlorinated derivatives of bisphenol A were between 18% and 63%. parabens showed detection frequencies between 37% and 100%, and methylparaben was quantified at an average concentration of 0.48 ± 0.66 ng/mL. In hair samples, bisphenols A, F, and S were detected at 95%–100%. chlorinated derivatives of bisphenol A were detected at 37%–68%, and parabens were detected at 100%.CONCLUSIONS: This awareness campaign may encourage health care institutions to adopt a policy of reducing endocrine disruptor exposure among their patients and professionals. a file could be allocated regarding the risks associated with EDs. Conducting a multicenter study is either the results herein and establish a system to prevent endocrine disruptor and environmental risks in health care systems could be valuable.	BMJ Open. 2020 Jun 21;10(6):e033509.	10.1136/bmjopen-2019-033509	32565448	ヒト	代謝(メタアナリシス)	-	-	-	-	-	メタアナリシス	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0230	C. M. Ribeiro, B. T. S. Bezerra, N. G. Silva, C. L. Lima, P. R. S. Rocha, M. S. Coelho, F. A. R. Neves and A. A. Amato	2020	Exposure to endocrine-disrupting chemicals and anthropometric measures of obesity: a systematic review and meta-analysis	OBJECTIVE: Endocrine disrupting chemicals (EDCs) are viewed as a major potential link between the environment and obesity development. We did a systematic review and meta-analysis to examine the association between exposure to EDCs and obesity.METHODS: We searched PubMed, Scopus, Web of Science, and Embase databases for studies published up to May 2019 that examined the association between exposure to EDCs and the age of 2 years and anthropometric measures of obesity or body fat. The Newcastle-Ottawa scale was used to assess the risk of bias. DATA EXTRACTION AND SYNTHESIS: Two independent reviewers screened and conducted data extraction and synthesis. A third reviewer resolved disagreements. RESULTS: A total of 35 studies investigating bisphenol A (12 286 individuals), organochlorine compounds (10 667 individuals), phthalates (5 181 individuals), polybrominated biphenyls (797 individuals), polycyclic aromatic hydrocarbons (1015 individuals), pyrethroids (989 individuals), heavy metals (3671 individuals) and polyfluoroalkyl substances (509 individuals) met our inclusion criteria. Most had a cross-sectional design and two or medium risk of bias. In qualitative analysis, bisphenol A and phthalates were associated with general and abdominal obesity in children and adolescents. Organochlorine compounds were associated with general obesity in children and adolescents. Heavy metals were associated with abdominal obesity in children and adolescents. Polybrominated biphenyls showed an association between exposure to bisphenol A and overweight (OR 1.256, 95% CI 1.065 to 1.481), obesity (OR 1.383, 95% CI 1.270 to 1.773) and increased waist circumference (OR 1.383, 95% CI 1.267 to 1.782) in adults, and between exposure to 2,4-dichlorophenol and obesity in children (OR 1.8, 95% CI 1.2 058 to 3.080). CONCLUSION: Most observational studies supported a positive association between obesity and exposure to EDCs. Although causality cannot be determined from these data, they underscore the need to limit human exposure to EDCs, in light of the evidence from animal and cell-based studies indicating the effects of these chemicals on adiposity. PROSPERO REGISTRATION NUMBER: CRD42020170538.	Sci Rep Vol.10 Issue 1 Pages 9367	10.1038/s41598-020-66379-x	32518293	動物	-	1	不明	0	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0231	A. Repouskou, A. K. Papadopoulou, E. Panagiotidou, P. Titchiri, C. Lindh, A. Bergman, C. Gennings, C. G. Bornehag, J. Klinge, E. Kitraki and A. Stamatakis	2020	Long term transcriptional and behavioral effects in mice developmentally exposed to a mixture of endocrine disruptors associated with delayed human neurodevelopment	Accumulating evidence suggests that gestational exposure to endocrine disrupting chemicals (EDCs) may interfere with normal brain development and predispose for later dysfunctions. The current study focuses on the developmental effects of a mixture of EDCs, based on the levels detected in pregnant women participating in the Swedish SELMA cohort. Specifically, we have previously found that EDC exposure was associated with language delay in their children. To study the long-term impact of developmental exposure to EDCs on certain physiological and behavior we administered this mixture to mice throughout gestation at doses 3-1-0.3 - 10-1 - 10-3 - and 100-1 the geometric mean of 555 400 mothers' concentrations, and examined their offspring in adulthood. Mixture 10-1 exposure increased active coping during swimming stress in both sexes, accompanied by increased hippocampal BDNF protein levels in females. Mixture 100-1 exposure increased anxiety-like behavior in the elevated plus maze in both sexes and in females in the novelty suppressed feeding test. Moreover, mixture 100-1 exposure altered social interaction in males. Female exposure to mixture 10-1 increased social interaction time, while mixture 100-1 exposure altered social recognition memory. Male exposure to mixture 100-1 altered social recognition memory. Female exposure to mixture 100-1 altered sociosexual behavior, as measured by ultrasonic vocalizations (USVs) and partner preference. Finally, male exposure to mixture 100-1 altered the number of ultrasonic vocalizations (USVs) during male-female social interaction. Principal component analysis revealed gene clusters associated with the observed behavioral responses, mostly related to the nitrinic axis. This integration of epidemiology-based data with an experimental model increases the evidence that prenatal exposure to EDC mixtures impacts later life brain functions.	Dermatitis Vol.35 Issue 5 Pages 467-475	10.1089/derm.2024.0018	38888884	ヒト	-	-	-	-	-	-	後ろ向き横断分析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0232	M. J. Reeder, A. Idrogo-Lam, S. R. Arasaratnam, E. M. Wenthaus, J. G. DeKoven, J. I. Silverberg, B. L. Asher, A. R. Atwater, J. S. Taylor, M. C. Houle, D. V. Belchis, J. Yu, N. Botto, C. M. Maxwell, C. A. Durocio, V. A. Dalusio and M. D. Pratt	2024	Occupational Contact Dermatitis in Construction Workers: A Retrospective Analysis of the North American Contact Dermatitis Group Data, 2001-2020	Background: Construction workers (CWs) are at risk for occupational contact dermatitis (CD) owing to workplace exposures. Objective: Determine the prevalence of occupational allergic CD and characterize common occupational allergens in CWs referred for patch testing in the United States and Canada. Methods: Retrospective cross-sectional analysis of patients patch tested by the North American Contact Dermatitis Group from 2001 to 2020. Results: Of 17,882 patch-tested patients, 681 (3.8%) were CWs. Compared with non-CWs, CWs were more likely to be male (95.8% vs 59.9%) have occupational skin disease (38.9% vs 11.6%) and have hand dermatitis (49.2% vs 29.4%; all P < .001). Common occupational allergens in CWs were epoxy resin (16.2%), fragrance mix I (15.2%), and cobalt dichloride (14.2%). Limitations: Lack of occupational/work-exposure information; only occupationally relevant allergens were grouped as dichromate (1,705; 10.2%; 26/258), bisphenol A epoxy resin (1.4%; 28/1,705), carba mix (0% per; 11/681; 26/1,705), cobalt (1) chloride hexahydrate (1% per; 24/1,705), and thiuram mix (1% per; 11/674; 26/1,705). Top sources of occupationally relevant allergens were cement/concrete/mortar (20.6%; 66/320), gloves (16.1%; 51/316), and coatings (paint/lacquer/shellac/varnish/stains) (9.8%; 31/316). Conclusions: Occupational CDs in North American CWs is common. In this group, frequently identified etiological sources of occupational allergic CD included resins, epoxy resin, and rubber.	Dermatitis Vol.35 Issue 5 Pages 467-475	10.1089/derm.2024.0018	38888884	ヒト	-	-	-	-	-	-	後ろ向き横断分析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0233	I. Rebai, J. O. Fernandes, M. Azzouz, K. Benmohammed, G. Bader, K. Benmbarek and S. C. Cunha	2021	Urinary bisphenol levels in plastic industry workers	Bisphenol A (BPA) is a known endocrine disruptor compound that is widely applied as a monomer base in polycarbonate plastics and as a binding agent in enamel epoxy resins. Plastic industry workers have usually been investigated exposure to BPA. Hence, the present work aims to assess the levels of BPA and their analogs (S, F, B, AF, Z, E, and BPS) in 100 urine samples from a plastic industry located in north Constantine (Algeria). This work was complemented with a questionnaire about sexual functions and evaluation of sexual hormone levels. The results showed a notable presence of BPS (average of 3.16 µg/L), accounting for more than 90% of the total BPs. Of the remaining BP analogs, only trace amounts of BPB were detected in three samples (average of 1.75 µg/L). Significant associations with BPS urinary levels were noted with age (p = 0.046), occupational level of exposure (p = 0.023), and years of experience (p = 0.001).	Environ Res Vol.202 Pages 111666	10.1016/j.envres.2021.111666	34265347	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0234	F. Rancière, J. Botton, R. Slama, M. Z. Lacroix, L. Debrauwer, M. A. Charles, P. Rouimi, B. Balkau and D. J. Magliano	2019	Exposure to Bisphenol A and Bisphenol S and Incident Type 2 Diabetes: A Case-Cohort Study in the French Cohort D.E.S.I.R	BACKGROUND: The question of whether exposure to bisphenol A (BPA) contributes to the development of type 2 diabetes is still unresolved. Most epidemiological evidence on the association between BPA and diabetes is from cross-sectional studies or longitudinal studies with single urinary measurements. No prospective study has examined exposure to BPA analogs such as bisphenol S (BPS) in relation to incident type 2 diabetes. OBJECTIVES: We aimed to investigate whether exposure to BPA and BPS, assessed at up to two time points, was associated with the incidence of type 2 diabetes. METHODS: We performed a case-cohort analysis. 756 participants without diabetes at baseline and followed-up over 9 y as part of the French prospective cohort Data from an Epidemiological Study on the Insulin Resistance Syndrome (D.E.S.I.R.) 494 glucose-tolerant (BPS-U- and BPS-glucuronide (BPS-G) were assessed in fasting spot urine samples collected during the health examinations at baseline and 3 y later. Associations with incident diabetes were examined using Prentice-weighted Cox proportional hazards models. RESULTS: Of the 494 participants, 71 developed diabetes. Urinary BPS-U concentrations were detectable in 19% of participants at baseline and 15% at 3 y. Urinary BPA-U concentrations were rarely above the LOD. Mean urinary BPS-U concentrations were 0.29 ± 0.70 and 0.22 ± 0.49 ng/mL at baseline and 3 y, respectively. Urinary BPS-U concentrations were associated with incident diabetes, with a hazard ratio (HR) = 2.64 (95% CI: 1.16, 5.65), 2.36 (95% CI: 1.07, 5.19), and 1.58 (95% CI: 0.68, 3.65), respectively. The detection of BPS-U in urine at one or both time points was associated with incident diabetes, with an HR = 2.85 (95% CI: 1.15, 6.53). CONCLUSIONS: This study shows positive associations between exposure to BPS and BPS and the incidence of type 2 diabetes, independent of traditional diabetes risk factors. Our results should be confirmed by recent, population-based observational studies in different populations and settings. Overall, these findings raise concerns about using BPS as a BPA substitute. Further research on BPS analogs is warranted. https://doi.org/10.1289/EHP5026	Environ Health Perspect. 2019 Oct;127(10):107013.	10.1289/ehp5159	31663775	ヒト	-	-	-	-	-	-	-	症例コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0235	V. Ramírez, P. González-Palacios, P. J. García-Serna-Domenech, S. Jaimez-Pérez, M. A. Baca, L. Rodrigo, M. J. Álvarez-Cubero, C. Monteagudo, L. J. Martínez-González and A. Rivas	2024	Influence of Genetic Polymorphisms on Cognitive Function According to Dietary Exposure to Bisphenols in a Sample of Spanish Schoolchildren	BACKGROUND: Neurodevelopmental disorders (NDDs) like intellectual disability (ID) are highly heritable, but the environment plays an important role. For example, endocrine disrupting chemicals (EDCs), including bisphenol A (BPA) and its analogues, have been termed neuroendocrine disruptors. This study aimed to evaluate the influence of different genetic polymorphisms (SNPs) on cognitive function in Spanish schoolchildren according to dietary bisphenol exposure. METHODS: A total of 182 children aged 8–12 years old were included. The SNPs in genes involved in brain development, synaptic plasticity, and neurotransmission (BDNF, GTF2I, GRIN2B, SLC6A4, and COMT) were genotyped. Cognitive function was assessed using the Wechsler Intelligence Scale for Children (WISC-V). RESULTS: The BDNF rs6265 T-carrier/BDNF rs11030104 A-carrier genotype was associated with a 5.6 point increase in the full-scale intelligence quotient (FSIQ) (β = 5.6; 95% CI: 1.16, 9.81), 3.36 (95% CI: 1.07, 5.55), and 1.98 (95% CI: 0.68, 3.30), respectively. The detection of BPS-U in urine at one or both time points was associated with incident diabetes, with an HR = 2.85 (95% CI: 1.15, 6.53). CONCLUSIONS: This study shows positive associations between exposure to BPS and BPZ and the incidence of type 2 diabetes, independent of traditional diabetes risk factors. Our results should be confirmed by recent, population-based observational studies in different populations and settings. Overall, these findings raise concerns about using BPS as a BPA substitute. Further research on BPS analogs is warranted. https://doi.org/10.1289/EHP5026	Nutrients. 2024 Aug 10;16(16):2639.	10.3390/nu16162639	39203776	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0236	S. Balmondo, M. L. Chiusano, M. Gentile, T. Gentile, F. Cuomo, R. Gentile, D. Danza, L. Sanzi, C. Crescenzo, M. Palmieri, S. Iaccarino, M. Iaccarino, A. Fortunato, F. Liguori, A. Esposito, C. Zullo, L. Soria, L. Sosa, I. Ferrara, M. Piscopo, T. Notari, E. Lacasera, A. A. Gentile and L. Montano	2024	Comparative analysis of the bioaccumulation of bisphenol A in the blood serum and follicular fluid of women living in two areas with different environmental impacts	INTRODUCTION: Bisphenol A (BPA) is a common contaminant widely used in many industrial sectors. Because of its wide use and dispersion, it can be accumulated in living human bodies through both oral assumption and inhalatory routes. BPA exhibits hormone-like properties, falling under the class of endocrine disruptors; therefore, it can alter relevant physiological functions. In particular, in women, it can affect folliculogenesis and, therefore reproduction, contributing not only to infertility, but also to endometriosis, and premature puberty. METHODS: We conducted a multicentric study on 81 women undergoing a first in vitro fertilization (IVF) treatment in the Campania region (Southern Italy). We investigated the presence and concentration of BPA in both serum and follicular fluids to assess the effects of its accumulation. The analysis was conducted on 20 women living in a low environmental impact (LEI) area, from the Dole Valley River and Cilento region, and 20 women living in a high environmental impact (HEI) area, the so-called "Land of Fires", a highly polluted area because of illegal waste disposal. RESULTS: Our results showed that BPA was detectable in the blood serum of 100% of the women and in the follicular fluid of 95% of them. In addition, our results show a correlation between BPA content in blood serum that in follicular fluid in the HEI area, with opposite observations in the LEI area. Moreover, in addition, our results also showed a lack of correlation between BPA content in follicular and serum fluids both in the overall population and in the HEI and LEI groups, with peculiar trends in different subsets of women. CONCLUSIONS: From our results, we revealed a heterogeneity in the distribution of BPA content between serum and follicular fluid. Further studies are needed to unravel the tissue accumulation mechanisms of BPA in highly polluted and nonpolluted areas.	Front Endocrinol (Lausanne) Vol.15 Pages 1392550	10.3389/fendo.2024.1392550	39439569	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0237	P. Radwan, B. Wielgomas, M. Radwan, R. Kiosidi, A. Klimowska, D. Kalela and J. Jurewicz	2020	Urinary bisphenol A concentrations and in vitro fertilization outcomes among women from a fertility clinic	Bisphenol A (BPA) is a widespread environmental endocrine disrupting chemical. Although many animals, and in vitro studies reported that BPA may affect female fertility through the effect on maturing oocyte, and embryo cell division, but the data from human studies are limited and inconclusive. The study was conducted to examine the association between urinary BPA concentration and in vitro reproductive outcomes. Immediate (1 DD) oocyte yield, top quality embryo, fertilization rate, implantation rate, biochemical and clinical pregnancy among women undergoing in vitro fertilizing clinic. The study participants were recruited in Poland. 350 women aged 24–40 (x = 33.51 ± 3.57) (n=1 oocyte) provided urine samples. The urinary concentrations of BPA were evaluated using validated gas chromatography–ion tandem mass spectrometry method. Clinical outcomes of IVF treatment were collected from medical documentation. The median BPA concentration was 1.61 ng/mL (interquartile range: 0.80–3.40 ng/mL). Detectable concentrations of BPA were found in 94% of urine samples. In women, not observed increased odds of general symptom (fever, fatigued) odds ratio (aOR) = 1.48 (95% C.I.: 0.98–2.24), local symptom (eye, tight = 1.34 (95% C.I.: 1.03–1.82), and emergency department visits (aOR = 1.17 (95% C.I.: 0.78–1.63) per 1ln-fold increase in BPA concentration. We also observed evidence of sexually disruptive effects: BPA concentrations were associated with increased odds of symptom dips and health care utilization only among men. Findings regarding BPS and BPF did not consistently point to associations with adverse symptoms or health-care utilization. CONCLUSION: We found evidence to suggest that BPA exposure, a predominantly low-income, minority pediatric cohort is associated with asthma morbidity and that associations may differ by sex. Our findings support additional studies, given the high pediatric asthma burden and widespread exposure to BPA in the United States.	Reprod. Toxicol. 2020 Sep;96:216-220	10.1016/j.reprotox.2020.07.009	32721521	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-
統合_0238	L. Quiró-Alcalá, N. N. Hansel, M. McCormack, A. M. Calafat, X. Ye, R. D. Peng and E. C. Matsui	2021	Exposure to bisphenols and asthma morbidity among low-income urban children with asthma	BACKGROUND: Bisphenol A (BPA) has been linked with pediatric asthma development and allergic airway inflammation in animal models. Whether exposure to BPA or its structural analogs bisphenol S (BPS) and bisphenol F (BPF) is associated with asthma morbidity remains unknown. OBJECTIVE: We examined associations between bisphenols and morbidity due to pediatric asthma. METHODS: We quantified concentrations of BPA, BPS, and BPF in 168 urine samples from 138 predominantly low-income, African American children (ages 5–17 years) with established asthma. We used Poisson models to examine associations between urinary bisphenols and symptoms, health care utilization, and pulmonary function and inflammation that were collected every 3 months over the course of a year. We used generalized estimating equations to examine associations between concentrations of detected bisphenols and asthma symptoms, health care utilization, and pulmonary function and inflammation. RESULTS: Urinary BPA concentrations were detected in 93% of urine samples, BPS in 39% of samples, and BPF in 1% of samples. Children with detectable urinary BPA concentrations had a 1.59-fold (95% CI: 1.08–2.34) increase in the number of days with albuterol use, a 1.61-fold (95% CI: 1.09–2.38) increase in the number of days with symptoms, and a 1.57-fold (95% CI: 1.08–2.28) increase in the number of days with albuterol use or symptoms, compared with children with undetectable urinary BPA concentrations. We observed evidence of sexually disruptive effects: BPA concentrations were associated with increased odds of symptom dips and health care utilization only among boys. Findings regarding BPS and BPF did not consistently point to associations with asthma symptoms or health-care utilization. CONCLUSION: We found evidence to suggest that BPA exposure, a predominantly low-income, minority pediatric cohort is associated with asthma morbidity and that associations may differ by sex. Our findings support additional studies, given the high pediatric asthma burden and widespread exposure to BPA in the United States.	J Allergy Clin Immunol. 2021 Feb;147(2):577-586.e7	10.1016/j.jaci.2020.05.031	32736870	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-
統合_0239	J. Qu, W. Mao, K. Liao, Y. Zhang and H. Jin	2022	Association between urinary bisphenol analogue concentrations and lung cancer in adults: A case-control study	Elevated urinary bisphenol A (BPA) concentrations have been associated with lung cancer in humans. However, toxicological studies demonstrated that the proliferation of lung cancer cells was inhibited by BPA exposure. Therefore, it is still necessary to determine whether exposure to BPA and other bisphenol analogues (BPs) is associated with lung cancer in humans. In this study, 294 lung cancer patients and 322 controls were randomly recruited. Concentrations of three BPs in human urine were quantified and their relationships with the risk of human lung cancer were evaluated. BPA (mean 1.03 ng/mL, IQR: 0.47 µg/g Cre) was the predominant BP in human urine, followed by bisphenol S (BPS) (0.72 ng/mL, 0.33 µg/g Cre) and bisphenol F (0.42 ng/mL, 0.17 µg/g Cre). Significant correlations between creatinine-corrected urinary BPA concentrations and the lung cancer risk (odds ratio: OR (adjusted) = 1.28, 95% confidence interval (CI): 1.17, 1.38) (Pinteract = 0.02) were found using logistical regression analysis. Creatinine-corrected urinary concentrations of BPS in participants showed significant correlations with the risk of lung cancer (OR (adjusted) = 1.44, 95% CI: 1.26, 1.56; Pinteract = 0.03). Significant interactions between the cigarette smoking status and BPA concentrations were found. The combined concentrations of BPA and the risk of lung cancer still increased in male participants (OR = 1.32, 95% CI: 1.09, 1.61; p = 0.002). This study demonstrates that elevated human exposure to BPA and BPS may be associated with the increased lung cancer risk.	Environ Pollut. 2022 Dec 15:315:120323.	10.1016/j.envpol.2022.120323	36191799	ヒト	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0240	W. Qiu, S. Yin, K. Abulizi, K. Li, Y. Lu, Q. Zhang, M. Zhao and J. Zhang	2024	Preconception exposure to bisphenol A and its alternatives: Effects on female fecundity mediated by oxidative stress and ovarian reserve	BACKGROUND: Various Bisphenol A (BPA) their alternatives have emerged in numerous personal products in recent years. However, it remains unclear whether BPA analogs affect female fecundity and possible biological mechanisms. OBJECTIVES: We aimed to evaluate the relationship of bisphenol analogs with female fecundability and infertility and whether oxidative stress, inflammation, and ovarian reserve may play a mediation role in such associations. METHODS: This prospective preconception cohort study included 967 couples who attempted pregnancy. BPA and its alternatives were measured in women's urine samples. Bisphenol exposure was categorized into tertiles. Cox proportional hazards models were used to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs). Mediation analysis was conducted to explore the role of oxidative stress, inflammation, and ovarian reserve in the relationship between bisphenol analogs and fecundity. We also quantified their interactions, including relative excess risk due to interaction (RERI), multiplicative term (AP), and the synergy index (S). RESULTS: Using an integrated analytical approach consisting of both single-pollutant and mixture models, we found that BPA and bisphenol AF (BPAF) were significantly associated with decreased fecundability. Women in the highest tertile of BPA (FR = 0.77, 95% CI: 0.61, 0.97) and BPAF (FR = 0.77, 95% CI: 0.61, 0.98) had a 23% and 23% lower chance of pregnancy, respectively, than those in the lowest tertile. The BPA-BPAF mixture also showed a 23% (FR = 0.77, 95% CI: 0.61, 0.96) reduction in fecundability. Mediation analysis revealed that increased concentrations of BPA and the risk of lung cancer still increased in male participants (OR = 1.32, 95% CI: 1.09, 1.61; p = 0.002). This study demonstrates that elevated human exposure to BPA and BPS may be associated with the increased lung cancer risk.	Sci Total Environ. 2024 Dec 20:957:177558.	10.1016/j.scitotenv.2024.177558	39547376	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-
統合_0241	R. X. Qin, X. Cao, S. Y. Zhang, H. Li, B. Tang, Q. L. Liao, F. S. Cai, K. Z. Pang and J. Zhang	2024	Decontamination promotes the release of incorporated organic contaminants in hair: Novel insights into non-invasive biomonitoring	Human hair is increasingly employed as a non-invasive biomonitoring matrix for exposure to organic contaminants (OCs). Decontamination procedures are generally needed to remove external contamination from hair prior to analysis of OCs. Despite various existing decontamination protocols, their impacts on internally incorporated (endogenous) OCs in hair remain poorly understood. This study aims to quantitatively assess the impact of decontamination procedures on the levels of OCs in hair. Hair samples were collected from 30 participants and divided into two portions. One portion was treated with a sequential rinsing procedure (dichloromethane [DCM], methanol [MeOH], and ultrapure water), while the other portion remained untreated. Thirty-seven OCs, including phthalate esters (PAEs), 2,4-dichlorophenoxyacetic acid (2,4-D), dichlorophenols (DCPs), and 3-phenoxybenzoic acid (3-PBA), were analyzed in hair extracts with different solvents (methanol, or hexane, acetone, ultrapure water, Triton X-100, and sodium dodecyl sulfate) were used to clear exposed guinea pig hair. All OCs and three metabolites (diphenyl phosphate [DPHP], dibutyl phosphate [DBP], and bis(1,3-dichloro-2-propyl) phosphate [BDCIPP]) were detected in the majority of washing solutions. The decontamination procedure apparently resulted in the release of endogenous OCs from hair. The percentages of residual OCs in hair exhibited a linear or exponential decrease with more washing cycles. Furthermore, the residuals of OCs in hair treated with organic and aqueous solvents showed significant differences, with the former exhibiting a greater ability to remove endogenous OCs from hair than the latter. Although the DCM/MeOH rinsing method is considered to be the most effective for the removal of exogenous OCs, the results obtained in this study provide compelling evidence that current hair decontamination procedures have significant impacts on the analysis of endogenous OCs in hair. Therefore, it is important to interpret quantitative data on hair OC concentrations with caution and to thoroughly consider each decontamination procedure during analysis.	Environ Pollut Vol.359 Pages 124696	10.1016/j.envpol.2024.124696	39122174	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0242	J. Puvvula, L. C. Song, K. J. Zalewska, A. Alexander, K. E. Marz, J. M. Braun, K. D. Pennell, E. A. DeFranco, S. M. Ho, Y. K. Leung, S. Huang, A. M. Yuong, S. S. Kim, Z. Percy, P. Bhartiyam, R. Lee, D. P. Jones, Y. Tran, D. V. Kim, A. M. Calafat, J. C. Botelho and A. Chen	2025	Global metabolomic alterations associated with endocrine-disrupting chemicals among pregnant individuals and newborns	BACKGROUND: Gestational exposure to non-persistent endocrine disrupting chemicals (EDCs) may be associated with adverse pregnancy outcomes. While many EDCs affect the endocrine system, their effects on metabolic pathways remain understudied. METHODS: We analyzed urine samples collected from 1,000 pregnant participants in the ECHO Cohort Program. Participants were enrolled in the study and delivered at the University of Cincinnati Hospital from 2015 to 2017. We measured maternal urinary biomarkers of paraben (ethyl (EP), methyl (MP), and propyl (PP)), phthalate (DEP, and monobenzyl phthalate (MBzP)), and bisphenol A (BPA) performance-matched (PM) urine samples (2) from the placenta collected during the delivery visit. Global nuclear metabolome profiles were analyzed from maternal blood (n = 72) and newborn (n = 80) cord blood samples collected at delivery. Fifteen of the 25 urinary biomarkers were excluded due to low detection frequency (<50%). We used Bayesian kernel machine regression (BKMR) models to examine associations between mixtures of urinary EDC biomarkers and metabolomic features. We used enrichment analysis to identify potential biomarkers in metabolic pathways. RESULTS: We observed metabolome-wide associations between maternal urinary concentrations of phthalate metabolites. There is also phthalate), phthalate replacements (mono (2-ethyl-5-carboxypentyl) terephthalate, mono (2-ethyl-5-hydroxyhexyl) terephthalate) and phenols. Bisphenol A, bisphenol (S) and maternal serum metabolome, using a value > 0.5 as a threshold. Additionally, associations of phthalate metabolites (mono-n-butyl phthalate, monobenzyl phthalate) and phenols (2,5-dichlorophenol, BPA) with the newborn metabolome were noted. Enrichment analysis revealed associations (γ-gamma (>0.05) cis-aconitic acid, carbohydrate, lipid, glycan, vitamin, and other cellular metabolism pathways. CONCLUSION: Maternal paraben, phenol, phthalate, and phthalate replacement biomarker concentrations at delivery were associated with maternal and newborn serum global metabolome.	Metabolomics Vol.21 Issue 1 Pages 20	10.1007/s11306-024-02219-7	39863779	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0243	J. Puvvula, J. M. Braun, E. A. DeFranco, S. M. Ho, Y. K. Leung, S. Huang, X. Zhang, A. M. Yuong, S. S. Kim, Z. Percy, A. M. Calafat, J. C. Botelho and A. Chen	2024	Gestational exposure to environmental chemicals and epigenetic alterations in the placenta and cord blood mononuclear cells	BACKGROUND: Exposure to environmental chemicals such as phthalates, phenols, and polycyclic aromatic hydrocarbons (PAHs) during pregnancy can increase the risk of adverse newborn outcomes. We explored the associations between maternal exposure to select environmental chemicals and DNA methylation in cord blood mononuclear cells (CBMC) and placental tissue (maternal and fetal sides) to identify potential mechanisms underlying these associations. METHOD: This study included 73 pregnant individuals who consented to give birth at the University of Cincinnati Hospital between 2014 and 2017. Maternal urine samples during the delivery visit were collected and analyzed for 17 biomarkers of phenols (2), phthalates (12), phthalate replacements (3), and PAHs (1). Cord blood and placenta tissue (maternal and fetal sides) were also collected to measure DNA methylation using the Illumina MethylationEPIC BeadChip. Robust linear regression models were used to examine associations between urinary biomarkers and DNA methylation in CBMC and placental tissue (n = 67 and maternal (n = 69) tissue) associated with gestational chemical exposures. Of the 473 biomarkers measured in this study. To account for multiple testing, we used a false discovery rate q-value < 0.05 and presented results by limiting results within a genomic inflation factor of 1±0.05. Additionally, gene set enrichment analysis was conducted using the Kyoto Encyclopedia of Genes and Genomics pathways. RESULTS: Among the 25 biomarkers assessed for differential methylation, maternal concentrations of PAH metabolites (1-hydroxynaphthalene, 2-hydroxynaphthalene, 3-hydroxyphenanthrene), monocarboxynonyl phthalate, mono (5-carboxypentyl) phthalate, and bisphenol A were associated with altered methylation in placenta (maternal or fetal side), driving exposure biomarkers associated with epigenetic changes in genes related to cellular metabolism, immune response, and neurodevelopment. Maternal urinary concentrations of 1-hydroxynaphthalene and 2-hydroxynaphthalene were associated with lipid metabolism and cellular processes of the placenta. Additionally, mono (5-carboxypropyl) phthalate was associated with neuronal systems and genetic information processing of the placenta. CONCLUSION: Among the 25 chemical biomarkers assessed during delivery, 1-hydroxynaphthalene and mono (5-carboxypropyl) phthalate were associated with DNA methylation in the placenta. GLYPHLINK"EHP13497 ERRATUM"ON: The online version contains supplementary material available at 10.1186/s13062-023-00327-7.	Epigenetics Commun. 2024;4(1):4.	10.1186/s43682-024-00027-7	38962689	ヒト	-	-	-	-	-	-	-	子宮	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0244	Y. Pu, Y. Du, J. Hu, S. He, Y. Chen, A. Cao and Y. Dang	2024	The mediating role of steroid hormones in the relationship between bisphenol A and its alternatives bisphenol S and F exposure and preeclampsia	Steroid hormone imbalance is believed to increase the odds of developing PE. Bisphenol A (BPA) and its substitutes (e.g., bisphenol S (BPS) and bisphenol F (BPF)) have estrogen-like effects, and its exposure may be related to the development of preeclampsia (PE). To explore the effects of bisphenol exposure on maternal serum steroid hormones and the potential mediating role of steroid hormones in the association between bisphenol exposure and PE, we conducted a nested case-control study in Wuhan, China, between 2021 and 2022. Maternal urine samples collected in the first trimester were analyzed for BPA, BPS, and BPF. Multivariable logistic and linear models were used to explore the associations of maternal urine bisphenols concentrations with both maternal steroid hormones and PE risk. Bidirectional mediation analysis was employed to evaluate the mediating role of steroid hormones in the association between bisphenols and PE. Results showed that maternal serum BPE concentrations were positively associated with testosterone (T) concentrations. The mediation analysis suggested that approximately 16.71% of the associations between BPA concentrations and the development of PE might be mediated by maternal T. In conclusion, maternal exposure to BPS during pregnancy is linked to higher maternal T concentrations, which might increase the odds of developing PE. T might mediate the association between BPA exposure and the development of PE.	J Steroid Biochem Mol Biol. 2024 Nov:244:106591.	10.1016/j.jsbmb.2024.106591	39059562	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0245	N. B. Patidhu, S. Vasishta, S. K. Bhat, M. B. Joshi, S. P. Kabekkodu, K. Satyamoorthy and P. S. Rai	2023	Distinct metabolic signatures in blood plasma of bisphenol A-exposed women with polycystic ovarian syndrome	Polycystic ovarian syndrome (PCOS) is a complicated endocrinopathy with an unclear etiology that affects fertility status in women. Although the underlying causes and pathophysiology of PCOS are not completely understood, it is suspected to be driven by environmental factors as well as genetic and epigenetic factors. Bisphenol A (BPA) is a well-established endocrine disruptor known to cause adverse reproductive outcomes in women. Hence, we hypothesized that BPA exposure in PCOS women may alter the metabolic signatures in blood plasma. To test this hypothesis, we recruited 50 PCOS women and 50 healthy women. Urinary BPA levels were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS), a metabolomics strategy that could generate a metabolic signature based on urinary BPA levels. mPCOS and healthy individuals. Towards this, we examined urinary BPA levels in PCOS and healthy women by ELISA and performed univariate and chemometric analysis to distinguish metabolic patterns among high and low BPA in PCOS and healthy females, followed by pathway and biomarker analysis employing MetaboAnalyst 5.0. Our findings indicated aberrant levels of certain steroids, sphingolipids, and others, implying considerable disturbances in steroid hormone biosynthesis, linoleic, linolenic, sphingolipid metabolism, and various other pathways across target groups in comparison to healthy women with low BPA levels. Collectively, our findings provide insight into metabolic signatures of BPA-impacted PCOS women, which can potentially improve management strategies and precision medicine.	Environ Sci Pollut Res Int. 2023 May;30(23):64025-64035.	10.1007/s11356-023-26820-w	37060405	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0246	S. P. Pirinen, M. Heinälä, H. Veijalainen, H. Salo, K. Suvanen, E. Parshintsev and T. Sartonen	2024	Environmental and occupational exposure to bisphenol compounds in Finland	The aim of the study was to assess non-occupational and occupational exposure to bisphenol compounds in Finland. The participants were 351 non-occupationally exposed volunteers and 15 potentially exposed employees of a sewage pipe refining company and a floor coating company. The following chemicals were measured in the urine samples: bisphenol A (BPA), bisphenol F (BPF), bisphenol A diglycidyl ether (BADGE), bisphenol F diglycidyl ether (BFDGE), and the metabolites of the latter two (bisphenol A (2,3-dihydroxypropyl) glycidyl ether (BADGE·H2O), bisphenol A bis(2,3-dihydroxypropyl) ether (BADGE·2H2O), bisphenol A (2-hydroxy-3-chloropropyl) (2,3-dihydroxypropyl) ether (BADGE·H2O·HCl), bisphenol A bis(2-hydroxy-3-chloropropyl) ether (BADGE·2HCl), bisphenol F (2,3-dihydroxypropyl) glycidyl ether (BFDGE·H2O), bisphenol F bis(2,3-dihydroxypropyl) ether (BFDGE·2H2O), bisphenol F (2-hydroxy-3-chloropropyl) (2,3-dihydroxypropyl) ether (BFDGE·H2O·HCl), and bisphenol F bis(2-hydroxy-3-chloropropyl) ether (BFDGE·2HCl). BADGE and BFDGE were also measured in breathing zone air samples, and hand wipe samples of the sewage pipe refining and floor coating workers. Non-occupational exposure to BPA has decreased in Finland. The BPF level of the non-occupationally exposed was higher than the respective levels of BPA, and BPF was detected in 99% of the urine samples. The urinary concentrations of BADGE·2H2O and BADGE·H2O·HCl were significantly higher in the workers than in the non-occupationally exposed. The concentrations of BADGE and BFDGE metabolites were found in some of the workers' urine samples. Elevated urine concentrations were also observed in the workers' urine samples before the next working. Some of the values for BADGE and BFDGE metabolite results correlated with the hand wipe results. The results show that occupational exposure to BADGE and BFDGE may occur in sewage pipe refining and floor coating work. They also indicate that dermal contamination plays a role in total exposure. Although the measured urinary levels indicate that the absorption of these bisphenol compounds are unlikely to pose a systemic health risk, the risk of dermal sensitization remains.	Toxicol Lett Vol.398 Pages 19-27	10.1016/j.toxlet.2024.06.001	38852895	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0247	S. M. Pourmoosaei, M. A. Behmanesh, S. Jarrati and H. Najafzadehvand	2019	Level of Bisphenol A in Follicular Fluid and Serum and Oocyte Morphology in Patients Undergoing IVF Treatment	Objective: To assess the correlation between the levels of BPA in the serum and follicular fluid (FF) using oocyte morphology. Materials and methods: In this cross-sectional research, oocyte, FF, and serum samples were obtained from 2 women's population consisting of 30 women undergoing in vitro fertilization (IVF) treatment. Enzyme-linked immunosorbent assay (ELISA) was used for the measurement of the BPA levels. In addition, oocyte morphology simultaneous with inverted optical microscopy. Results: Follicular fluid BPA levels had no significant effect on MII oocytes (p > 0.05). However, the mean levels of degenerated oocytes and germinal vesicle (GV) were significantly higher in the women with high BPA levels in the FF (p < 0.05). Moreover, the mean counts of MII oocytes and oocytes were significantly higher in the women with serum BPA levels of < 50 ng/ml (p < 0.05), while the mean count of GV oocytes was significantly higher in the women with serum BPA levels of ≥ 100 ng/ml (p < 0.05). Conclusion: According to the results, higher FF BPA levels were associated with the higher counts of GVs and oocytes, while oocytes with higher maturity can be achieved in lower levels of BPA in the serum of patients.	J Family Reprod Health Vol.13 Issue 3 Pages 154-159	-	32201490	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0248	R. C. N. Portnoi, B. A. Rocha, D. M. Garcia, L. A. Pereira, M. C. O. Souza, F. Barbosa, Jr. and E. M. Rocha	2020	Endocrine disrupting chemicals associated with dry eye syndrome	MACHADINHO. Dry eye syndrome (DES) is a multifactorial disease that causes changes in the tear film and occurs more frequently in women. Sex hormones (ShHs) influence tear production, and ShHs imbalance is associated with DES. Endocrine disrupting chemicals (EDCs) are exogenous substances that interfere with the action of ShHs. This study aimed to evaluate the association between exposure to EDCs and DES. This was a cross-sectional study with 200 women (100 in the active group and 100 in the control group). The active group was composed of women with DES, and the control group was composed of women without DES. The DES was confirmed by the Ocular Surface Disease Index (OSDI). DES was considered present when the OSDI score was ≥ 23 and one of the DES tests surpassed the established thresholds. INCLUSION CRITERIA: Women aged 18 to 45 years with regular menstrual cycles (21 to 35 days) and DES diagnosis. EXCLUSION CRITERIA: Pregnancy, breastfeeding, use of hormonal contraceptives, hormone therapy, and the presence of systemic diseases (other than DES) that could affect tear production. The following tests were performed: Schirmer test I (without anesthetic), tear film breakup time (TBUT), corneal fluorescein staining (Oxford scheme), and conjunctival impression cytology (CIC). The following EDCs were quantified in urine samples: bisphenol A (BPA), 2,5-dichlorophenol (2,5-DCP), 2,4-dichlorophenol (2,4-DCP), triclosan (TCS), and methylparaben (MeP). Statistical analysis was performed using the Mann-Whitney test, Fisher's exact test, and logistic regression. The significance level was set at 5%. Women in the active group had lower tear production (Schirmer test I) and TBUT, as well as higher corneal staining and goblet cell loss (CIC). Urinary concentrations of BPA, 2,5-DCP, and TCS were significantly higher in women with DES. Logistic regression showed that BPA, 2,5-DCP, and TCS were associated with DES, even after adjusting for confounding factors. The results suggest that exposure to EDCs, especially BPA, 2,5-DCP, and TCS, may contribute to the development of DES. Public health measures to reduce exposure to these chemicals may be important for preventing this disease.	Ocul Surf. 2020 Jul;18(3):487-493.	10.1016/j.jtos.2020.01.001	31958513	ヒト	-	その他(視聴覚器)	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0249	T. Pollock, S. Karthikeyan, M. Walker, K. Wery and A. St-Amand	2021	Trends in environmental chemical concentrations in the Canadian population: Biomonitoring data from the Canadian Health Measures Survey 2007-2017	Ten years of nationally representative biomonitoring data collected between 2007 and 2017 are available from the Canadian Health Measures Survey (CHMS). These data establish baseline environmental chemical concentrations in the Canadian population and provide an opportunity to examine trends in exposure. Here we present trends in environmental chemical concentrations measured in the first five-year cycles of the CHMS. We identified 94 chemicals that were measured in blood or urine in at least three cycles and had detection rates over 60% in the Canadian population. We calculated geometric mean concentrations for each cycle using the survey weights provided. We then conducted analyses of variance to test for linear trends over all cycles. We also calculated the percent difference in geometric means between the first and most recent cycle measured. Of the 94 chemicals examined, we found statistically significant trends in 66 chemicals. Trends were investigated for 19 chemicals found above detection frequencies in almost all samples, phenols and parabens, organophosphate pesticides, per- and polyfluoroalkyl substances, and phthalates. Significant reductions in chemical concentrations included di-2-ethylhexyl phthalate (DEHP), mono-2-ethylhexyl phthalate (MEHP), mono-ethyl phthalate (MEP), bisphenol A (BPA), triclosan (TCS), and perfluorooctanoic acid (PFOA) which decreased by 38%, 53% and 25%, 35%, 30% and 25% respectively. Trends were increasing for two quantified pesticide metabolites, including a 220% increase between 2007 and 2017 for 3-phenoxybenzoic acid (3-PBA). No significant trends were observed for the remaining 18 chemicals that included arsenic, mercury, fluoride, acrylamide, volatile organic compounds, and polycyclic aromatic hydrocarbons. National biomonitoring data indicate that concentrations, and therefore exposures, have decreased for many priority chemicals in the Canadian population. Concentrations for other chemical groups have not changed or have increased, although average concentrations remain below thresholds of concern derived from human exposure guidance values. Continued collection of national biomonitoring data is necessary to monitor trends in exposures over time.	Environ Int Vol.155 Pages 106678	10.1016/j.envint.2021.106678	34118655	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0250	T. Pollock, T. E. Arbuckle, M. Guth, M. F. Bouchard and A. St-Amand	2021	Associations among urinary triclosan and bisphenol A concentrations and serum sex steroid hormone measures in the Canadian and U.S. Populations	Exposure to triclosan, an antimicrobial agent, and bisphenol A (BPA), the monomer of polycarbonate plastics, is widespread. Endocrine disrupting impacts of these chemicals have been demonstrated in in vitro studies, raised toxicology studies, and some human observational studies. Here we compared survey concentrations of triclosan and BPA in the Canadian and U.S. populations using nationally representative data from the 2013-2014 Canadian Health Measures Survey (CHMS) and the 2013-2016 National Health and Nutrition Examination Survey (NHANES). We then examined the cross-sectional associations of urinary triclosan or BPA with sex steroid hormones, including estradiol (E_2), progesterone (P4), and testosterone (T), using multivariable linear regression. We observed differences in creatinine-adjusted concentrations between countries: urinary triclosan was higher in Canadian females aged 12-19 years, while BPA was higher in U.S. females aged 20-39 years. We also found significant associations among urinary chemicals and serum E_2 and T, but not P4, in females and males of reproductive age (12-39 years). Urinary triclosan was positively associated with E_2 in females aged 12-19 years, and inversely associated with T in females aged 12-19 and 20-39 years and males aged 12-39 years. Urinary BPA was positively associated with E_2 in females aged 20-39 years, and inversely associated with T in females and males aged 20-39 years. We observed sex-shared associations between urinary triclosan and E_2 in male adults aged 40-79 years, as associations between BPA and hormones were detected in adults. These results, in accordance with the in vitro and animal literature, suggest that triclosan and BPA exposures may be cross-sectionally associated with altered reproductive hormone levels, especially in children and adolescents. Further research and prospective studies are necessary to elucidate causal-type specific differences in chemical exposures and the potential public health significance of these findings.	Environ Int Vol.146 Pages 106229	10.1016/j.envint.2020.106229	33161203	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0251	A. Z. Pollack, J. R. Kroll, S. H. Swan and G. M. B. Louis	2022	Does Older Age Modify Associations between Endocrine Disrupting Chemicals and Fecundability?	Urinary concentrations of several endocrine disrupting chemicals, including phthalate metabolites, bisphenol A (BPA), and benzophenone-3(BP)-type ultraviolet (UV) filters, have been associated with a longer time-to-pregnancy (TTP). Potential modification of these associations by couple's age has not been studied. TTP was defined as the number of prospectively observed menstrual cycles until the occurrence of a human chorionic gonadotropin-detected pregnancy. Urinary concentrations of two BP-type UV filters and three phthalate metabolites were measured at baseline. Fecundability ratios and 95% confidence intervals (FR, 95% CI) were estimated using discrete survival models. Among 501 couples, 401 pregnancies occurred within 12 cycles of follow-up. We observed inverse associations between BMP, BBzP, DEHP, BP-3, and BP-8 concentrations and TTP. Associations between BMP, monobenzyl phthalate (MBzP), and BP-3 concentrations and TTP by partner's age, dichotomized at 35 years. Separate models were run for male and female partners. To quantify joint effects modification, we divided the sample into four age-by-BMP categories, but data were suggestive of a longer TTP among females aged ≥35 years, particularly for BP-3 (FR = 0.61, 95% CI: 0.36, 1.08) and 3-hydroxybenzophenone (FR = 0.71, 95% CI: 0.43, 1.09) reflecting 39% and 29% reductions in fecundability, respectively. We saw no evidence of effect modification by couples' age or associations between TTP and urinary phthalates or BPA metabolite concentrations. Across the EDCs, we examined, we found little evidence that age modifies TTP-exposure associations.	Int J Environ Res Public Health. 2022 Jun 30;19(13):8074.	10.3390/ijerph19138074	35805732	ヒト	-	生殖発生	-	-	-	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0252	K. M. Polemi, V. K. Nguyen, J. Heidt, A. Katana, O. Jolliet and J. A. Colacino	2021	Identifying the link between chemical exposures and breast cancer in African American women via integrated in vitro and exposure biomarker data	Among women, breast cancer is the most prevalent form of cancer worldwide and has the second highest mortality rate of any cancer in the United States. The breast cancer related death rate is 40 % higher in non-Hispanic Black women than non-Hispanic White women. Although the incidence rate is lower in Black women than White women, the mortality rate is higher, and the disease is more aggressive and diagnosed at younger ages in Black women than White women. The drivers of these differences are poorly understood. Here, we aimed to identify chemical exposures which may contribute to breast cancer disparities. Using chemical biomonitoring data from the National Health and Nutrition Examination Survey (NHANES) and biological activity data from the EPA's ToxCast program, we assessed the toxicological profiles of chemicals to which US Black women are disproportionately exposed. We conducted a literature search to identify known cancer targets in ToxCast to analyze the response of chemicals with exposure disparities in these assays. Forty-three chemical biomarkers are significantly higher in Black women. Investigation of these chemicals in ToxCast resulted in 23,887 assays for analysis, 10.7% of which contained known values for the concentration at which 50% activity occurs (AC50). Of these assays, 1,572 were associated with cancer. Black women have significantly higher urinary concentrations of 2,5-dichlorophenol, a chemical with known associations to breast cancer, and had higher hormone concentrations in Black women and moderate tanning and activity in ToxCast. The distribution of active concentrations for these chemicals in ToxCast assays are comparable to biomarker concentrations in Black women NHANES participants. Through this integrated analysis, we identify that multiple chemicals, including three, propylparaben, and p,p' DDE, have disproportionate exposures in Black women and have breast cancer-associated biological activity at harm exposure-relevant doses.	Toxicology Vol.463 Pages 152964	10.1016/j.tox.2021.152964	34600088	ヒト	-	バイオマーカー探索	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0253	C. Pirard and C. Charlier	2022	Urinary levels of parabens, phthalate metabolites, bisphenol A and plasticizer alternatives in a Belgian population: Time trend or impact of an awareness campaign?	A human biomonitoring study was carried out in 2015 within an adult population living in Liege (Belgium). Some phthalate metabolites and parabens were measured in the urine of 202 participants, and information were collected about their lead habits. On a pilot, and hence convenient to identify some predictors of exposure. Concomitantly, an awareness campaign was initiated by the Provincial Authorities of Liege and spread over 2 years. These years, later (2018), 92 of the initial participants provided again urine samples, and the levels of phthalate metabolites, phthalate substitute (DEHTA), parabens, bisphenol A and bisphenol alternatives (bisphenol A, F, S and B) were determined and compared to those obtained in 2015 to assess time trends. In 2015, methyl- and ethylparaben were the most abundant ones (GM = 19.2 and 1.1 µg/L, respectively), while propyl- and butylparaben were sparsely detected. Except for minor (2 ethylhexyl phthalate and di (iso-nonyl-propyl) phthalate, all other targeted phthalate metabolites were positively quantified in more than 70% of the samples. Bisphenol A was detected in 98% of the samples (GM = 1.1 µg/L), while bisphenol F was found in 20% of the samples and bisphenol S in 3% only. Significant associations between urinary phthalate metabolites or paraben levels and age, void or urban character of the residence place, and the use of some personal care products. However, all determination coefficients were found revealing that the usual covariates included in the models only explained a small part of the variance. Between 2015 and 2018, levels of parabens and phthalate metabolites significantly decreased from 2.1 to 2.5 fold except for monoethyl phthalate which seemed to remain quite constant. Contrariwise, all bisphenol alternatives and DEHTA metabolites were measured in higher concentrations in 2018 vs 2015 while BPA levels did not differ significantly. However, it was not feasible to unequivocally highlight an impact of the awareness campaign on the exposure levels of the population.	Environ Res Vol.214 Issue Pt 2 Pages 113852	10.1016/j.envres.2022.113852	35820649	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0254	E. M. Philips, S. Santos, E. A. P. Steegers, A. G. Asimakopoulos, K. Kannan, L. Trasande and V. W. V. Jaddoe	2020	Maternal bisphenol and phthalate urine concentrations and weight gain during pregnancy	MACHADINHO. Insufficient or excessive gestational weight gain are associated with increased risks of adverse birth and childhood outcomes. Increasing evidence suggests that exposure to bisphenols and phthalates may disrupt hormonal pathways and thereby influence gestational weight gain. OBJECTIVE: To examine the associations of early and mid-pregnancy bisphenol and phthalate urine concentrations with gestational weight gain and postpartum weight retention. METHODS: In a population-based prospective cohort study in Rotterdam, the Netherlands, we measured bisphenol A and phthalate metabolites in urine samples collected during early pregnancy (median gestational age 13.2 weeks) and mid-pregnancy (median gestational age 20.4 weeks) in 1,550 women. We used linear and logistic regressions to evaluate the associations of bisphenols and phthalates with total gestational weight gain, rate of weight gain, and total and central postpartum weight retention. RESULTS: Higher maternal total bisphenols and bisphenol S were associated with a lower total gestational weight gain at maximal level. Stratification by body mass index group showed that higher total bisphenols and bisphenol S were associated with lower total gestational weight gain specifically in normal weight women (respectively, 95% CI: -915, -100) and -186 g (95% CI: -322, -49)). Each log unit increase in early pregnancy total bisphenol and bisphenol A urine concentrations were associated with lower risk to take pregnancy gestational weight gain in the whole group (effect estimates: -32 g, 95% CI: -60, -4 and -31 g, 95% CI: -59, -3, respectively). Higher bisphenol A urine concentrations were associated with lower postpartum weight retention. Bisphenol and phthalate concentrations were not associated with gestational weight gain. DISCUSSION: Higher maternal bisphenol urine concentrations in early pregnancy may restrict maternal gestational weight in accordance of pregnancy. Further research is needed to assess the effects of maternal bisphenols and phthalates urine concentrations on placental and fetal growth and development.	Environ Int. 2020 Feb;135:105342.	10.1016/j.envint.2019.105342	31864031	ヒト	-	代謝	-	-	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0255	E. M. Philips, V. W. V. Jaddoe, A. Dosterlinck, A. G. Asimakopoulos, K. Kannan, E. A. P. Steegers and L. Trasande	2020	Exposures to phthalates and bisphenols in pregnancy and postpartum weight gain in a population-based longitudinal birth cohort	MACHADINHO. Experimental evidence suggests that exposures to phthalates and bisphenols may interfere with processes related to glucose and lipid metabolism, insulin sensitivity, and body weight. Few studies have considered the possible influence of chemical exposures during pregnancy on maternal weight gain or metabolic health outcomes postpartum. OBJECTIVE: To examine the associations of early and mid-pregnancy bisphenol and phthalate urine concentrations with gestational weight gain and postpartum weight retention. METHODS: In a population-based prospective cohort study in Rotterdam, the Netherlands, we measured bisphenol A and phthalate metabolites in urine samples collected during early pregnancy (median gestational age 13.2 weeks) and mid-pregnancy (median gestational age 20.4 weeks) in 1,550 women. We used linear and logistic regressions to evaluate associations of early and mid-pregnancy bisphenols and phthalate metabolites with weight change. Mediator and interaction models have been used to assess the role of gestational weight gain in the associations with postpartum weight retention. RESULTS: Higher maternal total bisphenols and bisphenol S were associated with a lower total gestational weight gain at maximal level. Stratification by body mass index groups showed that higher total bisphenols and bisphenol S were associated with lower total gestational weight gain specifically in normal weight women (respectively, 95% CI: -915, -100) and -186 g (95% CI: -322, -49)). Each log unit increase in early pregnancy total bisphenol and bisphenol A urine concentrations were associated with lower risk to take pregnancy gestational weight gain in the whole group (effect estimates: -32 g, 95% CI: -60, -4 and -31 g, 95% CI: -59, -3, respectively). Higher bisphenol A urine concentrations were associated with lower postpartum weight retention. Bisphenol and phthalate concentrations were not associated with gestational weight gain. DISCUSSION: Higher maternal bisphenol urine concentrations in early pregnancy may restrict maternal gestational weight in accordance of pregnancy. Further research is needed to assess the effects of maternal bisphenols and phthalates urine concentrations on placental and fetal growth and development.	Environ Int. 2020 Nov;144:106002.	10.1016/j.envint.2020.106002	32745783	ヒト	-	代謝	-	-	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0256	A. Phanumartwiwath, D. Liana and H. Duan	2025	Association of environmental phenol and paraben exposure with allergic biomarkers in eczema: findings from NHANES 2005-2006	Endocrine-disrupting chemicals such as phenols and parabens can promote allergic conditions including eczema. We aimed to analyze the association between exposure to environmental phenols and parabens and allergic biomarkers including total serum immunoglobulin E (IgE), C-reactive protein (CRP), and eosinophils in individuals with eczema, using the dataset from NHANES 2005-2006. This analysis was based on urinary phenol and paraben data, total IgE, CRP, and eosinophil counts from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. Multivariable linear regression models were used to assess associations between log-transformed urinary creatinine-adjusted phenol and paraben concentrations and total IgE, CRP, and eosinophil levels, controlling for potential confounders including demographic and lifestyle factors. Separate models were constructed for each exposure-outcome pair. Sensitivity analyses were conducted using Poisson regression models with robust variance estimation and Cox proportional hazards models with survey weights, respectively. Following data extraction, we obtained 309 individuals with a history of eczema and categorized them by age for analysis. Our findings showed positive correlations between bisphenol A, triclosan, butyl paraben, methyl paraben, and propyl paraben and allergic biomarkers in children with eczema aged 6 to 8 years. Notably, a significant positive correlation was observed between methyl paraben exposure and IgE levels. In adults with eczema, 8 men's polybrene demonstrated a significant positive association with both IgE levels and eosinophil counts. These findings suggest that exposure to these chemicals may exacerbate eczema symptoms.	Arch Dermatol Res Vol.317 Issue 1 Pages 452	10.1007/s00403-025-03981-x	39987402	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0257	W. Peng, M. Tamayo-Ortiz, L. Tang, B. N. Sánchez, A. Cantoral, J. D. Meeker, D. C. Dolinoy, Z. F. Ruberto, E. A. Martinez-Mier, H. Lamadrid-Figueroa, P. K. K. Song, A. S. Ettinger, R. Wright, M. Arora, L. Schnaas, D. J. Watkins, J. M. Goodrich, R. C. Garcia, M. Solano-González, L. F. Bautista-Arredondo, A. Mercado-García, H. Hu, M. Hernández-Avila, M. M. Téllez-Rojo and K. E. Peterson	2019	Early Life Exposure in Mexico to ENvironmental Toxicants (ELEMENT) Project	PURPOSE: The Early Life Exposure in Mexico to ENvironmental Toxicants (ELEMENT) Project is a mother-child pregnancy and birth cohort originally initiated in the mid-1990s to explore: (1) whether enhanced mobilization of lead from maternal bone stores during pregnancy poses a risk to fetal and subsequent offspring neurodevelopment; and (2) whether maternal calcium supplementation during pregnancy and lactation can suppress bone lead mobilization and mitigate the adverse effects of lead exposure on offspring health and development. Through utilization of carefully archived biospecimens to measure other prenatal exposures, banking of DNA and rigorous measurement of a diverse array of outcomes, ELEMENT has since evolved into a major resource for research on early life exposures and children's health. PARTICIPANTS: n=1,643 mother-child pairs sequentially recruited between 1994 and 2002 during pregnancy or at delivery from maternity hospitals in Mexico City, Mexico. FINDINGS TO DATE: Maternal bone (pg_patella, tibia) is an endogenous source of lead exposure for the developing fetus and young child, contributing to blood lead levels, neurodevelopment, and maternal health outcomes. Maternal calcium supplementation has been shown to reduce maternal bone lead mobilization and to protect offspring from lead-related deficits in postnatal growth. Prenatal lead exposure has been associated with deficits in attention, behavior, and cognitive function in childhood and adolescence, with effects on some outcomes modified by sex. Prenatal exposure to manganese, fluoride, and pesticides has been associated with neurodevelopmental outcomes, early life exposure to lead is associated with neurocognitive deficits, behavioral disorders, higher blood pressure and lower weight in offspring during childhood. Some of these relationships were modified by maternal nutritional status. Prenatal exposure to phthalates, bisphenol A, other metals (eg, mercury, manganese, cadmium), and pesticides (organochlorines, organophosphates) have been associated with some outcomes and also by sex. Prenatal exposure to phthalates, bisphenol A, other metals (eg, mercury, manganese, cadmium), pesticides (organochlorines, organophosphates) and fluoride affect hormones (eg, sex steroid hormones), sex ratio at birth, and fertility; other outcomes (eg, sexual maturation, metabolic syndrome, dental caries), and identification of novel mechanisms via epigenetic and metabolomics profiling. FUTURE PLANS: As the ELEMENT mothers and children age, we plan to (1) continue studying the long-term consequences of toxicant exposure during the perinatal period on adolescent and young adult outcomes as well as outcomes related to the original ELEMENT mothers, such as their metabolic and bone health during perimenopause; and (2) follow the third generation of participants (children of the children) to study intergenerational effects of in utero exposures. TRIAL REGISTRATION:CLINICALTRIALS.GOV NCT03509025.	BMJ Open. 2019 Aug 26;9(8):e030427.	10.1136/bmjopen-2019-030427	31455712	ヒト	-	生殖発生	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0258	W. Peng, N. M. Kacper, D. J. Watkins, B. N. Sánchez, J. D. Meeker, A. Cantoral, M. Solano-González, M. M. Téllez-Rojo and K. Peterson	2020	Exposure to Endocrine-Disrupting Chemicals During Pregnancy Is Associated with Weight Change Through 1 Year Postpartum Among Women in the Early-Life Exposure in Mexico to Environmental Toxicants Project	Background: The postpartum period may be a vulnerable life stage for a women's cardiometabolic health. We examined associations of exposure to common endocrine disrupting chemicals (EDCs) during pregnancy with weight change through 1 year postpartum. Methods: We measured 11 urinary EDCs in 1,006 pregnant women from Mexico City. Chemicals included bisphenol A (BPA), two butyl phthalate (BuP) metabolites (MBP, monobutyl phthalate; MHBP, monobutyl phthalate), BENP, mono-2-carboxyethyl phthalate (MCPP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), and monoethyl phthalate (MEP). We calculated summary scores for di-2-ethylhexyl phthalate metabolites (Σ DEHP) and dibutyl phthalate metabolites (Σ DBP). We calculated the geometric mean of each EDC across pregnancy for use in the analysis. At delivery and three additional times during the first year postpartum, we measured the women's weight. We used mixed effects linear regression models to estimate associations of each EDC with weight at delivery (kg) and weight change (kg/year) from delivery through 1 year postpartum. Covariates included maternal age, education, parity, and prepregnancy body mass index (BMI). Results: Each interquartile range increase in Σ DBP was associated with 0.61 kg (95% confidence interval: 0.01, 1.20) greater weight at delivery. Each 10% increase in BPA was associated with 0.08 kg (95% CI: 0.02, 0.14) greater weight at delivery. Each EDCs were inversely associated with weight at delivery, but became positively associated with weight change through 1 year postpartum. For example, each interquartile range of urinary Σ DEHP corresponded with 1.38 (95% confidence interval: 0.66-2.10) kg lower weight at delivery and 1.01 (0.61 - 1.41) kg/year slower rate of weight loss. We observed similar associations for other EDCs. Conclusions: Prenatal exposure to EDCs is associated with lower weight at delivery, but slower rate of weight loss through the first postpartum year.	J Womens Health (Larchmt). 2020 Nov;29(11):1419-1426.	10.1089/jwh.2019.8078	32233978	ヒト	-	生殖発生	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該性評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0259	S. Peng, S. Dong, C. Gong, X. Chen, H. Du, Y. Zhan and Z. Yang	2023	Evidence-based identification of breast cancer and associated ovarian and uterus cancer risk components in source waters from high incidence area in the Pearl River Basin, China	Breast cancer, ovarian cancer, and uterus cancer are among the most common female cancers. They are suspected to associate with exposures to specific environmental pollutants, which remain unidentified in source waters. In this work, we focused on the Pearl River Basin region in China, which experienced a high incidence of breast, ovarian, and uterus cancers. Combining cancer patient data, mammalian cell cytotoxicity analyses, and estrogen receptor-mediated luciferase reporter gene assays, we identified the cancer risk components in source waters and investigated their contributions. Results showed that the cytotoxicity of source waters on the estrogen receptor-mediated pathway. Therefore, the components that have previously been found to enhance the proliferation of estrogen-receptor-containing cells through endocrine disruption could be the crucial factor. Based on this, components that matched with the toxicological characteristics (i.e., estrogen like effect) were further identified in source waters, including (1) organic components: phthalates, bisphenol A, nonylphenols, and per-/polyfluoroalkyls; (2) inorganic components: Ba, Cu, As, and nitrate. Moreover, these identified risk/cancer components were present at levels comparable to other regions with high female cancer prevalence, suggesting that the potential risk of these components may not be exclusive to the study region. Together, multiple levels of evidence suggested that long-term co-exposures to source-water estrogenic components may be important for the development of breast, ovarian, and uterus cancers.	Sci Total Environ. 2023 Dec 10:903:166060.	10.1016/j.scitotenv.2023.166060	37543346	ヒト	発がん	-	-	-	-	-	-	生態学的研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0260	J. Peng, L. L. Du and Q. L. Ma	2023	Serum glycolipids mediate the relationship of urinary bisphenols with NAFLD: analysis of a population-based, cross-sectional study	BACKGROUND: Bisphenol A (BPA) and its substitutes bisphenol S (BPS) and bisphenol F (BPF) are endocrine-disrupting chemicals widely used in consumer products, which have been proposed to induce various human diseases. In western countries, one of the most common liver diseases is non-alcoholic fatty liver disease (NAFLD). However, studies on the associations of the three bisphenols with NAFLD in human beings are scarce. METHODS: We included 885 volunteers aged ≥ 20 years from the NHANES 2013–14 survey. Multivariate logistic regression models were used to evaluate the associations among bisphenols, glycolipid related markers and NAFLD. RESULTS: A total of 160 individuals (18.3%) were diagnosed with NAFLD. Logistic regression analysis and mediation effect analysis were used to evaluate the associations among bisphenols, glycolipid related markers and NAFLD. In the fully adjusted model, BPA and BPS were positively associated with NAFLD. The odds ratio (OR) (95% confidence interval (CI)) of NAFLD for participants in the highest tertile of BPA was 1.789 (95%CI: 1.060,3.019, p = 0.029) after full adjustment for confounders, elevated levels of BPA or BPS but not BPF were significantly associated with NAFLD. The odds ratio for NAFLD was 1.788 (95% confidence interval (CI): 1.2–2.676, p = 0.01) comparing the highest with the lowest tertile of BPS and 1.789 (95%CI: 1.060,3.019, p = 0.021) for BPS. Mediation effect analysis indicated that serum high-density lipoprotein cholesterol and glucose had a mediating effect on the relationships between bisphenols and NAFLD. (CI(BC):(-0.0258). The present study showed that high exposure levels of BPA and BPS increased NAFLD incidence, which might be mediated through regulating glycolipids metabolism. Further studies on the role of bisphenols in NAFLD are warranted.	Environ Health Vol.21 Issue 1 Pages 124	10.1186/s12940-022-00945-w	36588154	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0261	F. J. Peng, P. Palazzi, S. Mezzache, E. Adelis, N. Bourokba, P. Bastien and B. M. R. Appenzeller	2024	Glucocorticoid hormones in relation to environmental exposure to bisphenols and multiclass pesticides among middle aged-women: Results from hair analysis	Bisphenols and pesticides have been shown to alter circulating glucocorticoids levels in animals, but there is limited human data. Moreover, measurements from biological fluids may not be able to reflect long-term relationships between exposure to these compounds and glucocorticoids. Hair is a promising matrix for the assessment of long-term exposure to environmental pollutants. We investigated the associations between exposure pollutants among a healthy female population aged 25–55 years old. Concentrations of four glucocorticoids, four polychlorinated biphenyl congeners (PCBs), seven polychlorinated diphenyl ether congeners (PBDEs), two bisphenols and 126 pesticides and their metabolites were measured in hair samples collected from 196 Chinese women living in urban areas. Due to the low detection frequency of some pollutants, statistical analyses were performed on 4 PCBs, 5 PBDEs, 2 bisphenols, 11 pesticides and 4 glucocorticoids. Associations between pollutants (log-transformed), metabolic syndrome components (waist circumference, triglycerides, blood pressure, fasting glucose, and HDL-cholesterol), and glucocorticoids (cortisol, cortisone, and tetrahydrocortisone with S4, S5, S6 and S7 biomarkers of exposure to carbendazim, respectively), with bisphenol S, 4,4'-dichlorodiphenyldichloroethylene, and beta-cypermethrin (synthetic) biomarkers, were analyzed using multivariate linear regression models adjusted for age, BMI, menopausal status, and education level. Principal component analysis was performed to identify latent exposure patterns between various functional meta-estrogens and pollutants, namely dimethyl phosphate, 3-methyl-4-nitrophenol, cadmium, 2-cyclohexo, permethrin, fipronil, fluxtiazole, pirimiphos and benzovin. Some of these relationships were confirmed by single pollutant linear regression analyses. Overall, our results suggest that background level of exposure to bisphenols and currently used pesticides may interfere with the glucocorticoid homeostasis in healthy women.	Environ Pollut Vol.348 Pages 123839	10.1016/j.envpol.2024.123839	38522601	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0262	F. J. Peng, E. M. Hardy, R. Bérenger, S. Mezzache, N. Bourokba, P. Bastien, J. Li, L. C. Zeisa, C. Chevrier, P. Palazzi, J. Sosa and B. M. R. Appenzeller	2020	Human exposure to PCBs, PBDEs and bisphenols revealed by hair analysis: A comparison between two adult female populations in China and France	Humans are exposed to various anthropogenic chemicals in daily life, including endocrine-disrupting chemicals (EDCs). However, there are limited data on chronic, low-level exposure to such contaminants among the general population. Hair-based analysis was used to investigate the occurrence of four polychlorinated biphenyls (PCBs), seven polybrominated diphenyl ethers (PBDEs) and two bisphenols (BPs) in 261 Chinese women from Wuhan and 100 French women from Nancy. Concentrations of PCBs, PBDEs and BPs were detected in 100%, 100% and 97% of the samples, respectively, indicating widespread exposure to these EDCs among the women. In both cohorts, PCB 180 and BDE 47 were the dominant PCB and PBDE congener, respectively. PCB 180 was found in 82% of the French women and 46% of the Chinese women, with corresponding values for BDE 47 were 58% and 23%, respectively. A discriminant analysis further demonstrated the differences in PCBs and PBDEs exposure profile between the two cohorts. These results demonstrate that hair analysis is sufficiently sensitive to detect exposure to these pollutants and highlight differences in exposure between populations even at environmental levels. Although BPA and BPS were found in 100% of the hair samples in both cohorts, the French women had significantly higher levels of BPA and BPS than the Chinese women. The median concentrations of BPA were one order of magnitude higher than BPS in both the Chinese (16.9 versus 1.83 pg/mg) and the French women (128 versus 9.01 pg/mg respectively). Our results suggest that both French and Chinese populations were extensively exposed to BPS and BPF.	Environ Pollut Vol.267 Pages 115425	10.1016/j.envpol.2020.115425	32882460	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0263	C. Y. Peng, E. M. Tsai, T. H. Kao, T. C. Lai, S. S. Liang, C. C. Chiu and T. N. Wang	2019	Canned food intake and urinary bisphenol a concentrations: a randomized crossover intervention study	Bisphenol A (BPA) is an endocrine disruptor. To evaluate the effect of canned food consumption on internal BPA dose, urinary BPA concentrations were measured before and after intake of canned foods. This study recruited 75 healthy participants who were randomly assigned to consume canned food (n = 38) or fresh food (n = 37) for 5 days. Urine samples were collected at 0 h, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h, 24 h, 36 h, 48 h, 60 h, 72 h, 84 h, 96 h, 108 h, and 120 h after the intervention started. Second-void urine samples were collected immediately before meals and 2 h after meals. A mixed-effects model was used to analyze the data. Our results showed urinary BPA concentrations increased after consumption of canned food. Specifically, urinary BPA concentrations significantly differed between consumption of canned food and fresh food at 2 h, 4 h, and 6 h after intake (p values of 0.001, < 0.001, and < 0.001, respectively). Mean BPA concentrations at 2 h, 4 h, and 6 h after meals were 2.5-fold, 2.4-fold, and 1.9-fold higher, respectively, than the BPA concentrations before meals. Urine concentration profiles of canned food intake showed that peaks were at 2 h, the increase diminished at 6 h, and returned to baseline levels at 24 h after intake. Therefore, dietary intervention and a 1-day washout period are effective for limiting internal BPA burden. This study provides convincing evidence of a human exposure route to BPA and a basis for designing interventions to mitigate exposure.	Environ Sci Pollut Res Int Vol.26 Issue 27 Pages 27999-28009	10.1007/s11356-019-05534-y	31352597	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0264	K. Pelch, J. A. Wignall, A. E. Goldstone, P. K. Ross, R. B. Blain, A. J. Shaughn, S. D. Holmgren, J. H. Hsieh, D. Svoboda, S. S. Auerbach, F. M. Parham, S. A. Masten, V. Walker, A. Rooney and K. A. Thayer	2019	A scoping review of the health and toxicological activity of bisphenol A (BPA) structural analogues and functional alternatives	Recent studies report widespread usage or exposure to a variety of chemicals with structural or functional similarity to bisphenol A (BPA), referred to as BPA analogues or derivatives. These have been detected in foodstuffs, house dust, environmental samples, human urine or blood, and consumer products. Compared to BPA, relatively little is known about potential toxicity of these compounds. This scoping review aimed to characterize the peer-reviewed literature on BPA analogues and to identify potential hazards associated with exposure to these chemicals. We identified 14 BPA analogues for which 741 records were compiled from literature searches conducted through March 15, 2018, in The National Toxicology Program's Research Report 8 (NTP RR-8), Systematic Review of Bisphenol A (BPA) Structural Analogues and Functional Alternatives". Study details are presented in interactive displays using Tableau Public. In total, 1218 records were screened for inclusion. One hundred sixty seven studies were included from NTP RR-8 and 175 studies were included from the updated literature search through April 2018. In total, there are 22, 127, and 231 human epidemiological, experimental animal, or in vitro studies included. The most frequently studied BPA analogues are bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF). Notable changes in the literature since 2013 include the growing body of human epidemiological studies and in vivo rodent studies, the emergence of in vitro high-throughput screening data, and the publication of physiologically based pharmacokinetic (PBPK) models for BPS and BPF. Across all evidence streams, the most neurodevelopmental outcomes or impacts on the developing mammary or prostate glands, which are known to be susceptible to disruption by BPA. Further, there remains a critical need for better exposure information in order to prioritize experimental studies. Moving forward, researchers should also ensure that full dose-response are performed for all main effects. In order to support hazard and risk characterization efforts. The evidence gathered here suggests that hazard and risk characterizations should expand beyond BPS in order to consider BPA structural and functional analogues.	Toxicology. 2019 Aug 1:424:152235.	10.1016/j.tox.2019.06.006	31201879	ヒト、in vitro	-	-	-	-	-	-	スコープレビュー	1	1	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0265	F. M. Peirado, I. Landínez, R. Solelo, L. M. Iribarne-Durán, J. Fernández-Parra, F. Vela-Soria, N. Olea, M. F. Fernández, C. Freire, J. Lozano, B. Pérez-Cabrera, O. Ocón-Hernández and F. Artacho-Cordón	2020	Association of Urinary Levels of Bisphenols A, F, and S with Endometriosis Risk: Preliminary Results of the EndEA Study	Aim: The aim of this study was to explore associations of urinary concentrations of bisphenols A (BPA), S (BPS), and F (BPF) and of thiobutiric acid reactive substances (TBARS) with the risk of endometriosis in women undergoing surgery. Methods: The EndEA study is a case-control study. Cases were women undergoing surgery for endometriosis, and controls were women undergoing surgery for other reasons (controls). Endometriosis was diagnosed (cases) or ruled out (controls) by laparoscopic inspection of the pelvis and the biopsy of suspected lesions. Histological diagnosis. Fasting urine samples were collected before surgery to determine concentrations of BPA, BPS, BPF, and TBARS. Associations of bisphenol and TBARS concentrations with endometriosis risk were explored with multivariate logistic and linear regression analyses. Results: After adjustment for urinary creatinine, age, BMI, parity, and smokers, endometriosis risks were increased in cases (n = 39) with BPA (OR 1.5; 95%CI 1.1–2.2) and bisphenols (OR 1.6; 95%CI 0.9–2.7) but were not associated with the presence of BPS and BPF. Classification of the screen by tertiles of exposure revealed statistically significant associations between endometriosis risk and the highest tertiles of BPA (OR 3.0; 95%CI 1.1–8.2) and bisphenols (OR 3.3; 95%CI 1.1–9.9). Urinary concentrations of TBARS were also associated with endometriosis risk (OR 2.4; 95%CI 1.0–5.7). Associations between bisphenols and TBARS (β 0.2; 95%CI 0.0–0.5) and TBARS and endometriosis (β 0.2; 95%CI 0.0–0.5) were also statistically significant. Conclusion: Exposure to bisphenols may increase the risk of endometriosis, and oxidative stress may play a crucial role in this association. Further studies are warranted to verify these findings.	Int J Environ Res Public Health. 2020 Feb 13;17(4):1194.	10.3390/ijerph17041194	32069886	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0266	F. M. Peirado, L. M. Iribarne-Durán and F. Artacho-Cordón	2023	Human Exposure to Bisphenols, Parabens, and Benzophenones, and Its Relationship with the Inflammatory Response: A Systematic Review	Bisphenols, parabens (PNs), and benzophenones (BPs) are widely used environmental chemicals that have been linked to several adverse health effects due to their endocrine-disrupting properties. However, few articles have reviewed the relationship between exposure to these chemicals and the inflammatory response in humans. The aim of this study was to review the scientific literature published to date to provide evidence on the relationship between human exposure to these chemicals and levels of inflammatory biomarkers. A systematic review of peer-reviewed original research articles published up to February 2022 was conducted using the MEDLINE, Web of Science, and Scopus databases. A total of 28 articles met the inclusion/exclusion criteria. Most of the reviewed studies reported significant associations between any of the assessed chemicals/metabolites and inflammatory biomarkers (including C-reactive protein and interleukin-6, among others). Taken together, this systematic review has identified consistent positive associations between human exposure to some chemicals and levels of pro-inflammatory biomarkers, with very few studies exploring the associations between PNs and/or BPs and inflammation. Therefore, a larger number of studies are required to get a better understanding on the mechanisms of action underlying bisphenols, PNs, and BPs and the critical role that inflammation could play.	Int J Mol Sci Vol.24 Issue 8	10.3390/ijms24087325	37108488	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0267	Z. Pei, L. Zhang, Y. Bao, J. Li and Q. Zhuo	2025	The negative impacts of bisphenols on thyroid function in adults with bisphenol A exposure level exceeding the tolerable daily intake	In 2023, European Food Safety Authority (EFSA) published a re-evaluation of the safety of bisphenol A (BPA), establishing the new tolerable daily intake (TDI) as 0.2 ng/kg bw/day with a 20,000-fold reduction compared to 2015, which reignited public concern about the impact of bisphenols (BPs) on human health. In order to explore the health risk to thyroid function of BPs, in this study, we examined the internal exposure levels of BPs and the relationships between urinary BPs and thyroid function in general adults. We carried out a cross-sectional study in Chengdu, China, recruiting 1189 adults without special tendencies and diseases. Aged 18–60, and collected their urine samples and questionnaire information. Urinary concentrations of BPA, BPS, BPF, BPAF, BPB, BPP, BPZ, and BPTMC were detected by UPLC-MS/MS. The results showed that the detection rates of BPA, BPS, BPF, BPAF, BPB, BPP, BPZ, and BPTMC were 99.7%, 98.2%, 97.6%, 0.3%, 0.3%, 0.3%, 0.3%, and 0.3%, respectively. The concentrations of BPA were significantly higher than other BPs, with a median value of 1.61 ng/mL, which was nearly two orders of magnitude. Using multivariate regression models, we observed a negative association between BPA and T3 and TT3 (P < 0.05). Trend tests indicated that higher BPA levels were correlated with higher rates of subclinical hypothyroidism (SCH) in males (OR=1.283, 95 % CI (1.024, 1.607)). We also observed that bisphenol F (BPF) contributed to the occurrence of thyroid globulin antibody positivity (TGAb+) in both males and females. Although the use of BPs has been restricted, the adverse health effects still deserve public attention.	Ecotoxicol Environ Saf Vol.290 Pages 117790	10.1016/j.ecoenv.2025.117790	39862696	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0268	M. M. Poulsen, N. Iszatt, A. K. Sakhi, M. Kvalvi, S. L. Brodwell, E. Papadopoulou, H. M. Wetlesen, B. Granum, A. L. Brantsæter, C. Thomsen and L. S. Haug	2025	Environmental contaminants, heavy metals, and essential elements in Norwegian children and adolescents: Data from the Norwegian environmental biobank	We are daily exposed to various environmental contaminants, including heavy metals, with suspected adverse health effects, and children's vulnerability is particularly concerning. Human biomonitoring is crucial for assessing exposure and potential health risks. The Norwegian Environmental Biobank (NEB) is a national biobank established to monitor environmental contaminants in human samples. Collecting blood and urine and questionnaire data systematically since 2018, identifying population subgroups at elevated risk is essential for implementing protective measures. This study aimed to describe concentrations of environmental contaminants and essential elements in Norwegian children and explored potential clustering among different contaminants. Additionally, we examined differences across groups defined by family socioeconomic factors, dietary patterns, and contaminant concentrations. Blood samples from 1,000 children aged 2–17 years were collected from 2018 to 2021. Concentrations of 24 environmental contaminants were quantified in 1,927 ml of the samples, along with nine essential elements. Mixture-related contaminant levels were assessed using Quantile-based g-computation (QGC). Moreover, exceedance of children-specific blood lead (Pb-B) levels exceeding the updated tolerable daily intake set by the European Food Safety Authority (EFSA), and 50 % lead blood concentrations of the four most common per- and polyfluoroalkyl substances (PFAS) exceeding EFSA's old criteria. Statistically significant differences in contaminant levels were observed between groups defined by sociodemographic variables such as sex, age, region, and degree of urbanization. Network analysis indicated clear clusters of correlated contaminants. This study shows that Norwegian children are exposed to a broad range of environmental contaminants, with levels similar to those reported in other studies from Europe and globally.	Environ Int Vol.202 Pages 109633	10.1016/j.envint.2025.109633	40614348	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0269	M. M. Poulsen, L. S. Haug, A. K. Sakhi, C. Thomsen and A. L. Brantsæter	2025	Associations between dietary patterns and environmental contaminants in children from the Norwegian Environmental Biobank: A cross-sectional analysis	Diet is a well-known source of environmental contaminants. This cross-sectional study explored children's dietary patterns and their associations with contaminant exposure in the Norwegian Environmental Biobank. Parent-completed questionnaires provided data on children's frequency of intake of 30 foods and beverages, and socio-demographics. Several environmental contaminants were measured in urine, plasma, and whole blood from the children. Data were available for 898 children aged 7–13 years. Two dietary patterns, denoted "healthy" and "unhealthy," were identified using data-driven factor analysis. We examined associations between diet, dietary patterns and contaminant concentrations, using linear regression, adjusting for potential confounders. Children's mean age was 10.1 years, and 51.2 % were girls. The healthy pattern was positively associated with urinary bisphenol A (BPA) concentration. Likelihood of exceeding health-based guidance value (HBM-GV) was examined using generalized linear model with Poisson family and log-link function. Children in the highest tertile of the healthy pattern had a 1.39 (95 % CI: 1.04, 1.86) times higher likelihood of exceeding the HBM-GV for BPA, compared to children in the lowest tertile. The unhealthy pattern was positively associated with urinary concentrations of bisphenol S (BPS) and plasma concentrations of perfluorooctanoic acid (PFOA). Multiple regression analyses showed that age and total breastfeed consumption were associated with higher BPA (β: 0.05, and 0.14, and 0.1) higher concentrations per additional month, year, serving, respectively ($P < 0.001$). For the sum of urinary dichlorophenols (2,4-dichlorophenol (2DCP), 2,5-dichlorophenol (2,5DCP)), 32 % higher concentration was observed per weekly serving of sweets/desserts. The urinary BPA concentration was 3 % higher per extra weekly serving of fast food ($P = 0.001$). These results highlight the need for societal measures to reduce contaminant exposure through food.	Environ Res Vol.280 Pages 121871	10.1016/j.envres.2025.121871	40381717	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0270	J. Patel, H. Chaudhary, S. Panchal, B. Parekh and R. Joshi	2024	Connecting Bisphenol A Exposure to PCOS: Findings from a Case-Control Investigation	Polycystic Ovary Syndrome (PCOS) is a multifaceted condition influenced by genetic, hormonal, and environmental factors. Among environmental factors, Bisphenol A (BPA) a recognized endocrine disruptor has been implicated in the development of PCOS. The study aimed to compare BPA levels in women diagnosed with PCOS with those in healthy controls, using the high-performance liquid chromatography (HPLC) technique. The study included 100 participants, 50 PCOS patients and 50 healthy controls, aged 18–40 years, recruited from Ahmedabad, Gujarat. Blood samples were collected from each participant and underwent centrifugation to separate serum. Serum samples were then subjected to BPA extraction using the Solid Phase Extraction technique followed by HPLC analysis. Clinical parameters such as Body Mass Index (BMI), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Dehydroepiandrosterone Sulfate (DHEA-S), Thyroid-Stimulating Hormone (TSH), and Anti-Müllerian Hormone (AMH) were also measured. The World Assessment Model (WAM) HPLC Furthermore, BPA levels were measured using the HPLC technique. Women with PCOS exhibited significantly higher mean age and BMI compared to healthy controls ($p < 0.01$, $p < 0.0001$ respectively). Additionally, higher levels of testosterone ($p < 0.01$), LH ($p < 0.01$) and AMH ($p < 0.0001$) were observed in women with PCOS. However, estradiol, FSH, TPG, LH/FSH ratio, and TSH levels were not significantly different between the two groups. HOMA-IR levels were not recorded for the control group. A notable positive relationship emerged between Bisphenol A and luteinizing hormone (LH) levels ($r = 0.72$, $p < 0.05$), also significant negative correlation appeared between Bisphenol A and thyroid-stimulating hormone (TSH) levels. This study found that women with PCOS have elevated BPA levels compared with healthy controls, showing a need for further research on the relationship between BPA exposure and the development of PCOS.	Reprod Sci. 2024 Aug;31(8):2273-2281.	10.1007/s43032-024-01548-1	38637475	ヒト	卵巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0271	J. Patel, H. Chaudhary, S. Panchal, T. Joshi and R. Joshi	2024	Endocrine-disrupting chemicals and hormonal profiles in PCOS women: A comparative study between urban and rural environment	Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrine disorder, affects a significant proportion of women globally, with its etiology rooted in both genetic and environmental factors. This study delves into the environmental aspect, particularly focusing on the role of endocrine-disrupting chemicals (EDCs) in the context of urbanization and industrialization. This research examines the impact of endocrine-disrupting chemicals (EDCs) - Bisphenol A (BPA), Mono-ethyl Hexyl Phthalate (MEHP), and Di-ethyl Hexyl Phthalate (DEHP) - on 40 women with Polycystic Ovary Syndrome (PCOS) across urban and rural Gujarat. Employing High-Performance Liquid Chromatography (HPLC), the study quantifies these EDCs in urine samples and correlates their levels with hormonal profiles, including testosterone, LH, FSH, and AMH concentrations, highlighting the environmental exposure differences. Notably, urban exposure to MEHP and DEHP correlated with a marked decrease in estradiol levels, while rural DEHP exposure was associated with an increase in estradiol but a decrease in prolactin and DHEAS levels. These findings illuminate the variable effects of EDC exposure on hormonal profiles in PCOS, influenced by geographical and environmental contexts. The study underscores the critical need for tailored environmental health policies to mitigate the diverse impacts of EDCs, advocating for a nuanced approach in PCOS management that considers environmental exposures. Our insights contribute to the understanding of PCOS's hormonal dynamics, emphasizing the significance of addressing EDC exposure in different settings.	Reprod Toxicol Vol.125 Pages 108562	10.1016/j.reprotox.2024.108562	38417580	ヒト	-	-	-	-	-	-	比較研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

曝露性評価（動物）1：該当、0：該当しない　曝露性評価（疫学）1：該当、0：該当しない　曝露性評価（in vitro）1：該当、0：該当しない　曝露性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに曝露性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で除害に基づき除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	曝露性評価基準適合論（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0272	J. Patel, H. Chaudhary, S. Panchal and R. Joshi	2025	Plasticizer exposure and reproductive dysfunction: Assessing bisphenol A and phthalate esters impact on ovarian reserve in women with PCOS-associated infertility	Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder among women of reproductive age, frequently causing infertility. This study investigates the influence of endocrine disrupting chemicals (EDCs) on ovarian reserve parameters in women with PCOS-related infertility. A cohort of 92 women with PCOS, aged 29.92 ± 3.64 years, was recruited from Dr. Nagori's Institute for Infertility in Ahmedabad, Gujarat. Serum level of bisphenol A (BPA) and phthalate esters (DEHP, DBP, BBP, DEP) were measured using HPLC and GC-MS, respectively. Ovarian reserve was assessed through antral follicle count (AFC) and anti-Müllerian hormone (AMH) levels. Hormonal profiles and metabolic parameters were also analyzed. Correlations between EDCs and ovarian reserve markers were evaluated using Pearson correlation and regression analysis. The study found serum mean levels of BPA (77.80 ± 51.82 ng/ml), MEHP (37.43 ± 19.81 µg/ml), and DEHP (5.77 ± 7.21 µg/ml). Participants exhibited typical PCOS hormonal imbalances, including elevated LH/FSH ratios and increased testosterone levels. Correlation analysis revealed a positive relationship between BMI levels and AFC (r = 0.417, p = 0.01). However, no significant associations were found between EDC exposure and ovarian reserve markers. A high prevalence of adenomyosis and bilateral polycystic ovaries was noted among the participants. While metabolic and hormonal disruptions are prominent in PCOS, the direct impact of EDCs on ovarian reserve parameters appears minimal. This study highlights the necessity of addressing metabolic health and environmental exposures in managing PCOS-related infertility to improve reproductive outcomes.	Reprod Toxicol. 2025 Aug;135:108949.	10.1016/j.reprotox.2025.108949	40379154	ヒト	卵巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0273	M. Pastor-Garcia, S. Gimeno-Martos, Ó. Zuniga, J. V. Sanfi and C. Cuenca-Carbunell	2020	[Congenital heart defects in the Valencian Community 2007-2014: The Population-Based Registry Of Congenital Anomalies]	INTRODUCTION: Congenital heart defects (CHDs) are the most prevalent and severe type of major congenital anomalies. (Cita). The objective of this study was to determine the frequency and distribution of CHDs in the Valencian Region from 2007 to 2014, describing common characteristics of the patients and their mothers. MATERIAL AND METHODS: We retrieved data on CHDs in live births, stillbirths and cases of termination of pregnancy for fetal anomaly between 2007 and 2014 (codes Q20-Q26 in the 10th Revision of the International Classification of Diseases-British Paediatric Association, ICD10-BPA) from the population-based Registry of congenital anomalies of the Valencian Region. We calculated the prevalence per every 10,000 births of CHDs overall and by subtype, analyzed temporal trends and the geographic distribution of cases, and documented the characteristics of the mothers and patients. RESULTS: We registered 1,534 cases of CHDs (1,512 live births, 19 stillbirths and 3 terminations of pregnancy). The overall prevalence was 127.9 (95% confidence interval [CI], 121.6-134.4) per 10,000 births, which remained stable throughout the study period. The most frequent CHDs were ventricular septal defects, atrial septal defect and patent ductus arteriosus (38.1 [CI, 35.2-41.1], 19.4 [CI, 17.4-21.5] and 13.9 [CI, 12.2-15.8] per 10,000 births, respectively). The most frequent associated extracardiac malformations were musculoskeletal, and 30.5% of patients had syndromes. The most frequent maternal diseases were diabetes mellitus, hypothyroidism and urinary tract infections. CONCLUSIONS: The prevalence of CHD and atrial septal defects was higher compared to European data, while the prevalence of ventricular septal defects was similar. Musculoskeletal malformations were the noncardiac CAs most frequently associated with CHDs.	An Pediatr (Engl Ed). 2020 Jan;92(1):13-20.	10.1016/j.anpedi.2018.12.019	31122878	ヒト	生殖発生	-	-	-	-	-	-	疫例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0274	S. Y. Park, J. H. Jeon, K. Jeong, H. W. Chung, H. Lee, Y. A. Sung, S. Ye and E. H. Ha	2021	The Association of Ovarian Reserve with Exposure to Bisphenol A and Phthalate in Reproductive-aged Women	BACKGROUND: Exposure to endocrine disrupting chemicals (EDCs) that influence the hormonal and homeostatic systems is known to be associated with gynecologic health risks in many countries. In this study, we evaluated exposure to EDCs, associated with diminished ovarian reserve (DOR) and gynecologic health risks. METHODS: This cross-sectional study was performed from September 2013 to November 2015 and included 307 Korean reproductive-aged women. Anthropometric measurements, laboratory tests with urine and blood sampling and pelvic ultrasound examinations were performed. RESULTS: Urinary bisphenol A (BA-B) level was significantly higher in the DOR group than in the non-DOR group (1.5 ± 0.1 vs. 1.2 ± 0.1 ng/mL, p = 0.042). Urinary phthalate metabolite concentrations were not significantly different between the two groups. In the DOR group, urinary BA-B was significantly correlated with age, body mass index, and urinary BPA levels. Logistic regression analysis suggested an increase in infertility in high BPA exposure group and the odds ratio (OR, 1.038) was statistically significant after adjustment for age, birth control pills, and the age of menarche, parity, and waist circumference. High phthalate exposure was associated with endometrial polyp after adjustment (OR, 2.782; CI[95%] 1.0555-7.3). CONCLUSIONS: BPA exposure might be associated with DOR and infertility. Meanwhile, endometrial polyp is increased in women with high phthalate exposure. Therefore, the risk of exposure to EDCs for reproduction should be a matter of concern in reproduction-aged women.	J Korean Med Sci Vol.36 Issue 2 Pages e1	10.3346/jkms.2021.36.e1	33429469	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0275	S. Park and C. Chung	2021	Effects of a dietary modification intervention on menstrual pain and urinary BPA levels: a single group clinical trial	BACKGROUND: Exposure to endocrine disrupting chemicals (EDCs) occurs mainly through dietary intake. Due to current lifestyle trends, young people tend to consume fast food, to eat disposable products, and to utilize plastic containers frequently. Exposure to EDCs is known to be associated with menstrual pain, which is a common symptom experienced by women during their reproductive years. Most women suffer from menstrual pain during their menstrual cycles. In female college students who experienced severe menstrual pain, We also analyzed participants' adherence to the intervention and examined whether their level of adherence was associated with differences in the effects of the intervention. METHODS: A single group pretest and repeated posttest experimental design was employed. Thirty female college students with a score of 5 or higher on a menstrual pain scale were recruited through convenience sampling. During three menstrual cycles, menstrual pain was scored on a 10-point scale for each cycle, and urinary BPA levels were measured from the first spot urine collected after each cycle. The intervention involved three components: small group education, follow-up monitoring, and peer support via social network communication. Statistical analyses were conducted using repeated measures analysis of variance (RM-ANOVA) and generalized estimating equations (GEE). RESULTS: The RM-ANOVA ($F = 3.16$, $p = 0.048$) and GEE ($\chi^2 = 6.16$, $p = 0.013$) results revealed statistically significant effects on menstrual pain scores at all three time points of menstrual cycles 2 ($t = -2.84$, $p = 0.008$) and cycle 3 ($t = -2.84$, $p = 0.008$) when compared with baseline. We had significant effects on menstrual pain scores at all three time points of menstrual cycles 2 ($t = -2.84$, $p = 0.008$) and cycle 3 ($t = -2.84$, $p = 0.008$) when compared with baseline. Urinary BPA levels also decreased significantly ($F = 7.96$, $p = 0.006$), but did not differ according to adherence level. CONCLUSIONS: The dietary modification intervention was effective and sustainable for reducing menstrual pain, and urinary BPA levels. Detailed information about EDCs, and dietary experiences centered to encourage the young women to become more concerned about EDCs and to perform self-protective actions. Further experimental research is suggested to examine the relationships of EDCs with various health indicators. (trial no. TRN: KCT0005778, KCT0006372 on 2019-11-5 retrospectively registered.	BMC Womens Health. 2021 Feb 9;21(1):58.	10.1186/s12905-021-01199-3	33563271	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0276	C. Park, M. Hwang, Y. Baek, S. Jung, Y. Lee, D. Paek and K. Choi	2019	Urinary phthalate metabolite and bisphenol A levels in the Korean adult population in association with sociodemographic and behavioral characteristics: Korean National Environmental Health Survey (KoNEHS) 2012-2014	BACKGROUND: Phthalates and bisphenol A (BPA) have been used in a variety of consumer products, and are detected widely in both humans and the environment. Demographic and socio-economic characteristics like gender, age, and household income have been associated with exposure to phthalates and BPA in previous studies. However, the results have been inconsistent. Also, there is relatively little is known about the socio-demographic characteristics that influence exposure to these chemicals among nationally representative populations of Asia. METHODS: Data are obtained from the Korean National Environmental Health Survey (2012-2014). In total, 6,078 adults (aged 19 and older) were recruited and sampled for urinary levels of major phthalate metabolites and bisphenol A. In addition, demographic and behavioral characteristics were collected through questionnaires. Multivariate linear regression models were used to examine the associations between the urinary levels of BPA, phthalate diester (DEHP) and phthalate (DBP) metabolites of Korean adults (aged 19 and older). RESULTS: Urinary bisphenol A (BPA) levels were higher than those reported from adults in the United States and Canada. Similar to other nationally representative populations, females and older adults showed higher creatinine-adjusted phthalate metabolite and BPA levels among the Korean population. Meanwhile, monthly household income and education were negatively associated with urinary phthalate metabolites. Among personal care products, nail polish use was positively associated with both phthalate metabolites and BPA concentrations. In urine. CONCLUSIONS: Our observations, based on a nationally representative population of Korea show that socio-demographic determinants for these urinary chemicals vary by country, and should be considered for developing appropriate mitigation measures, and policies.	Int J Hyg Environ Health Vol.222 Issue 5 Pages 903-910	10.1016/j.ijheh.2019.02.003	30773337	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0277	H. Parada, Jr., M. D. Gammon, H. L. Ettore, J. Chen, A. M. Calafat, A. I. Neugut, R. M. Santella, M. S. Wolff and S. L. Teitelbaum	2019	Urinary concentrations of environmental phenols and their associations with breast cancer incidence and mortality following breast cancer	BACKGROUND: Environmental phenols, compounds used widely in personal care and consumer products, are known endocrine disruptors. Few epidemiologic studies have examined the association of phenol biomarkers with breast cancer incidence and survival. METHODS: We measured urinary concentrations of 11 phenols in spot samples collected on average within three months of diagnosis among 1,508 women with breast cancer and subsequent mortality, and examined their exposure modification by body mass index (BMI). METHODS: Participants included 711 women with breast cancer and 698 women without breast cancer who were interviewed for the population-based Long Island Breast Cancer Study Project. Among women with breast cancer, phenol biomarkers were quantified in spot urine samples collected on average within three months of a first diagnosis of primary in situ or invasive breast cancer. In 1996-1997, Women with breast cancer were followed for died cases using the National Death Index. After a median follow-up of 17.9 years, we identified 276 deaths, including 98 deaths from breast cancer. We examined creatinine-corrected phenol concentrations and the sum of parabens (7 parabens) in association with breast cancer incidence using logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs), and breast cancer mortality using Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs. We used restricted cubic spline models to evaluate nonlinear trends in nested models. RESULTS: The highest (vs lowest) quintiles of urinary methylparaben, propylparaben, and 3 parabens were associated with risk of cancer mortality HRs ranging from 0.58 to 0.77. Associations for breast cancer incidence were more pronounced among women with BMI < 25.0 kg/m2 than among women with BMI ≥ 25.0 kg/m2; however, associations for mortality were more pronounced among women with BMI ≥ 25 kg/m2 than among women with BMI < 25 kg/m2. CONCLUSIONS: Select parabens may have differential associations with risk of developing breast cancer and mortality following breast cancer.	Environ Int. 2019 Sep;130:104890.	10.1016/j.envint.2019.05.084	31228785	ヒト	発がん	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0278	D. Paoli, F. Pallotti, A. P. Dima, E. Albani, C. Aloigi, F. Cavolo, C. C. Dioguardi, A. Conforti, R. Cosimina, G. Falcucci, G. Giuffrida, R. Guattieri, M. G. Minasi, S. Ochetti, V. Pirotano, C. Racca, L. Rienzi, E. Savina, C. Scanzi, G. Tomasi, C. Verlengia, R. Villeggia, F. Zullo, A. Lenzi, F. Baldi and L. De Santis	2020	Phthalates and Bisphenol A: Presence in Blood Serum and Follicular Fluid of Italian Women Undergoing Assisted Reproduction Techniques	BACKGROUND: Infoliculogenesis is a strictly regulated process that may be affected by endocrine disrupting chemicals (EDCs) through sometimes not so clear molecular mechanisms. METHODS: we conducted a multicentric observational study involving six fertility centers across Italy, prospectively recruiting 132 women attending a fertility treatment. Recruited women had age ≤42 years, and normal ovarian reserve. Dissolved follicular fluid samples were taken for EDCs measurement using liquid chromatography tandem mass spectrometry and each woman completed an epidemiological questionnaire. RESULTS: The main EDCs found were monobutyl phthalate (MBP) (median blood: 8.90 ng/mL; follicular fluid:10.42 ng/mL), monoethylhexyl phthalate (MEHP) (median blood: 9.26 ng/mL; follicular fluid: 7.58 ng/mL) and bisphenol A (BPA) (median blood: 1.89 ng/mL; follicular fluid: 1.68 ng/mL). Women undergoing ICSI showed significantly higher blood MBP ($p = 0.0001$) and BPA ($p = 0.0001$) than women undergoing IVF. Women with a BMI ≥ 25 kg/m^2 had much higher blood MBP ($p = 0.0001$) and much lower for MEHP, indicating that the Two frequently detected biophenols have different placental transfer behaviors. The placental transfer of Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) and Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP) was also investigated. MEHHP, MEOHP and MECPP were detected in all follicular fluid samples, which were significantly higher than the PTE of BPAP. The PTE of BPAP was much higher than other BPs, indicating its strong maternal transfer and high fetal accumulation. The PTEs of bisphenols were inversely correlated, and passive diffusion was suggested as the potential mechanism of placental transfer. Significant concentration correlations of the five main bisphenols between maternal plasma and cord plasma were observed ($p < 0.05$). Meanwhile, significant associations of BPAP concentrations in maternal/cord plasma with some maternal characteristics and adverse birth outcomes were also identified ($p < 0.05$).	Toxics. 2020 Oct 21;8(4):91.	10.3390/toxics8040091	33096627	ヒト	卵巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0279	M. K. Pant, A. H. Ahmad, M. Nabhani and J. Pant	2022	Plastic bottle feeding produces changes in biochemical parameters in human infants - A pilot study	BACKGROUND: Plastic bottles are widely used by people to feed their infants when breastfeeding is not possible. Bisphenol A (BPA), an endocrine disruptor is widely used in the manufacturing of plastic scams and is leached out from these plastic scams on exposure to high temperature, changed pH, or cleaning the plastic scam by harsh detergents. PURPOSE: Feeding the infants from plastic bottles over prolong duration is suspected to expose the infants to leached BPA. Hence the present study was taken up to compare the effects of breastfeeding and plastic bottle feeding on biochemical parameters in infants and also detect for the presence of free BPA in the plasma and urine samples of the infants. METHODS: Twenty infants (10 male and 10 female) in the age group of 1-6 months were recruited for the present study. Ten infants were breastfed and plastic bottle fed. Further, plasma and urine samples of the infants were subjected to Liquid chromatography mass spectrometry analysis for detecting free BPA and BPA glucuronide. RESULTS: Biochemical changes in form of raised triglycerides, cholesterol, low-density lipoproteins, very low-density lipoproteins and increase in CK-MB, serum urea were observed in plastic bottle fed infants. BPA glucuronide was also detected in the urine of these infants. Free BPA was not detected in plasma or urine samples of the infants except in one plasma sample from bottle fed group. CONCLUSION: Plastic bottle feeding may lead to toxic changes in the functioning of organs which manifest as altered biochemical parameters.	Clin Exp Pediatr Vol.65 Issue 9 Pages 459-465	10.3345/cep.2022.00234	35588762	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0280	Y. Pan, M. Deng, J. Li, B. Du, S. Lan, X. Liang and L. Zeng	2020	Occurrence and Maternal Transfer of Multiple Bisphenols, Including an Emerging Derivative with Unexpectedly High Concentrations, in the Human Maternal-Fetal-Placental Unit	In this study, a set of 13 bisphenols (BPs) and one emerging derivative (3-hydroxyphenyl-3-isopropylphenylindone, BPIDP) were analyzed in 60 pairs of maternal plasma, cord plasma, and placenta samples from pregnant women in South China. A total of 6 of the 13 target BPs, i.e., BPA, bisphenol F (BPF), bisphenol AF (BPAF), and bisphenol B (BPB), were frequently detected in the three human biological matrices. The derivative BPIDP was found to be the predominant BP analogue in placenta, with a median concentration of 1.08 ng/g, which was significantly higher than those of BPA (0.29 ng/g), BPF (0.12 ng/g), and BPAF (0.11 ng/g). The concentration of BPIDP was much higher in BPAF and much lower in BPAF, indicating that the Two frequently detected bisphenols have different placental transfer behaviors. The placental transfer efficiencies (TEs) of BPA, BPF, and BPAF were similar, which were significantly higher than the TFE of BPBP. The TFE of BPAF was much higher than other BPs, indicating its strong maternal transfer and high fetal accumulation. The TFEs of bisphenols were inversely correlated, and passive diffusion was suggested as the potential mechanism of placental transfer. Significant concentration correlations of the five main bisphenols between maternal plasma and cord plasma were observed ($p < 0.05$). Meanwhile, significant associations of BPAF concentrations in maternal/cord plasma with some maternal characteristics and adverse birth outcomes were also identified ($p < 0.05$).	Environ Sci Technol Vol.54 Issue 6 Pages 3476-3486	10.1021/acs.est.0c00206	32092248	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0281	R. Pan, C. Wang, R. Shi, Y. Zhang, Y. Wang, C. Cai, G. Ding, T. Yuan, Y. Tian and Y. Gao	2019	Prenatal Bisphenol A exposure and early childhood neurodevelopment in Shandong, China	BACKGROUND: Several epidemiological studies suggest that prenatal exposure to BPA may interfere with the neurodevelopment of pre-school and school age children. However, a limited number of studies are available for effects during children at a younger age, especially in China. METHODS: Based on Laizhou Wan Birth Cohort (LWBC), BPA concentrations were measured in urine areas 538 pregnant women during their hospital admission for delivery and neurodevelopment of their children were assessed using the Gesell Developmental Schedules at 12 months (n = 395) and 18 months (n = 388) of age. Generalized linear models were used to analyze the association between prenatal BPA exposure and the children's developmental quotient scores (DQs). RESULTS: The median of maternal BPA concentrations was 3.08 µg/L at 1.48 µ g/g creatinine. Prenatal BPA exposure was negatively associated with the gross motor DQ (GMDQ) at 12 months of age, especially among girls. Each 10-fold increase in BPA was associated with a 3.29 (95% CI: −5.83, −0.74) decrease in GMDQ. After stratified by gender, prenatal BPA concentrations were adversely associated with the adaptive domain DQ among boys (β = −3.62) and girls (β = −3.13) at 12 months of age. BPA was also negatively associated with the social domain DQs (β = −3.03) among girls. At 18 months of age, the significant adverse association was only found in the language domain among girls (β = −1.69, 95% CI: −3.23 to −0.15, p = 0.032). CONCLUSIONS: Based on a Chinese population, we found potential impacts of prenatal BPA exposure on childhood neurodevelopment at 12 and 18 months of age, especially among girls.	Int J Hyg Environ Health. 2019 Jun;222(5):896-902.	10.1016/j.ijheh.2019.03.002	30981646	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0282	K. Pan, J. Xu, Y. Xu, C. Wang and J. Yu	2024	The association between endocrine disrupting chemicals and nonalcoholic fatty liver disease: A systematic review and meta-analysis	Nonalcoholic fatty liver disease (NAFLD) is one of the leading causes of chronic liver disease worldwide. Epidemiological studies have reported that exposure of the population to environmental endocrine disrupting chemicals (EDCs) is associated with NAFLD. However, EDCs are of different types, and there are inconsistencies in the relevant evidence and descriptions, which have not been systematically summarized so far. Therefore, the purpose of this study was to systematically summarize the relationship between EDCs and NAFLD and to provide a reference for the prevention of NAFLD. Studies included in this study: Methodological quality, heterogeneity, and publication bias of the included studies were assessed using the Newcastle-Ottawa scale, I2 statistics, Begg's test, and Egger's test. The estimated effect sizes of the included studies were pooled and evaluated using the random-effects model (I2 > 50%) and the fixed-effects model (I2 < 50%). The pooled estimated effect sizes showed that population exposure to Phthalates (PAEs) (OR = 1.18, 95 % CI:1.09-1.28), cadmium (Cd) (OR = 1.37, 95 % CI:1.08-1.73), and bisphenol A (OR = 1.23, 95 % CI:1.12-1.34) were significantly correlated with the risk of NAFLD. Exposure to mercury (Hg) (OR = 0.48, 95 % CI:0.27-1.00) tended to increase the risk of "elevated alanine aminotransferase". On the contrary, no significant association was identified between perfluoroalkyl substances (OR = 0.99, 95 % CI:0.90-1.10), polychlorinated biphenyls (OR = 1.00, 95 % CI:0.99-1.01), and polybrominated diphenyl ethers (OR = 1.00, 95 % CI:0.99-1.01) and the risk of NAFLD. Nevertheless, the current meta-analysis results of some of the meta-analyses were not stable and demonstrated high heterogeneity. The evidence for these associations is limited, and more large-scale population-based studies are required to confirm these findings.	Pharmacol Res. 2024 Jun;206:107251.	10.1016/j.phrs.2024.107251	38862070	ヒト	肝毒性(メタアナリシス)	-	-	-	-	-	-	システマティックレビュー・メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0283	Y. I. Palmieri, M. G. Gyngyetten, A. J. Arcari, V. Umido and A. Y. Feixe	2025	Endocrine disruptors as risk factors for idiopathic precocious thelarche in girls: A case-control study	Introduction: Idiopathic premature thelarche (IPT) is defined as breast growth in girls before age 8 without activation of the gonadotropic axis. Among the probable etiologies, endocrine disruptors (EDC) with estrogenic action have been suggested. Objective: To evaluate whether there is an association between exposure and degree of exposure to the main EDs with estrogenic action in our environment and the development of IPT. Methodology: Case-control study between 2021 and 2023 in girls aged 6 months to 8 years. Cases: girls with IPT. Controls: girls without breast development, matched for age and sex. Variables: considering the degree of exposure according to weekly frequency. Results: Categories of ED score (T1-2-3-4 years) and number of ED (1-2-3 years) were interested. An association was found between IPT and exposure to phytoestrogens in food (OR: 16.6 95%CI 1.8-158 p<0.011), the use of BPA containers exposed to temperature changes (OR 2.6; 95%CI 1.1-6.9; p<0.05), contact with phthalates (OR 2.6; 95%CI 1.2-7.4; p<0.03) and pesticides (OR 2.7; 95%CI 1.2-6.4; p<0.02). In all the detailed EDs, we also found an association of IPT according to their degree of exposure. Conclusions: Exposure and degree of exposure to different sources of phytoestrogens, BPA, pesticides, and phthalates were associated with the development of IPT.	Arch Argent Pediatr. 2025 Jun 1;123(3):e20241050.	10.5546/aap.2024-10501.eng	40168507	ヒト	乳房	-	-	-	-	-	-	疫例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0284	E. Polak, W. Lebiedzińska, S. Arciszewski, M. Sołtysińska, P. Pierzyński, W. Wiczkowski, B. Z ołzowska-Rutkowska, G. N. Nikiforuk, D. Puntkowska-Tyczko and S. Walczyński	2021	The Association between Bisphenol A, Steroid Hormones, and Selected MicroRNAs Levels in Seminal Plasma of Men with Infertility	Bisphenol A (BPA), the most common endocrine disrupting chemical, has been associated with male reproductive dysfunctions. Recently, it has been shown that BPA may also affect miRNAs expression. Hereto, we aimed to evaluate the association of BPA levels with steroid hormone concentrations and circulating miRNAs levels to investigate the potential direct effect of BPA on hormonesis in the testis environment. The level of BPA in the seminal plasma of azoospermic men was significantly higher compared to the healthy control. The concentrations of estradiol (E2) and androstenedione (A) were significantly decreased in the seminal plasma of azoospermic men compared to the normospermic men. The levels of miR-34c-5p, miR-34c-3p, and miR-34b-3p were significantly up-regulated, and the level of miR-518-5p was significantly down-regulated in the seminal plasma of azoospermic men compared to the control group. Moreover, the level of miR-34c-5p was significantly positively correlated with the level of miR-34b-3p and miR-34c-3p, the level of miR-34b-3p was correlated with the level of miR-34c-3p, and miR-34c-5p and miR-34c-3p were correlated with miR-518-5p levels. Our results suggest that BPA may negatively affect sperm quality. Moreover, BPA correlated with the miR-34-5p, miR-34-3p, and miR-518 levels in seminal plasma, which suggests that BPA may act directly in seminal plasma, affecting the testicular environment.	J Clin Med. 2021 Dec 18;10(24):5945.	10.3390/jcm10245945	34945242	ヒト	精子	-	-	-	-	-	-	疫例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については≦100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0285	M. Ciga and J. Jurewicz	2025	Environmental exposure to selected non-persistent endocrine disrupting chemicals and polycystic ovary syndrome: a systematic review	Polycystic ovary syndrome (PCOS) is an endocrine disorder manifesting with symptoms such as irregular menstrual cycles, hyperandrogenism, and/or polycystic ovaries. The exact cause of PCOS remains unknown, but it is considered multifactorial, involving genetic predisposition, lifestyle factors, and environmental influences. Non-persistent endocrine disrupting chemicals (EDCs) are a group of exogenous substances that can interfere with the endocrine system. EDCs, in addition to genetic and hormonal ones, also may influence PCOS. This is one of the first systematic reviews dealing with the exposure to non-persistent endocrine disrupting chemicals and PCOS. The review summarizes the existing knowledge about the association of EDCs with PCOS based on significant findings on the toxicity of various non-persistent environmental EDCs and polycystic ovaries syndrome risk. A systematic search of the literature was conducted in order to identify proper studies using PubMed, Scopus, Elsevier, and Springer databases. The results of the studies suggest that there is a positive association between bisphenol A (BPA), phthalates, octocrylene, and PCOS. The data concerning triclosan and PCOS were inconclusive. Additionally, no link between the exposure to parabens and PCOS was observed. Three results of the presented studies highlight the urgent need for continued research on EDCs and their role in PCOS, for Clin Exp Med Environ Health. 2025;26(2):99-121.	Int J Occup Med Environ Health Vol.38 Issue 2 Pages 98-121	10.13075/ijomeh.1896.02551	40200737	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0286	R. Gveli, N. N. Yenigl, S. Dilbaz, B. Dilbaz, O. Aldemi, I. Kaplanoğlu, F. Gl et, E. Bayer and M. Tekin Ö	2024	The Association of ICSI Outcomes with Semen and Blood Bisphenol A Concentrations of the Male Partner	This study investigated the association of blood and semen Bisphenol A (BPA) levels of the male partner on the reproductive outcome in intracytoplasmic sperm injection (ICSI) treatment cycles. For this prospective study, 100 couples undergoing ICSI treatment were included. Blood and semen samples were collected from male partners on the day of oocyte retrieval. Couples were divided into two groups according to their live-birth outcomes, while men with normal seminogram-free semen underwent ICSI due to tubal factor infertility were taken as the study group. Habitual consumption of drinking water from plastic surface bottles (PBW) at home was also questioned in both groups, as it was considered as chronic BPA exposure. The association of ICSI outcome with blood BPA (bBPA) and semen BPA (sBPA) levels was analyzed in both groups. No significant correlation was found between sperm parameters and bBPA levels in both groups. A negative correlation was found between sBPA levels and total sperm count and progressive sperm motility in men who consumed PBW. Embryo development arrest was found to be significantly higher in patients who have high sBPA levels. Although sBPA levels were not different in PBW consumers, sBPA levels were found to be significantly higher in patients who have high bBPA levels. Elevated bBPA were associated with a significant decrease in clinical pregnancy rate. Considering the widespread human exposure to BPA, the effects of BPA on female reproductive system needs to be further examined.	Reprod Sci. 2024 May;31(5):1323-1331.	10.1007/s43032-023-01446-y	38212582	ヒト	精巣	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0287	F. Ouyang, G. H. Zhang, K. Du, L. She, R. Ma, X. Wang, X. Wang and J. Zhang	2020	Maternal prenatal urinary bisphenol A level and child cardio-metabolic risk factors: A prospective cohort study	Exposure to endocrine disrupting chemicals during the first 1000 days of life may have long-lasting adverse effects on cardio-metabolic risk in later life. This study aimed to examine the associations between maternal prenatal urinary bisphenol A (BPA) concentrations and cardio-metabolic risk factors in children at 2 and 12 years of age. Mother-child pairs were recruited from Wuhan, China between 2010 and 2011. Maternal BPA concentration was measured in prenatal and child 2-year cast urine samples, and classified into high, medium and low tertiles. Child adiposity anthropometric measurements, resting glucose, glucose, serum insulin, and lipids (high density lipoprotein, low-density lipoprotein, cholesterol, triglyceride), systolic (SBP) and diastolic blood pressure (DBP) were measured. Linear regression was used to evaluate the associations between maternal BPA and child cardio-metabolic risk factors. Mediation analysis was conducted to explore the role of child BMI in the BPA-risk factor associations. A total of 1,346 and 1,109 mother-child pairs were successfully followed up at 2 and 12 years, respectively, and 95.6% of children at age 2 years. Compared to those with low prenatal BPA, mean SBP was 2.73 (95%CI: 0.99-4.47) mmHg higher, and BMP was 0.4 (95%CI: 0.11-0.70) mmHg higher in girls with high prenatal BPA levels, but these associations were not found in boys. In boys, medium maternal prenatal BPA level was associated with 0.38 (95% CI: 0.03-0.68) mmol/L higher plasma glucose. No associations were found between prenatal BPA and child BMI, skinfold thickness, serum lipids, or insulin in either girls or boys. There were no associations between concurrent child urinary BPA and cardio-metabolic risk factors in children. These results suggest that BPA exposure during prenatal period, susceptible time for fetal development, may be associated with increase in child BP and plasma glucose in a sex-specific manner. Further independent cohort studies are needed to confirm the findings.	Environ Pollut. 2020 Oct;265(Pt A):115008.	10.1016/j.envpol.2020.115008	32574892	ヒト	心血管	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0288	M. Ouidir, A. H. Cissé, J. Botter, S. Lyon-Caen, C. Thirman, A. K. Sakhi, A. Sabaredzovic, S. Bayat, R. Slama, B. Heude and C. Philippat	2024	Fetal and Infancy Exposure to Phenols, Parabens, and Phthalates and Anthropometric Measurements up to 36 Months, in the Longitudinal SEPAGES Cohort	BACKGROUND: Endocrine disrupting chemicals may play a role in adiposity development during childhood. Until now literature in this scope suffers from methodologic limitations in exposure assessment using one or two urine samples collected during pregnancy and childhood. OBJECTIVES: We studied the associations of exposure to phenols, parabens, and phthalates, measured in repeated urine samples collected from mother-child pairs from the SEPAGES mother-child cohort recruitment (2014-2017) and follow-up visits, with anthropometric measurements from birth to 3 years. METHODS: We studied the associations of four phenols, four parabens, seven phthalates, and one hundredfold dilution factor newly quantified urine samples collected from the mother during second and third trimesters (median 28 and 30 gestational weeks, respectively) and infant at 2 and 12 months of age, and child growth until 36 months. We relied on repeated measures of weight, weight and head circumference from study visits and the child health booklet to predict growth outcomes at 2 and 36 months using the Jenss-Bayley nonlinear mixed model. We assessed associations with individual chemicals using adjusted linear regression and mixtures of chemicals using a Bayesian kernel machine regression model. RESULTS: The antipyrethroid pesticide metabolite 3-phenoxybenzoic acid (3-PBA) was frequently detected in pregnancy urine samples (detection frequency = 89%), whereas detection frequencies were lower than 50% for the other chemicals. Prenatal phthalate (DnBP) or 3-PBA urinary concentrations were not associated with body mass index (BMI), weight, and head circumference at 36 months. Mixture analysis revealed positive associations between exposure at 12 months and BMI and weight at 36 months, with DnBP showing the highest effect size within the mixture. CONCLUSIONS: This study suggests that exposure to early infancy may be associated with increased weight and BMI in early childhood, which are risk factors of obesity in later life. Furthermore, this study highlighted the impact of BPA, a compound replacing bisphenol A, which has never been studied in this context. https://doi.org/10.1289/EHP13644.	Environ Health Perspect. 2024 May;132(5):57002.	10.1289/ehp13644	38728218	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0289	E. Ougier, F. Zeman, J. P. Antignac, C. Rouveelle, R. Lange, M. Kolossa-Gehring and P. Apel	2021	Human biomonitoring initiative (HBM4EU): Human biomonitoring guidance values (HBM-GVs) derived for bisphenol A	The "European Human Biomonitoring Initiative" (HBM4EU) derives human biomonitoring guidance values (HBM-GVs) for the general population (HBM-GVGenPop) and/or occupationally exposed adults (HBM-GVWorker) for several priority substances and substance groups as identified by policy makers, scientists and stakeholders at EU and national level, including Bisphenol A (BPA). Human exposure to BPA is widespread and the substance is known to cause reproductive toxicity in animal studies. Therefore, the derivation of HBM-GVs for BPA is of high relevance for public health protection. The derivation of HBM-GVs for BPA is considered to be most toxicologically and/or from the conjugated forms (e.g. BPA-glucuronide (BPA-G) and BPA-sulfate (BPA-S)). As measurement is blood provides the superior surrogate of the biologically effective dose. However, considering the difficulty of implementing blood sampling in large HBM cohorts, as well as the current analytical capacities complying with the quality assurance (QA)/quality control (QC) schemes, total BPA in urine (i.e. the sum of free and conjugated forms of BPA measured after an hydrolysis step) was identified as the most relevant matrix and biomarker for BPA. HBM-GVGenPop for total BPA in urine of 200 µg/L and 230 µg/L for adults and children, respectively, were developed on the basis of toxicological data. To derive these values, the concentrations of urinary total BPA consistent with a steady-state internal dose of 0.5 µg/kg bw/day, which is 5 times lower than the TDI of 4 µg/kg bw/day established by the European Food Safety Authority (EFSA) in 2015, were calculated by means of a PBPK model developed by Karrer et al. (2018) was used, assuming an oral exposure to BPA at the 1 TDI level and repeated over 24 h. Dermal uptake of BPA is suspected to contribute significantly to the total BPA body burden, which in comparison with the oral route, is generating a higher ratio of free BPA to total BPA in blood. Therefore, an alternative approach for calculating the HBM-GVGenPop according to the estimated relative contributions of free and conjugated BPA to the internal dose was developed. HBM-GVWorker for total BPA in urine of 1500 µg/L was derived by dividing the HBM-GVGenPop by a factor of 10 to take into account the lower tolerance of the BPA in adults. Considering the limited amount of data on the toxicokinetics in humans, the European Chemicals Agency (ECHA) and EFSA, as well as the BPA industry, have established an assessment factor of 4 for workers. The predicted concentration of urinary total BPA at steady-state is equivalent to, or exceeds the 95th percentile of total BPA in urine measured in different European HBM studies conducted in the general population. Thus, no HBM-GVWorker was proposed, as the high background level of BPA coming from environmental exposure – mostly through food intake – is making the discrimination with the occupational exposure to BPA difficult.	Environ Int Vol.154 Pages 106563	10.1016/j.envint.2021.106563	33894553	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0290	S. Onkar, M. S. Wolff, S. L. Teitelbaum and J. A. Stingone	2021	Identifying environmental exposure profiles associated with timing of menarche: A two-step machine learning approach to examine multiple environmental exposures	BACKGROUND: Variation in the timing of menarche has been linked with adverse health outcomes in later life. There is evidence that exposure to hormonally active agents (or endocrine disrupting chemicals; EDCs) during childhood may play a role in accelerating or delaying menarche. The goal of this study was to generate hypotheses on the relationship between exposure to multiple EDCs and timing of menarche by applying a two-stage machine learning approach. METHODS: We examined data from the National Health and Nutrition Examination Survey (NHANES) for years 2013-2018. Data were analyzed for participants 12-19 years of age who had blood and urine biomarker measures of 13 environmental exposures, all with <75% above limit of detection, in seven classes of chemicals. We modeled risk for earlier menarche (≤12 years of age vs. older) with weighted elastic net regression (Stage 1) and then applied Bayesian Kernel Machine Regression (Stage 2) to examine the joint effects of the exposures identified in Stage 1. RESULTS: Stage 1 regression results identified associations between exposure profiles ("combinations") and timing of menarche. NHSS 13,187 identified urinary concentrations of monoethyl-hexyl phthalate (MEHP) as the most important feature in partitioning girls into homogenous subgroups followed by bisphenol A (BPA) and 2,4-dichlorophenol (2,4-DCP). In this first stage, we identified 21 distinct exposure biomarker profiles, containing five different classes of EDCs, associated with menarche. Stage 2 BKMR analysis identified a positive association between MEHP and earlier menarche (OR = 1.28 ng/mL vs. 0.36 ng/mL; adjusted95% CI: 0.96, 1.61). Additionally, we found a negative association between BPA and earlier menarche (OR = 0.78 ng/mL vs. 2.39 ng/mL; adjusted95% CI: 0.58, 1.00). Combinations of lower MEHP with benzophenone-3 (2.32 ng/mL) or BPA had similar associations with earlier menarche, though slightly weaker in those smaller subgroups. For girls not having lower MEHP, exposure profiles included other biomarkers (BPA, antimicrobial, monobenzyl phthalate, cis-lauric, and 3-hydroxycotinine); these showed largely null associations in the second-stage analysis. Adjustment for covariates did not materially change the estimates or CIs of these models. Bio-statistical tools or null effect estimates for some exposure biomarker profiles and relevant profiles consisted of no more than two EDCs, possibly due to small sample sizes in subgroups. CONCLUSION: A two- stage approach incorporating machine learning was able to identify comparable constellations of biomarkers in relation to timing of menarche; these should be further explored in prospective studies. Machine learning methods can serve as a valuable tool to identify patterns within data and generate hypotheses that can be investigated within hybrid, targeted analyses.	Environ Res Vol.195 Pages 110524	10.1016/j.envres.2020.110524	33249040	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0291	S. Onkar, A. A. Balallan and J. A. Stingone	2024	Identifying critical windows of prenatal phenol, paraben, and pesticide exposure and child neurodevelopment: Findings from a prospective cohort study	BACKGROUND: This study aimed to investigate how exposure to a mixture of endocrine disrupting chemicals (EDCs) during two points in pregnancy affects early childhood neurodevelopment. METHODS: We analyzed publicly available data from a high-risk cohort of mothers and their children (2007-2012) that measured six EDCs, including methyl-, ethyl- and propyl paraben, (MEPB, EPB, PRPB), Bisphenol (BPA), 2,5,6-trichloro-3-pyridinol (TCPY), 3-phenoxybenzoic acid (3-PBA) in prenatal urine samples during the second and third trimesters. Neurodevelopmental scores were assessed using Mullen Scales of Early Learning (MSEL) at age 3. We used Bayesian kernel machine regression (BKMR) to examine associations between EDC mixtures and MSEL scores, and to identify critical windows of exposure. RESULTS: The analytic sample included 350 children. For females, the relationship between BPA and 3PBA with MSEL score varied between the two trimesters. In the second trimester, BPA had similar associations with earlier menarche, though slightly weaker in those smaller subgroups. For girls not having lower MEHP, exposure profiles included other biomarkers (BPA, antimicrobial, monobenzyl phthalate, cis-lauric, and 3-hydroxycotinine); these showed largely null associations in the second-stage analysis. Adjustment for covariates did not materially change the estimates or CIs of these models. Bio-statistical tools or null effect estimates for some exposure biomarker profiles and relevant profiles consisted of no more than two EDCs, possibly due to small sample sizes in subgroups. CONCLUSION: A two- stage approach incorporating machine learning was able to identify comparable constellations of biomarkers in relation to timing of menarche; these should be further explored in prospective studies. Machine learning methods can serve as a valuable tool to identify patterns within data and generate hypotheses that can be investigated within hybrid, targeted analyses.	Sci Total Environ. 2024 Apr 10:920:170754.	10.1016/j.scitotenv.2024.170754	38369152	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0292	W. J. Grzeljaiak, A. E. Charkiewicz, M. Garley, W. Radzjczak-Wrona, J. Czernicki, E. Jabłkowska, M. Cechowska-Pasko and W. Miłyk	2022	Bisphenol A: Potential Factor of Miscarriage in Women in the Context of the Phenomenon of Neutrophil Extracellular Traps	Humans are exposed to a number of environmental pollutants every day. Among them, endocrine disruptors are particularly harmful to human health. Bisphenol A (BPA) is a xenoestrogen that has been shown to disrupt the functioning of the endocrine system in humans and animals. The aim of the study was to assess the concentration of BPA in the serum of women in the first trimester of pregnancy. The serum levels of cytoplasmic and PMN-perinuclear antinuclear antibodies were also determined. Samples were collected from healthy women and women who had miscarriage in the first trimester of pregnancy. The serum levels of cytoplasmic and PMN-perinuclear antinuclear antibodies were also determined using an immunoenzymatic method. The concentrations of key pro-inflammatory cytokines TNF-α and IL-17, as well as human neutrophil elastase subunits (hNE) and hCG, were also measured in the serum samples. The serum concentration of BPA was determined using gas chromatography. The results showed that the concentrations of BPA were significantly elevated in the serum of women in the first trimester of pregnancy compared to the control group, with the highest concentration found in the "hETs positive" group. The levels of hCG-1 and TNF-α were significantly higher in the "hETs positive" group compared to the "hETs negative" and control groups. The levels of hNE1 and hCG-1 were also higher in the "hETs positive" group compared to the "hETs negative" group. The study showed that BPA could play a role in the course of miscarriage through the formation of hETs. The results indicate the need to limit the exposure of women planning pregnancy to xenoestrogens, including BPA.	Arch Immunol Ther Exp (Warsz) Vol.70 Issue 1 Pages 24	10.1007/s00005-022-00661-w	36181646	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0293	Y. Okubo, A. Handa and T. Ikeiri	2019	Serial cross-sectional study for the association between urinary bisphenol A and paediatric obesity: Recent updates using NHANES 2003-2014	BACKGROUND: Several studies have reported bisphenol A (BPA) as a potential risk factor for paediatric obesity, but the findings were inconsistent among these studies. METHODS: Using data from the National Health and Nutrition Examination Survey from 2003 to 2014, we conducted a serial cross-sectional study to examine the association between urinary BPA and paediatric obesity among children aged 6 and 19 years. The analytical sample included 6,826 children. Urinary BPA was measured using high-performance liquid chromatography-tandem mass spectrometry. Obesity was defined as BMI ≥ 95th percentile. RESULTS: We observed increasing trends in urinary BPA concentrations from 2003 to 2014. The associations between urinary BPA concentrations and obesity were inconsistent across the years of survey and even after different models for urinary creatinine adjustments were used. Children with obesity were positively associated with urinary creatinine concentrations, but was not with creatinine-adjusted models. Furthermore, children with higher urinary BPA concentrations had elevated odds of obesity during 2003 to 2008, whereas these associations were inconsistent during 2009 to 2014. CONCLUSIONS: The associations between paediatric obesity and urinary BPA concentrations differed across the years of survey and creatinine adjustments. Further studies are required to assess these discrepancies.	Pediatr Obes Vol.14 Issue 12 Pages e12566	10.1111/ijpo.12566	31364316	ヒト	-	-	-	-	-	-	-	連続横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0294	J. Oh, S. Shah, K. A. Lee, E. Park, D. W. Lee, Y. C. Hong, S. Song, S. Y. Kim, H. Park, H. C. Kim, K. S. Jeong and E. Ha	2025	Sex-specific effects of prenatal exposure to phthalates and bisphenol A on adverse birth outcomes: Results from The Korean Children's Environmental Health Study (Ko-CHENS)	OBJECTIVES: Although previous epidemiological studies have reported the effects of fetal exposure to phthalates and phenols on birth outcomes, evidence is still limited. The objective of this study was to investigate whether prenatal exposure to endocrine-disrupting chemicals (EDCs), phthalates and bisphenol A (BPA), is associated with birth outcomes and whether there are sex-specific effects. METHODS: We used data from the Korean Children's Environmental Health Study (Ko-CHENS) cohort. Exposure to phthalates and BPA was measured by urine tests, and the information on outcomes and confounders was obtained from delivery records, questionnaires, and medical records. Multivariate linear and logistic regression models were used to examine associations between prenatal exposure and birth outcomes. Additionally, to evaluate the effects of EDC mixture exposure, we performed weighted quantile sum regression analysis. Subgroup analysis was further performed by sex and birth outcomes to examine potential differences in associations. RESULTS: This study included 2,176 mother-child pairs from the Ko-CHENS. We observed a significant association between the risk of PTB and exposure to BPA during early pregnancy and mono-carboxyoctyl phthalate (MCOP) during late pregnancy, with odds ratios of 1.23 (95% CI: 1.01, 1.49) and 1.29 (95% CI: 1.08, 1.55), respectively. Additionally, there was a significant association between exposure to MCOP during early pregnancy and the risk of LBW (OR: 1.30, 95% CI: 1.03, 1.64). For male infants, in particular, exposure to MCOP during early pregnancy was associated with the risk of LBW (OR: 1.61, 95% CI: 1.22, 2.13), and exposure to MCOP during late pregnancy was associated with the risk of PTB (OR: 1.46, 95% CI: 1.10, 1.92). CONCLUSIONS: This study suggests a potential association between exposure to BPA during early pregnancy and PTB, while exposure to MCOP during late pregnancy was associated with increased PTB risk in male infants.	Environ Int. 2025 May:199:109518.	10.1016/j.envint.2025.109518	40359600	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0295	N. Numcioksuket, T. Tawanathada, C. Bongsebandh u-Phubhakdi, S. Anuparkkongkol, K. Chi and V. Supornkchai	2023	Exposure to Bisphenol A and Its Analogs among Thai School-Age Children	Bisphenol F (BPF) and bisphenol S (BPS) have become popular substitutes for bisphenol A (BPA) in the plastic industry due to concerns over BPA's adverse effects. However, there is limited information on children's exposure to these chemicals. This study aims to assess the levels of BPA, BPF, and BPS in urine samples of Thai children. Spot urine samples and relevant factors that influence exposure to these chemicals were collected from 172 children, 6–7 years old, recruited between October 2019 and 2020. Two first-morning voids were collected one week apart. Demographic and exposure-related information was gathered. Urinary concentrations of bisphenols were analyzed by liquid chromatography–tandem mass spectrometry. Intraclass correlation coefficients (ICCs) were calculated to assess the reproducibility of the urinary bisphenol concentrations. Bisphenol exposure was estimated using a time-weighted average model. BPA, BPF, and BPS were detected at 79.6%, 11.0%, and 8.0%, with geometric mean (GM) concentrations of 1.41, 0.013, and 0.012 ng/mL, respectively. Dietary children aged ≤ 10 years exhibited 1.3–1.4 times higher GM levels of all bisphenols compared to older children. Exposure to food stored in plastic containers was associated with higher levels of BPF and BPS. In conclusion, BPA was the most frequently detected bisphenol in urine samples from Thai children, followed by BPF and BPS.	Toxics Vol.11 Issue 9	10.3390/toxics11090761	37755771	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0296	Y. Niu, B. Wang, R. Yang, Y. Wu, Y. Zhao, C. Li, J. Zhang, Y. Xing and B. Shao	2021	Bisphenol Analogues and Their Chlorinated Derivatives in Breast Milk in China: Occurrence and Exposure Assessment	Concentrations of bisphenol S (BPS) and its analogues (together with their chlorinated derivatives are referred to as BPs) were measured in 181 breastmilk samples collected from 9 provinces in China in 2016. Twelve BPs were more found. The BP concentrations ranged from not detected to 5.922 μg/L. BPA was the predominant BP, followed by bisphenol F (BPF) and bisphenol S (BPS). The mean BPA, BPF, and BPS levels were 0.041, 0.012, and 0.011 μg/L, respectively. Significant correlations were found between BPA and BPF (r = 0.5, p < 0.01) and between BPA and BPS (r = 0.4, p < 0.01). Higher BP levels were found in urban and southern regions. BPA accounted for approximately 70% of the BPs and BPF accounted for more than 50% of the BPs in these milk samples. The high correlations between BPA and BPF/BPS and regions, not only BPA should receive attention. The upper-bound daily intakes of BPs for infants 0-6 months old were 0.810-1.291 μg/kg bw/day. Despite the absence of tolerable daily intake data, attention should be paid not only on BPA but also BPF.	J Agric Food Chem Vol.69 Issue 4 Pages 1391-1397	10.1021/acs.jafc.0c06938	33480683	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0297	Y. Nishimura, K. Moriya, S. Kobayashi, A. Araki, F. Sata, T. Mitsui, S. Itoh, C. Miyashita, K. Chi, M. Kon, M. Nakamura, T. Kitta, S. Murai, R. Kishi and N. Shinohara	2020	Association of exposure to prenatal phthalate esters and bisphenol A and polymorphisms in the ESR1 gene with the second to fourth digit ratio in school-aged children: Data from the Hokkaido study	Phthalates and bisphenol A (BPA) are estrogenic endocrine disruptors. Polymorphisms in the gene encoding estrogen receptor 1 (ESR1) may contribute to the ratio of the lengths of the second and fourth digits (2D:4D), which is considered an index of prenatal exposure to sex hormones. Thus, we investigated whether ESR1 polymorphisms modify the effects of prenatal exposure to phthalates and BPA on 2D:4D in a birth cohort. Maternal urine samples were collected during pregnancy, and the concentrations of 11 phthalate metabolites and BPA were measured. Finger length was measured in 1,066 children (529 boys and 537 girls) at 6 years of age. We successfully performed genotyping for 10 nonsynonymous SNPs, particularly Pro87 (T → C, rs9340799), Ala594 (G → A, rs2077647), and Ala594Val (A → G). The associations among compound exposure, mean 2D:4D, and ESR1 polymorphisms were assessed by multiple linear regression adjusted for potential confounding factors. Boys with the AG/GG genotype at rs2077647 in the group exposed to high levels of mono(2-ethylhexyl) phthalate (MEHP) (≥ 2.52) and bisphenol A (BPA) (≥ 0.84) showed increased 2D:4D compared with boys with the AA genotype at rs2077647 who had low exposure to MEHP (< 2.52) and BPA (< 0.84). Increases in mean 2D:4D of 1.55%, 95% confidence interval (CI): 0.43–2.63, 2.06% increase in mean 2D:4D of 1.17%, 95% CI: 0.31–2.02). No significant differences were found among girls. There were no associations between mean 2D:4D and metabolites other than MEHP or BPA. These data suggest that ESR1 polymorphisms modify the effects of prenatal exposure to DEHP on mean 2D:4D among boys.	Steroids. 2020 Jul:159:108637.	10.1016/j.steroids.2020.108637	32165209	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0324	N. Moharoj, S. Prasanth, P. Rajapriya, G. Vinothkumar, V. M. Vinothini, R. Lenin, R. Jananthan and P. Venkatraman	2023	Bisphenol A accelerates the vascular complications in patients with Type 2 diabetes mellitus through vascular calcification-a molecular approach	PURPOSE: Environmental pollutant Bisphenol A (BPA) strongly interacts with insulin resistance, which leads to type 2 diabetes mellitus (T2DM). Uncontrolled glucose levels in both bloodand urine develops vascular complications in T2DM patients. However, glucose controlled diabetic patients are also affected by vascular complications due to vascular calcification, and there is a lack of clinically relevant data on BPA levels in T2DM patients with vascular calcification. Therefore, we investigated the association of BPA with T2DM and T2DM associated vascular complications and also BPA levels in T2DM with vascular calcification vitalsignsexpression. METHODS: This study involved 120 participants with T2DM and its associated vascular complications. Serum and urinary BPA were estimated using ELISA kit, and gene expression of the study participants in peripheral blood mononuclear cells (PBMCs) was studied with quantitative real-time PCR. RESULTS: Serum and urinary BPA levels were higher in T2DM and its associated vascular complications than in healthy controls. Moreover, T2DM patients with vascular calcification had significantly higher BPA levelshigher significance with both Scr (p < 0.001, r = 0.995), Rand2 (p < 0.01, p = 0.990) and IL-1beta (p < 0.001, p = 0.993) and TNF-alpha (p < 0.001, p = 0.993) in comparison to the study groups, but T2DM alone significant with Scr and BPA (p < 0.05). CONCLUSION: BPA levels were positively correlated with serum Scr and increased level in T2DM associated vascular complications patients. Also, higher expression of IL-1beta and TNF-alpha was observed in T2DM associated vascular complications patients. Our study is the first to associate BPA levels with vascular calcification in patients with T2DM and its associated vascular complications.	Int Arch Occup Environ Health Vol.96 Issue 9 Pages 1291-1299	10.1007/s00420-023-02007-1	37698613	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0325	L. Mínguez-Alarcón, L. Fruh, P. L. Williams, T. James-Todd, I. Souter, J. B. Ford, K. M. Rexrode, A. M. Calafat, R. Hauser and J. E. Chavarro	2022	Pregnancy urinary concentrations of bisphenol A, parabens and other phenols in relation to serum levels of lipid biomarkers: Results from the EARTH study	The epidemiologic literature on associations between urinary phenol concentrations and lipid profiles during pregnancy is limited. We examined whether urinary concentrations of phenol and phenol replacement biomarkers were associated with serum lipid levels among pregnant women. This cross-sectional study included 176 women attending the Massachusetts General Hospital Fertility Center who enrolled in the Environment and Reproductive Health (EARTH) Study between 2007 and had matched urine and serum samples collected. Urinary phenol biomarkers and serum lipids during pregnancy. We used linear mixed models to assess the relationship between groups of urinary phenol and phenol replacement biomarkers and serum lipid levels (total cholesterol, high density lipoprotein (HDL), non-HDL, low-density lipoprotein (LDL), cholesterol, and triglycerides). Models were adjusted for age, race, body mass index, and gestational age at urine collection. We found positive associations between urinary bisphenol A (BPA) and serum lipids. Women in the highest urinary bisphenolate concentrations, in the highest tertile had 236 (95% CI: 11, 461 mg/dL), 22% (95% CI: 2, 38 mg/dL) and 28% (95% CI: 1, 55 mg/dL) higher mean total, non-HDL and LDL cholesterol, respectively, compared to women with concentrations in the lowest tertile. Similar relations were observed for urinary bisphenol S concentrations. Urinary bisphenol S, benzophenone-3, triclosan, methylparaben, ethylparaben, and butylparaben were unrelated to serum lipids. Among pregnant women, urinary concentrations of bisphenol A and propylparaben were associated with higher serum levels of total, non-HDL and LDL cholesterol.	Sci Total Environ Vol.833 Pages 155191	10.1016/j.scitotenv.2022.155191	35421480	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0326	L. Mínguez-Alarcón, A. Ballesta, A. J. Gaskins, J. E. Chavarro, J. B. Ford, I. Souter, A. M. Calafat, R. Hauser and P. L. Williams	2021	Paternal mixtures of urinary concentrations of phthalate metabolites, bisphenol A and parabens in relation to pregnancy outcomes among couples attending a fertility center	BACKGROUND: Few epidemiologic studies have evaluated the impact of paternal environmental exposures, particularly as mixtures, on couples' pregnancy outcomes. OBJECTIVE: We investigated whether mixtures of paternal urinary bisphenol A (BPA), parabens, and phthalates were associated with pregnancy outcomes among couples attending a fertility center. METHODS: We included 216 couples undergoing 384 in vitro fertilization (IVF) cycles between 2007 and 2017 in the Environment and Reproductive Health (EARTH) Study. Paternal urine samples were collected on the day of oocyte retrieval and analyzed for 15 phthalate metabolites, 2 parabens, and BPA. We used Bayesian kernel machine regression (BKMR) analysis (PCA) to identify correlations of biomarker concentrations and multivariable Cox proportional hazards models for discrete survival time to estimate the fecundability ratio (FR) and 95% CIs for the associations between PCA-derived factor scores and probability of failing to achieve a live birth. Interactions were also included in the models to examine strength of associations over three consecutive periods. Analyses transfer to IVF cycle outcomes were restricted to 1,004 IVF cycles among 384 couples. RESULTS: Paternal urinary concentrations of BPA, parabens, and phthalates were correlated. Men with higher intensity of fertility diagnosis, and when PCA factor scores, sensitivity analyses with further adjustment for maternal PCA factor scores, were performed. RESULTS: We identified three correlated components of phthalate, phthalate (DEHP) metabolites, BPA and non-DEHP metabolites, and parabens, accounting for 58%, 35%, and 28%, respectively, of the total variance explained. An interquartile range (25th-to-75th percentile) increase in the DEHP-related factor score was associated with elevated probability of failing prior to live birth (FR = 1.11; 95% CI: 1.00, 1.23) and the association was stronger between intermediate (time to pregnancy) or unsuccessful (no live birth) outcomes and between clinical pregnancy and live birth compared to before implantation. The overall 19% of failure for the BPA/non-DEHP-related and paraben-related factor scores were FR = 1.26 (95% CI: 0.97, 1.64) and FR = 0.96 (95% CI: 0.85, 1.10). We found similar FRs when additionally adjusting for maternal PCA factor scores. CONCLUSION: Paternal mixtures of urinary concentrations of DEHP metabolites were related to higher infertility treatment failure.	Environ Int. 2021 Jan;146:106171.	10.1016/j.envint.2020.106171	33069985	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0327	A. Mira, G. Bouzios, I. Papoutsis, G. Kaparas, P. Christopoulos, E. Kaseta, M. Mastrominas, S. Athanasiadis and G. Makrakakos	2022	Bisphenol A correlates with fewer retrieved oocytes in women with tubal factor infertility	PURPOSE: Serum and urinary bisphenol A (BPA) concentrations have been associated negatively with the number of retrieved oocytes after in vitro fertilization (IVF). The impact of BPA upon women with polycystic ovary syndrome (PCOS) and severe endometriosis (endometrioma) has not been investigated. To this purpose, associations among serum and urinary and follicular fluid (FF) BPA concentrations and the number of retrieved and fertilized oocytes and comparisons between pregnancy rates were evaluated. METHODS: This was a cross-sectional study conducted at a university-affiliated assisted conception unit between January and December 2019, including 93 women of reproductive age (PCOS: 30; TFI: 28; following IVF: 35 women). Unconjugated BPA in serum and urine samples was measured by gas chromatography-mass spectrometry method. The number of retrieved and fertilized oocytes and pregnancy rate were documented and evaluated. RESULTS: The number of oocytes retrieved from PCOS women was significantly higher than that of TFI women (p = 0.001) and women following IVF (p = 0.001). Serum BPA concentrations were significantly higher in PCOS than in TFI women (p = 0.001). Serum BPA concentrations in TFI women (p = 0.001) and women following IVF (p = 0.001) were significantly higher than in PCOS women. Serum and FF urine BPA concentrations did not significantly affect the number of retrieved oocytes, and pregnancy rate in both groups. CONCLUSION: FF BPA concentrations were lower in all PCOS women and in some eight/nine/ten PCOS than in TFI women. In TFI women, FF BPA concentrations correlated negatively with retrieved oocytes. Confirmation of these findings might lead to moderation of use of BPA-containing products by women undergoing IVF.	Hormones (Athens) Vol.21 Issue 2 Pages 305-315	10.1007/s42000-022-00370-1	35524040	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0328	R. L. Miller, Y. Wang, J. Kalkbrug, A. N. Akinbiwaidiash, D. H. Bennett, C. V. Breton, J. P. Buckley, D. Dabelea, A. L. Dunlop, A. Ferrara, G. Gao, A. Gaylord, D. R. Gold, T. Hartert, L. Hazlehurst, L. Hertz-Picciotto, L. A. Hoepner, M. Karagas, C. J. Kerr, W. S. Kelly, C. Khatchikian, M. Liu, L. D. Meeker, T. G. O'Connor, A. K. Peterson, S. Sathyanarayana, J. Sordillo, L. Trasande, S. T. Weiss and Y. Zhu	2025	Prenatal exposure to environmental bisphenols over time and their association with childhood asthma, allergic rhinitis and atopic dermatitis in the ECHO consortium	Concerns persist about the potential impact of prenatal exposure to bisphenols (BP) and their replacement analogues on childhood asthma and allergies. Previous studies on single and small cohorts had limited statistical power, few investigated analogues of BPA and BPS, and even those examined mixed outcomes. Our objective was to assess whether prenatal exposures to individual environmental bisphenols (BPA, BPF, BPS) influence risk of childhood asthma, allergic rhinitis, and atopic dermatitis. Data from the U.S. Environmental Influences on Child Health Outcomes (ECHO) consortium were harmonized on measures of prenatal urinary BPA, BPF, and BPS and asthma, allergic rhinitis, and atopic dermatitis (ever/never; up to age 5 years) from 1983 to 2019 in 1,460 children. Urine samples were collected between 1998 and 2019. In 1,460 pairs from nine cohorts with urine bisphenol analysis, median BPA levels decreased from 1.11 ng/ml (n 5,89 ng/ml, median BPF levels decreased from 0.01 ng/ml (n 2,89 ng/ml, and median BPS levels increased from 0.23 ng/ml (n 0.41 ng/ml (detection frequency 41%). Associations between prenatal bisphenol exposure and asthma, allergic rhinitis, and atopic dermatitis were examined using multivariable logistic regression models. Effects were tested for modification by child sex, race/ethnicity, household income, and maternal education. Prenatal BPA exposure was associated with a reduced odds of asthma (adjusted odds ratio [aOR] 0.87, 95% CI 0.77–0.98). Each doubling of asthma (odds ratio [OR] 0.87, 95% confidence interval [CI] 0.78, 0.98) or eczema (odds of prenatal BPA was associated with reduced odds of atopic dermatitis (OR 0.92, 95% CI 0.83, 0.99). The ongoing and changing patterns of exposure to bisphenols in the U.S. population require further study with additional attention to time-windows of exposure and co-occurring social determinants of health, to continue to inform current policies and evaluate the importance of limiting exposure to BPA and its analogues on childhood asthma, allergic rhinitis, and atopic dermatitis.	Environ Pollut. 2025 Feb 1;366:125415.	10.1016/j.envpol.2024.125415	39615574	ヒト	免疫	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0329	J. Milczarek-Banach, D. Rachoń, T. Bednarczuk, K. Wysocka-Czapla, A. Wasik and P. Miś Kiewicz	2020	Exposure to Bisphenol A Analogs and the Thyroid Function and Volume in Women of Reproductive Age-Cross-Sectional Study	Bisphenols (BPs) are commonly known abocitlons that are widely used in industry. The knowledge about the impact of BPs on thyroid function is scarce. Proper thyroid functioning is especially important for women of reproductive age, as hypothyroidism affects fertility, pregnancy outcomes and the offspring. There are no studies analyzing the influence of BPs on thyroid function and volume in non-pregnant young women. The aim of this cross-sectional study was to evaluate the relationship between bisphenol A and its 13 analogs (BPC, BPE, BPF, BPG, BPM, BPP, BPZ, BPS, 4-HPPH, 4-HPPOH, TMBPF, TMBPS) exposure and thyroid function and volume in women of reproductive age. Inclusion criteria were: females as per 18-50 years. Exclusion criteria were history of any thyroid disease, pharmacotherapy influencing thyroid function, pregnancy or puerperium, and diagnosis of autoimmune disease other than Hashimoto's thyroiditis. Thyroid function was assessed by measuring serum concentrations of TSH, fT4, fT3, TPOAb, TgAb, and TRAb. Thyroid volume was assessed by ultrasonography. Ultrasound examination of thyroid gland was performed. Five hundred eighty participants were included into the study. A negative correlation was found between urine BPZ and bisphenol A (BPA) (R = −0.266, p < 0.0001). Patients with detected urine BPC presented smaller thyroid glands than those with not detected urine BPC (p = 0.00002). A positive correlation was found between TSH and urine BPC (R = 0.216, p = 0.002). Patients with detected urine BPC presented higher concentrations of TSH versus those with not detected urine BPC (p = 0.003). There were no relationships between any of serum BPs as well as the urine ones BPs and thyroid function and its volume. The only BP that demonstrated the relationship between thyroid function and its volume was BPC, probably because of its chemical structure that most resembles thyroxine. Exposure to this BP may result in the development of hypothyroidism that could have a negative impact on pregnancy and the offspring.	Front Endocrinol (Lausanne) Vol.11 Pages 587252	10.3389/fendo.2020.587252	33547704	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0330	M. Milanović, N. Milošević, I. Sučić, S. Stojanoski, M. Abenavoli, Krstonošić, A. Rjelica, N. Milić and M. Medić Stojanoska	2020	Can environmental pollutant bisphenol A increase metabolic risk in polycystic ovary syndrome?	BACKGROUND: Bisphenol A (BPA), a widespread industrial substance is recognized as endocrine-disrupting chemical and therefore could be associated with polycystic ovary syndrome (PCOS) related metabolic disturbances. METHODS: In this study 75 women of reproductive age with diagnosed PCOS were enrolled. METHODS: BPA in urine samples was analyzed by gas chromatography-mass spectrometry. RESULTS: BPA was detected in urines of 66.28% participants. The crude no-height ratio (WHtR) was statistically significant higher in PCOS BPA(+) in comparison to PCOS BPA(-) women (p = 0.026). PCOS BPA(+) women had 6.89 times (95% CI 1.160-33.068, p = 0.034, p = 0.026) higher risk for waist circumference above 88 cm and 5.49 odds (95%CI 1.009-29.896, p = 1.981, p = 0.038) to have WHtR over 0.5 when compared to PCOS BPA(-). Statistically significant positive association between BPA urine concentrations, and insulin serum levels (p = 0.038) was obtained. BPA urine values were associated with elevated HOMA-IR values, and reduced HOS, levels with statistical significance (p = 0.038, p = 0.026). Conclusion: There was 51% (95% CI 0.769-0.777) BPA(+) women in the PCOS group. There was a 3.896 (p = 0.004) higher risk for PCOS BPA(+) women to have testosterone levels above reference values. CONCLUSION: The obtained results suggested that the BPA exposition in PCOS women was followed by increased metabolic risk through promotion of obesity, especially the visceral type, hyperinsulinemia, insulin resistance, dyslipidemia and elevated androgen levels.	Clin Chim Acta Vol.507 Pages 257-263	10.1016/j.cca.2020.05.009	32387634	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0331	F. M. Metwally, H. Rashad, H. M. Zoidan and A. F. Hashish	2020	Impact of Bisphenol A on Gonadotropic Hormone Levels in Children with Autism Spectrum Disorders	Early developmental exposures to endocrine disruptors including bisphenol A (BPA) may affects the body's endocrine system producing adverse neurologic, reproductive, cardiovascular, metabolic, and immune effects in humans. Many studies show the effect of BPA on human reproductive or/ even concentrations than that of safety limit recommendations. However, limited studies have investigated the possible association between environmental exposure of BPA and gonadotropic hormone levels in children with autism spectrum disorders (ASDs). This study was done to evaluate association between the serum levels of hormones; follicle-stimulating (FSH), follicle (E2H2B), and estradiol (E2) and BPA in the ASD children compared with 30 healthy control children. Serum levels of FSH, E2H2B, and E2 were lower in ASD group than that of control. Correlations between BPA and FSH, E2H2, and E2 within autistic children were not significant. The observed results revealed that BPA may cause endocrine dysfunction in ASD children.	Indian J Clin Biochem Vol.35 Issue 2 Pages 205-210	10.1007/s12291-018-0801-7	32226252	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0332	M. Medlin, C. Beausoleil, F. A. Zeman, J. P. Antignac, M. Kolossa-Gehring, C. Rousselle and P. Apel	2022	Human Biomonitoring Guidance Values (HBM-GVs) for Bisphenol S and Assessment of the Risk Due to the Exposure to Bisphenols A and S, in Europe	Within the European Joint Programme HBM4EU, Human Biomonitoring Guidance Values (HBM-GVs) were derived for several prioritised substances. In this paper, the derivation of HBM-GVs for the general population (HBM-GVGeneral) and workers (HBM-GVworker) referring to bisphenol S (BPS) is presented. For the general population, this resulted in an estimation of the total urinary concentration of BPS at 0.5 µg/L according to 23 h continuous exposure to BPS. For workers, the modelling was refined in order to reflect continuous exposure during the working day, leading to a total urinary concentration of BPS of 5.0 µg/L. The usefulness for risk assessment of the HBM-GVs derived for BPS is discussed by comparing them to the HBM-GVs derived for bisphenol A (BPA) in a previous publication. Due to the similarities between BPA and bisphenols, with a very low NOA regarding exposure to BPS, contrary to that observed for BPS. This may be due to the endocrine-mediated endpoints selected to derive the HBM-GVs for BPS, whereas the values calculated for BPS are based on the temporary Tolerable Daily Intake (t-TDI) from EFSA set in 2013, in comparison with the revised TDI recently opened for comments by EFSA is also discussed. Regarding the occupational field, results indicate that the risk from occupational exposure to both bisphenols cannot be disregarded.	Toxics Vol.10 Issue 5	10.3390/toxics10050228	35622642	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0333	H. Meng, Y. Zhou and Y. Jiang	2020	Association of bisphenol A with puberty timing: a meta-analysis	OBJECTIVES: The results of existing studies on bisphenol A (BPA) and puberty timing did not reach a consensus. Thereby we performed this meta-analytic study to explore the association between BPA exposure in urine and puberty timing. METHODS: Meta-analysis of the pooled odds ratio, OR), premature ratios (PR) or hazards ratios (HR) with 95% confidence intervals. CI) were calculated and estimated using fixed-effects or random-effects models based on between-study heterogeneity. RESULTS: A total of 10 studies involving 5611 subjects were finally included. The meta-analysis showed that BPA exposure was unrelated to precocious puberty (OR = 0.96, 95% CI: 0.63–1.45), early menarche (OR = 0.96, 95% CI: 0.63–1.45), or early menstruation (OR = 0.96, 95% CI: 0.63–1.45). CONCLUSIONS: The meta-analysis results found between BPA exposure and precocious puberty (OR: 0.96, 95% CI: 0.63–1.45), premature menarche (OR: 0.96, 95% CI: 0.63–1.45), or early menstruation (OR: 0.96, 95% CI: 0.63–1.45). There was no strong correlation between BPA exposure and puberty timing. Further studies with large sample sizes are needed to verify the relationship between BPA and puberty timing.	Rev Environ Health. 2020 Dec 14;ahead ofprint(ahead ofprint):459-466.	10.1515/reveh-2020-0091	34651495	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0334	A. Mehlsen, L. Hallund, H. Bips, H. Frederiksen, A. M. Andersson, S. Bruun, S. Huzby, T. K. Jensen and C. A. G. Timmermann	2022	Pregnancy exposure to bisphenol A and duration of breastfeeding	INTRODUCTION: Bisphenol A (BPA) is frequently used in the production of plastics. It is an endocrine disruptor, and BPA exposure in mice has been associated with reduced offspring growth due to insufficient milk production. However, human studies of associations between BPA exposure and duration of breastfeeding are sparse. METHODS: Pregnant women from the Odense Child Cohort (n = 730) donated a third-trimester morning urine sample, which was analyzed for BPA by LC-MS/MS. Information about duration of exclusive and any breastfeeding was obtained through questionnaires three and 18 months postpartum, and a subgroup of 400 participants was interviewed by telephone about breastfeeding duration. Associations between BPA exposure and duration of breastfeeding were analyzed using Cox regression models. RESULTS: The median urinary BPA concentration was 1.29 ng/mL. Compared to women within the lowest tertile of BPA exposure, women in the second and third tertiles had 8% and 14% shorter breastfeeding at any given time. HRs (95% CI) were 1.08 (0.87, 1.34) and 1.16 (0.93, 1.27), respectively, and in terminate exclusive breastfeeding at any time up to 26 weeks after birth. HRs (95% CI) were 1.07 (0.86, 1.28) and 1.06 (0.85, 1.27), respectively. However, confidence intervals were accountable with an effect or even a protective effect. DISCUSSION: This study indicated that high BPA exposure in pregnancy is associated with shorter duration of breastfeeding. Although our findings were not statistically significant, all estimates were above one suggesting increased risk of early breastfeeding termination with high exposure. Using a single spot morning urine sample to estimate BPA has likely caused imprecision as it might not adequately reflect long-term exposure. Future studies, should consider measuring BPA more than once, including other timepoints during pregnancy and after birth.	Environ Res. 2022 Apr 15:206:112471.	10.1016/j.envres.2021.112471	34861228	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0335	S. E. Madellín-Gallbq, L. E. Alcántara-Quintana, A. S. Rodríguez-Báez, J. Sagahón-Azúa, M. Rodríguez-Aguilar, M. L. A. Hernández Cueto, J. E. Muñoz-Medina, R. D. C. Milián-Segovia and R. Flores-Ramírez	2023	Urinary phthalate metabolite and BPA concentrations in women with cervical cancer	Environmental pollutants are involved in the development and progression of numerous cancers, including cervical cancer (CC). One possible explanation for this is the ability of several pollutants to mimic natural hormones, thus altering the endocrine system. Phthalates and bisphenol A (BPA) are ubiquitous pollutants that have been classified as endocrine disruptors (EDs). This study aimed to evaluate the association between CC risk and urinary concentrations of 10 phthalate metabolites and BPA. A case-control study (n = 70, 35 cases/subjects with CC and 35 controls/subjects without CC) was conducted in Mexico. Urine samples were analyzed for BPA, seven hydroxyl phthalate (OHMP), seven oxo-phthalate (oxoMP), and seven carboxyl phthalate (cxMP) using high-performance liquid chromatography coupled to a tandem mass detector. The detection rate of environmental pollutants was 100%, with a median concentration in the control group and cases and inter-range was 0.5-5.9, 5.3, 96.6, and 129 µg/g Cr (1.5-11, 13.1-193.1, 163, and 362 µg/g Cr) and 1.9, 10.8, 3.5, and 9.1 µg/g Cr for BPA, MEHP, MBP, and MEP, respectively. This study reveals high levels of phthalates, particularly MEHP, in urine samples of women in CC associated with human papillomavirus (HPV) infection. Further studies are needed to evaluate the possible role of phthalates in synergy with HPV in progression to CC.	Environ Sci Pollut Res Int Vol.30 Issue 8 Pages 21033-21042	10.1007/s11356-022-23654-w	36264455	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0336	C. M. McKinney, B. G. Lemus, A. L. Semirado, A. Kim, Z. Liu, S. Samy and S. Sathyanarayana	2020	A Prospective Cohort Study of Bisphenol A Exposure from Dental Treatment	Laboratory studies show that bisphenol A (BPA) leaches from bisphenol A glycidyl methacrylate (bisGMA)-based dental materials. We aimed to quantify the extent to which children are exposed to BPA from dental treatment with bisGMA materials, by amount of treatment and type of sealants. We hypothesized that posttreatment urinary BPA (uBPA) concentrations would be higher among patients with more surfaces treated with bisGMA sealants and composite restorations. We recruited children undergoing dental treatment at the University of Rochester Medical Center (URMC) Dental Clinics. Urine samples were collected before dental treatment. We measured uBPA concentrations in urine before treatment and at 3 and 6, 6 and 24 hr posttreatment. We elaborated treatment data (surfaces treated) from the chart. We generated descriptive statistics and compared pre- and posttreatment uBPA concentrations using generalized estimating equations. Participants were 53% female, 65% non-White, and 73% publicly insured. The median age was 8.1. The mean number of tooth surfaces exposed to BisGMA materials (composites/sealants) was 7.5 (SD 5.5). Overall, uBPA concentrations were 80% higher (95% confidence interval (CI) 20% to 165%, P = 0.002) at 3–6 posttreatment compared with pretreatment concentrations. The uBPA concentrations 3–6 posttreatment versus pretreatment tended to be higher (112%, 95% CI 0.5% to 296%) among those receiving treatment on >5 surfaces than those receiving treatment on ≤5 surfaces (48%, 95% CI −11% to 151%), but the difference was not statistically significant (P = 0.2). Urine collection was challenging for young children undergoing general anesthesia. Among all findings, uBPA concentrations returned to baseline by 6 hr. Children experience short-term increases in BPA from dental treatment. The impact of relatively high, short-term BPA exposure on child health is unknown. Given the widespread use of BisGMA-based dental materials, and that chronic low-dose BPA exposure may adversely affect child health, strategies that minimize BPA exposure could potentially improve child health.	J Dent Res Vol.99 Issue 11 Pages 1262-1269	10.1177/0022034520934725	32579872	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則として精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合論（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0337	G. McGee, M. Gérard-Walton, P. L. Williams, T. J. M. Koesser, J. E. Chavarro, J. D. Meeker, J. M. Braun, M. A. Brazier, J. B. Ford, A. M. Calafat, L. Souter, R. Hauser and L. Mínguez-Alarcón	2023	Associations of Maternal Urinary Concentrations of Phenols, Individually and as a Mixture, with Serum Biomarkers of Thyroid Function and Autoimmunity: Results from the EARTH Study	The associations between urinary phenol concentrations and markers of thyroid function and autoimmunity among potentially susceptible subgroups, such as euthyroid women, have been understudied, especially when considering chemical mixtures. We evaluated cross-sectional associations of urinary phenol concentrations, individually and as a mixture, with serum markers of thyroid function and autoimmunity. We included 138 women attending a fertility center who provided one spot urine and one blood sample at enrollment (2009-2015). We quantified four phenols in urine using isotope-dilution high-performance liquid chromatography tandem mass spectrometry: bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), and triclosan (TCS). We measured serum concentrations of thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), and thyroglobulin (Tg) antibodies (TgAb) to assess using electrochemiluminescence assays. We fit linear and logistic regression models to investigate the association between urinary phenols (each individually and as a mixture) and serum thyroid function and autoimmunity, adjusted for confounders. As a sensitivity analysis, we also applied Bayesian Kernel Machine Regression (BKMR) to investigate non-linear and non-additive interactions. Urinary bisphenol A was associated with thyroid function; in particular, FT3 (mean difference for a 1 ng/mL increase in concentration: -0.088; 95% CI: -0.151, -0.025) and FT3/FT4 (-0.004; 95% CI: -0.012, -0.003). Urinary methylparaben and triclosan were also associated with several thyroid hormones. The overall mixture was negatively associated with serum FT3 concentrations (mean difference comparing all four mixture components at the 75th vs. 25th percentiles: -0.19; 95% CI: -0.33, -0.05). We found no evidence of non-linearity or interactions. These results add to the current literature on phenol exposures and thyroid function in women, suggesting that some phenols may alter the thyroid system.	Toxics Vol.11 Issue 6	10.3390/toxics11060521	37368621	ヒト	疫学								横断研究	1	1																		
統合_0338	C. F. McCabe, V. Padmanabhan, D. C. Dolinoy, S. E. Domino, T. R. Jones, K. M. Bakulski and J. M. Goodrich	2020	Maternal environmental exposure to bisphenols and epigenome-wide DNA methylation in infant cord blood	Maternal prenatal exposures, including bisphenol A (BPA), are associated with offspring's risk of disease later in life. Alterations in DNA methylation may be a mechanism through which altered prenatal conditions (e.g. maternal exposure to environmental toxicants) elicit this disease risk. In the Michigan Mother-Infant Pairs Cohort, maternal first-trimester BPA, bisphenol S (BPS), and bisphenol F (BPF) concentrations were tested for association with DNA methylation patterns in infant umbilical cord blood leukocytes (N = 99). We used the Illumina Infinium MethylationEPIC BeadChip to quantitatively evaluate DNA methylation across the epigenome. We identified differentially methylated positions (DMPs) and regions (DMRs) associated with maternal bisphenol concentrations using robust linear regression models and the comb-p algorithm, and tested for an association between BPA-associated DMRs and placental DNA methylation. Finally, we used the Comparative Toxicogenomics Database to identify genes with curated associations between BPA exposure and disease, and tested for enrichment of BPA-associated DMRs in these genes. Maternal first-trimester urinary BPA was associated with DNA methylation at 875 of significant sites. BPA exposure-associated DNA methylation sites were enriched for 38 pathways significant at FDR <0.05. The pathway or gene set with the greatest odds of enrichment for differential methylation (FDR <0.05) was type I diarrhoea receptor binding. This study provides a novel understanding of fetal response to maternal bisphenol exposure through epigenetic change.	Environ Epigenet. 2020 Dec 23;6(1):dvaa021.	10.1093/eep/dvaa021	33391824	ヒト	遺伝毒性								コホート研究	1	1							1	1	1											
統合_0339	C. F. McCabe, J. M. Goodrich, K. M. Bakulski, S. E. Domino, T. R. Jones, J. Colacino, D. C. Dolinoy and V. Padmanabhan	2023	Probing prenatal bisphenol exposures and tissue-specific DNA methylation responses in cord blood, cord tissue, and placenta	The early gestational fetal epigenome establishes the landscape for fetal development and is susceptible to disruption via environmental stressors, including chemical exposures. Research has explored how cell- and tissue-specific DNA methylation (DNAm) responds to bisphenol exposures, but few studies have compared responses across tissues. We leveraged the Michigan Mother-Infant Pairs cohort to evaluate DNAm in four previously identified genes across matched cord blood (CB), cord tissue (CT), and placental (PL) samples from 35 mother-infant pairs. In the Michigan Mother-Infant Pairs study, evaluated associations between prenatal exposure to bisphenols (BPA, BPF, and BPS) and DNA methylation (DNAm) by tissue type; compared epigenome-wide DNAm of CB and PL; and explored associations between prenatal bisphenol exposure and epigenome-wide DNAm in PL. Bisphenol concentrations were quantified in first-trimester maternal urine. DNAm was assessed at four genes via pyrosequencing in three tissues: epigenome-wide DNAm analysis via Infinium MethylationEPIC array was completed in CB and PL. Candidate gene analysis revealed tissue-specific differences across all genes. In adjusted linear regression, BPA and BPF were associated with DNAm across candidate genes in PL, but not CB and CT. Epigenome-wide comparisons of matched (fetal) PL DNAm revealed tissue-specific differences at most CpG sites, and modest associations between maternal first-trimester bisphenol exposures and PL, but not CB DNAm. These data endorse inclusion of a variety of tissues in perinatal exposure studies. Overlapping and divergent responses in CB, CT, and PL demonstrate their utility in combination to capture a fuller picture of the epigenetic effect of developmental exposures.	Reprod Toxicol. 2023 Jan;115:74-84.	10.1016/j.reprotox.2022.11.005	36473650	ヒト	遺伝毒性								コホート研究	1	1							1	1	1											
統合_0340	A. Martínez-Ibarra, L. D. Martínez-Razo, E. R. Vázquez-Martínez, N. Martínez-Cruz, R. Flores-Ramírez, E. García-Gómez, M. López-López, C. Ortega-González, I. Camacho-Arroyo and M. Cerbón	2019	Unhealthy Levels of Phthalates and Bisphenol A in Mexican Pregnant Women with Gestational Diabetes and Its Association to Altered Expression of miRNAs Involved with Metabolic Disease	Several studies indicate that bisphenol A (BPA) and phthalates may have a role in the development of metabolic diseases using different molecular pathways, including epigenetic regulatory mechanisms. However, it is unclear whether exposure to these chemicals results in even levels of miRNAs associated with gestational diabetes mellitus (GDM) risk. In the present study, we evaluated the urinary levels of miRNAs associated with GDM (miR-9-5p, miR-16-5p, miR-29a-3p and miR-330-5p) and urinary levels of phthalate metabolites (mono-n-butyl phthalate (MBP), mono-isobutyl phthalate (MiBP), mono-benzyl phthalate (MBzP) and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)) and BPA in pregnant women with GDM ($n = 30$) and healthy pregnant women ($n = 30$). Urinary BPA levels were higher ($p = 0.0001$) in pregnant women with GDM compared to non-diabetic subjects. Phthalates were detected in 87 (58%) of urine samples, while BPA was in 60%. Urinary MEHHP and BPA concentrations were higher in women exposed to previously reported data. Unadjusted MEHP levels and adjusted BPA levels were higher in non-diabetics than in GDM patients ($p = 0.03$, $p = 0.02$). We found positive correlations between adjusted urinary MEHP levels and miR-16-5p expression levels ($p = 0.04$), adjusted MEHP concentrations and miR-29a-3p expression levels ($p = 0.05$). We also found negative correlations between unadjusted and adjusted MEHP concentrations and miR-29a-3p expression levels ($p = 0.004$, $p = 0.04$), unadjusted MiBP concentrations and miR-29a-3p expression levels ($p = 0.01$). Urinary MEHP levels reflect a striking exposure in di(2-ethylhexyl) phthalate (DEHP) in Mexican women. This study highlights the need for a regulatory strategy in the manufacture of several items containing endocrine disruptors in order to avoid involuntary ingestion of these compounds in the Mexican population.	Int J Mol Sci Vol.20 Issue 13	10.3390/ijms20133343	31284700	ヒト									横断研究	1	1																		
統合_0341	E. Martínez Steele, N. Khandpur, M. L. da Costa Louzada and C. A. Monteiro	2020	Association between dietary contribution of ultra-processed foods and urinary concentrations of phthalates and bisphenol in a nationally representative sample of the US population aged 6 years and older	Ultra-processed food consumption has been associated with several health outcomes such as obesity, hypertension, cardiovascular disease and cancer. The deleterious nutrient profile of these products, and the presence of food additives, reactive vapour compounds and contact materials such as phthalates and bisphenol may be some of the potential pathways through which ultra-processed food formulations decrease cancers. The aim of this study was to examine the association between dietary contribution of ultra-processed foods and urinary biomarker concentrations of parent compounds or their metabolites, including DiDP-ethylhexyl phthalate (1.3EHP), Di-2-ethylhexyl phthalate (1.5EHP), Monoisobutyl phthalate (mDiP), Mono (3-carboxypropyl) phthalate (mCPP), Monobenzyl phthalate (mBzP), Bisphenol A (BPA) and Bisphenol S (BPS). Participants from the cross-sectional 2009-2010 National Health and Nutrition Examination Survey, aged 6+ years, with urinary measures and with one 24 hour dietary recall were included in the study. Ultra-processed foods were identified according to the NOVA classification. Survey-weighted linear regression models were used to estimate the percentage difference in urinary creatinine-standardised concentrations across quintiles of energy contribution of ultra-processed foods. Models incorporated survey-sample weights and were evaluated for different sociodemographic and lifestyle variables. Adjusted geometric means of 1.3 EHP, mCNP, mCPP, mBzP and BPF increased monotonically from the lowest to the highest quintile of ultra-processed food consumption. As both phthalates, bisphenol and ultra-processed foods have been previously associated with insulin resistance, diabetes, general abdominal obesity and hypertension, our results suggest the possibility of contact materials in ultra-processed foods as one link between ultra-processed food and these health outcomes. Future studies could confirm findings and further explore these mechanisms of action.	PLoS One Vol.15 Issue 7 Pages e0236738	10.1371/journal.pone.0236738	32735599	ヒト									横断研究	1	1																		
統合_0342	M. Martínez, A. Salas-Huetos, M. Fernández de la Puente, C. Valle-Hita, M. Marqués, C. Del Egido-González, E. Davila-Cordova, C. Montes, M. S. Petersen, N. Balbis and J. Salas-Salvadó	2024	Exploring the association between urinary bisphenol A, S, and F levels and semen quality parameters: Findings from Led-Fertyl cross-sectional study	Infertility is recognized as a multifactorial condition affecting approximately 15% of couples globally, influenced by various factors, including genetic predisposition and environmental exposures. Among these environmental factors, endocrine disrupting chemicals (EDCs) have garnered attention for their potential impact on reproductive health. Bisphenols, a group of EDCs commonly found in plastics and other consumer products, are substances such as bisphenol A (BPA) and bisphenol F (BPF) have emerged. Animal studies have demonstrated a dose-dependent decline in testicular function and embryotoxicity following these exposures in BPA. However, literature data on human studies are limited and heterogeneous. Additionally, even less is known about the relationship between exposure to the BPA analogues (BPF) and BPS and sperm quality. Therefore, the present study aimed to examine the association between urinary concentrations of BPA, BPF, and BPS and semen quality parameters among 195 adult Spanish men from the Led-Fertyl study using multiple linear regression models adjusted by potential confounding variables. Our results revealed an inverse association between log-transformed creatinine-adjusted concentration (ng/mg) of BPA and BPF levels and the percentage of sperm with DNA damage (β: -0.06; 95%CI: -0.11, -0.01; p = 0.02 and β: -0.06; 95%CI: -0.11, -0.01; p = 0.02, respectively). Moreover, men in the highest tertile of BPA concentrations (≥ 1.5 ng/mL) showed lower values in the lowest quartile (Q1: 6.38 %; 95%CI: 5.60 to 7.15 and Q1: 9.60 %; 95%CI: 8.15 to 11.05; p = 0.04, respectively). These results supply epidemiological evidence establishing a relationship between bisphenols, urine exposure and sperm quality, suggesting that a re-evaluation of the current safety of BPA alternatives is warranted.	Environ Res Vol.263 Issue Pt 2 Pages 120086	10.1016/j.envres.2024.120086	39353529	ヒト									横断研究	1	1																		
統合_0343	M. Martínez, M. Marqués, A. Salas-Huetos, N. Babio, J. L. Domingo and J. Salas-Salvadó	2022	Lack of association between endocrine disrupting chemicals and male fertility: A systematic review and meta-analysis	The incidence of infertility currently affects about 15% of the world's population. Male factors are estimated to be responsible for up to 30-50% of these cases. While the cause of these reproductive disorders is still unknown, endocrine disrupting chemicals (EDCs) have emerged as a possible factor. The aim of this study was to systematically review the literature published to date (2000-2021) on the association between EDCs and male reproductive health. Cross-sectional studies reporting whether human male exposure to EDCs affects male fertility, Clinical and observational studies assessing the exposure to EDCs using urine quality, human semen reproductive disorders, sperm DNA damage, sperm oxidative stress, fertilization rate, implantation rate, clinical pregnancy rate, live birth rate, and miscarriage rate were included. The quality assessment tool from the NHLBI-NIH was used to assess their studies. Ten standardized quality criteria, Sensitivity analysis and heterogeneity among studies was assessed. Overall, the 32 selected articles, including 7835 individuals in the systematic review, explored 13 families of EDCs. The results revealed a high heterogeneity among studies. In relation to the association between exposure to EDCs and the endpoints analyzed. Meta-analyses were performed with data from 3 studies including 1240 men. The pooled estimates revealed a significant association between exposure to EDCs and sperm DNA damage (standardized mean difference (SMD) = 0.33; 95% CI: 0.04, 0.62). However, the conventional significant positive association between PCB153 exposure and sperm concentration. However, it would not be clinically relevant. No positive or inverse associations were found within for BPA, nor for PCB153 and the rest of sperm parameters analyzed. The high disparity between studies made difficult to draw conclusions on the potential harmful effects of EDCs on male fertility. Consequently, to delineate the potential relationship that EDCs can have on male fertility, an important conditions crossing the health system, further investigations are required.	Environ Res. 2023 Jan 15:217:114942.	10.1016/j.envres.2022.114942	36436552	ヒト									メタアナリシス	1	1							1	1	1		1							
統合_0344	M. Martínez, N. González, A. Marí, M. Marqués, J. Rovira, V. Kumar and M. Nadal	2021	Human biomonitoring of bisphenol A along pregnancy: An exposure reconstruction of the EXHES-Spain cohort	This study was aimed at reconstructing the exposure to bisphenol (BPA) of 60 pregnant women from the EXHES-Spain cohort. A biomonitoring study was conducted by determining BPA levels in urine samples over the three trimesters of pregnancy. Moreover, the correlations between BPA levels and the role of different potential exposure sources, with special emphasis on the dietary intake, were also studied. Urine samples were subjected to dispersive liquid-liquid microextraction and the analysis was performed by gas chromatography–mass spectrometry. BPA was detected in 76% of the collected samples. Significant decrease of urinary BPA levels was observed along pregnancy, as mean concentrations of creatinine-adjusted BPA were 3.82, 4.86 and 2.51 μg/g in the first, second and third trimester, respectively. This decrease was essentially associated with the lower BPA concentrations found in the third trimester samples. Estimated daily intakes (EDIs) were calculated for the three trimesters of pregnancy, and were found to be dissimilar. Very interestingly, significant differences in urine BPA levels were found according to the fish consumption pattern, as women who ate more citrus fruits showed lower BPA concentrations in urine. The reconstructed exposure to BPA was estimated to 0.072, 0.088 and 0.048 μg BPA/kg of body weight/day in the first, second and third trimesters, respectively. These values are far below the temporary tolerable daily intake (t-TDI) established by the EFSA.	Environ Res Vol.196 Pages 110941	10.1016/j.envres.2021.110941	33647302	ヒト									バイオモニタリング	1	1																		
統合_0345	D. Martín-Way, I. Puche-Sanz, J. M. Cozar, A. Zafra-Gomez, M. D. C. Gomez-Regalado, C. M. Morales-Alcaraz, A. F. Hernandez, L. J. Martinez-Gonzalez and M. J. Alvarez-Cubero	2022	Genetic variants of antioxidant enzymes and environmental exposures as molecular biomarkers associated with the risk and aggressiveness of bladder cancer	Bladder cancer (BC) is one of the top 10 most common cancers worldwide however, no molecular markers are currently available for tumor management and follow-up. BC could benefit from molecular biomarkers in environmental disease, which provide mechanistic understanding of individual susceptibility to exposure-related cancers and allow characterizing genetic alterations in the molecular pathway for malignancy. This case-control study performed a molecular analysis in 99 BC and 125 controls. Buccal swabs were collected to assess SNPs in eleven genes coding for xenobiotic detoxification enzymes, cellular antioxidant defenses, and hormone synthesis and signaling (NAT2 rs1801280, SPINK1 rs17438068 and rs7849382, TAYSB1 rs1125900, PRSS1 rs17438062, PRSS2 rs6465651, GSTT1 rs17856199, GSTT2 rs17856272 and GSTT2 rs17856273). A structured questionnaire was administered to study participants to assess environmental and dietary chemical exposures. Several mRNAs associated to BC and aggressiveness were also analyzed in tumor tissues and matched controls (TERT, CLDN3, EGFR, ERBB2, PTEN, and GPX3). Urine samples were collected from BC patients to assess environmental pollutants (polycyclic aromatic hydrocarbons and endocrine-disrupting chemicals) were determined in urine from a subsample of BC cases and controls. We found that CYP1A1, GSTT2, ERBB2, PTEN, and GPX3 (rs17856199T) were associated with BC risk. Furthermore, exposure to smoke and/or diet, and alcohol intake were identified as risk factors for BC. Increased urinary levels of benzo[a]pyrene and bisphenol A were observed in BC patients relative to controls, along with an increased expression of miR-100b, miR-27b, and miR-97-5p in BC. Nevertheless, further studies with a larger sample size are warranted to confirm these exploratory results. This study also shows that the combination of genetic markers (PON1 and CYP27A1) and miRNA (miR-21) 3p and miR-92-1p) opens new scenarios in the use of non-invasive biomarkers in the classification of BC to guide personalized medicine, which is extremely urged in the current clinical setting.	Sci Total Environ. 2022 Oct 15:843:156965.	10.1016/j.scitotenv.2022.156965	35764155	ヒト									症例対照研究	1	1							1	1										
統合_0346	J. Martín, J. L. Santos, I. Aparicio and E. Alonso	2019	Exposure assessment to parabens, bisphenol A and perfluoroalkyl compounds in children, women and men by hair analysis	Population is continuously exposed to endocrine disrupting compounds present in everyday products such as parabens, bisphenol A (BPA), and perfluoroalkyl compounds (PFCs). The aims of this study were: first, to evaluate human exposure to three parabens (methylparaben (MeP), ethylparaben (EtP) and propylparaben (PrP)), BPA and six PFCs (perfluorobutanoic acid, perfluoropentanoic acid, perfluorohexanoic acid (PFHxA), perfluoroctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS)) through the analysis of hair samples from children, women and men and, then, to evaluate possible relationships between the concentrations found in hair and several factors potentially influencing exposure. Hair samples were collected from 100 children (50 girls and 50 boys) and 100 women and 100 men from Madrid (Spain). Analytical methods based on ultrasound-assisted extraction (UAE) followed by ultra-high performance liquid chromatography–tandem mass spectrometry (UHPLC-MS/MS) were developed and validated for the analysis of hair samples. The highest concentrations and frequency of detection (DF) of the analytes were found in the case of MeP and PrP (up to 11,100 and 9888 ng/g, respectively). BPA was found in 85% of the samples at concentrations in the range from 26 to 1227 ng/g whereas PFCs were detected at concentrations in the range from 0.6 to 13.3 ng/g, being PFHxA and PFOS the ones most frequently detected (85% and 76%, respectively). Concentrations of BPA and parabens in adults were statistically higher than those in children. The results of this study reveal the suitability of hair for biomonitoring endocrine disrupting compounds of high concern: PFCs, parabens and BPA) to which population is internally or/and externally but continuously exposed.	Sci Total Environ Vol.695 Pages 133864	10.1016/j.scitotenv.2019.133864	31421338	ヒト									バイオモニタリング	1	1																		
統合_0347	V. Marotta, L. Grumetto, I. Nori, G. Russo, A. Tortora, G. Izzo, I. Parravicini, D. Rocco, L. Pezzullo and M. Vitale	2023	Exposure to Bisphenol A increases malignancy risk of thyroid nodules in overweight/obese patients	Bisphenol A (BPA) is a widespread thyroid disruptor, but evidence about an association with thyroid cancer is weak. Excess body weight is a risk factor for thyroid cancer and affects activity of endocrine disruptors. Aim of the study was to investigate the association between BPA exposure and thyroid cancer, verifying the effect modification related to body weight. We performed a multicentric, cross-sectional study including consecutive patients undergoing thyroid surgery for nodules. Urinary BPA was measured by high-performance liquid chromatography-tandem mass spectrometry. Logistic regression models were used to detect risk factors for malignancy detection. Ninety-six patients were included: 50 benign nodules, 46 thyroid cancers, 28 normal weight, and 68 overweight/obese. BPA was detected in 79 subjects. The overall median BPA value was 0.6 ng/mL and in the group with BMI<25 kg/m2 BPA exposure was not significantly correlated to thyroid cancer (p = 0.08 and 0.759, respectively). In the group with BMI≥25 kg/m2, BPA-exposed subjects showed significantly higher risk of malignancy (OR 5.2, p = 0.026). In multivariate analysis, such association was independent of smoking, alcohol consumption, occupational exposure, and phthalates exposure (p = 0.025 and 0.026, respectively), but was lost after adjustment for the presence of metabolic syndrome (p = 0.089). In overweight/obese subjects, BPA exposure was significantly associated with higher thyroid-stimulating hormone levels. Our study suggests that BPA exposure is a risk factor for thyroid cancer in overweight/obese subjects.	Environ Pollut Vol.316 Issue Pt 1 Pages 120478	10.1016/j.envpol.2022.120478	36306887	ヒト									横断研究	1	1																		
統合_0348	V. S. Malik, K. Ravindra, P. Rattan, D. Dayal and S. V. Attri	2021	Environmental exposure to urinary Bisphenol-A in North Indian children aged between 6 and 16 years and its association with body mass index	This study investigates the effect of environmental risk factors among North Indian children aged between 6 and 16 years associated with body mass index by comparing fasting and non-fasting urine Bisphenol-A, urine creatinine, and anthropometric measurements. Urine samples were collected from 200 children (100 fasting and 100 non-fasting) and analyzed for Bisphenol-A and creatinine using HPLC and UV-Vis spectrophotometer, respectively. Children were grouped into obese, non-obese, and underweight categories based on age- and gender-specific Centre for Disease Control (CDC) 2000 growth chart and compared according to their body mass index. The overall mean ± SD (standard deviation) of age (years) was 10.65 ± 2.38 (boys, age 10.58 ± 2.38 and girls age 10.65 ± 2.45). Urinary Bisphenol-A concentration (ng/mL ± SD) was higher among obese (2.48 ± 0.42) than non-obese (1.98 ± 0.32) and underweight (1.52 ± 0.29) children. Urinary Bisphenol-A concentration (ng/mL ± SD) was higher among females (2.08 ± 0.42) than males (1.89 ± 0.32). Urinary Bisphenol-A concentration (ng/mL ± SD) was higher among fasting (2.04 ± 0.42) than non-fasting (1.93 ± 0.32) children. Urinary Bisphenol-A concentration (ng/mL) was significantly ($p < 0.05$) higher among obese subjects than non-obese and underweight subjects. Urinary Bisphenol-A concentration (ng/mL) was significantly ($p < 0.05$) higher among females than males and fasting than non-fasting

別添-2　統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性懸念等不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	遺伝毒性試験	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性生評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0350	J. Majewska, A. Berg, J. Jurewicz, K. Daroszek, R. Zajdel, A. Kilanowicz, A. Wasik and D. Rachoń	2024	Bisphenol A analogues and metabolic syndrome in women with polycystic ovary syndrome	Bisphenols (BPs) have become a chemical group of special interest due to their ability to interfere with the endocrine system and their ubiquitous presence in the environment. As some of them possess mild estrogenic and anti-androgenic effects, they might be associated with the diagnosis of polycystic ovary syndrome (PCOS). Acting on multiple tissues, BPs exposure may lead to metabolic derangements, characteristic for metabolic syndrome (MetS). The aim of the study was to assess the relationship between exposure to bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), bisphenol AF (BPAF), and bisphenol AP (BPAP) and MetS in women with PCOS. In 1 year, women who were diagnosed with PCOS (study group; n = 100) and who were not (control group; n = 100) were enrolled in the study. BP concentrations were measured in the fasted state in serum samples using a validated method based on liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Women who were overweight or obese (BMI ≥ 25 kg/m2) were more likely to be diagnosed with PCOS (adjusted OR (95%CI) 0.45 (0.25–0.80), P = 0.007) and MetS (0.37 (0.19–0.74), P = 0.005, correspondingly). Serum concentrations of BPs were not associated with the MetS diagnosis in the PCOS group. There was a negative correlation between the concentrations of serum BPAP and total serum cholesterol (r = − 0.19, P = 0.050), BPA and serum cholesterol (r = − 0.18, P = 0.032) as well as BPS and HDL cholesterol (r = − 0.208, P = 0.036). There was a positive correlation between the concentrations of BPAP and serum triglycerides (r = 0.20, P = 0.036). Our results point to the potential association between exposure to BPA, BPS, and the diagnosis of PCOS, along with the impact of BPAP, BPS, BPC, and BPF on the metabolic features of the MetS.	Reprod Toxicol Vol.123 Pages 108511	10.1016/j.reprotox.2023.108511	37984601	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0351	V. Magalhães, M. Severo, S. A. Costa, D. Correia, C. Carvalho, D. Torres, S. Casal, S. Cunha and C. Lopes	2024	Bisphenol A and cardiometabolic risk in adolescents: Data from the Generation XXI cohort	BACKGROUND AND AIMS: Bisphenol A (BPA), an endocrine-disruptor widely used in food contact materials, has been linked to a worse health profile. This study intends to estimate the association between BPA exposure and cardiometabolic patterns at adolescence. METHODS AND RESULTS: Data from the Portuguese population-based birth cohort Generation XXI at the age of 13 were used (n = 288 providing 3-day food diaries and fasting blood samples). BPA exposure was measured in 24 h urine samples (n = 288) and then predicted at participants' age using a validated mixed model. Multivariate regression models were applied to associate BPA. Three cardiometabolic patterns were identified (normal, modified lipid profile and higher cardiometabolic risk), using a probabilistic Gaussian mixture model. Multinomial regression models were applied to associate BPA exposure with the cardiometabolic patterns. Adolescents with higher BPA exposure were more likely to present a modified lipid profile (OR (95%CI) 1.03 (1.00–1.06), P = 0.030) and higher cardiometabolic risk (1.04 (1.01–1.08), P = 0.009), when compared to normal cardiometabolic pattern. Boys with higher BPA exposure had higher medium and lower levels of total, LDL and HDL cholesterol (β = -0.04, P = 0.030; β = -0.04, P = 0.040; β = 0.04, P = 0.040, respectively). Adolescents with higher BPA exposure had higher medium and lower levels of total, LDL and HDL cholesterol (β = -0.04, P = 0.030; β = -0.04, P = 0.040; β = 0.04, P = 0.040, respectively). Boys with higher BPA exposure had higher levels of body fat (kg) (β = 0.04, P = 0.040) and trunk fat (kg) (β = 0.04, P = 0.040). Girls

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	透明性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0363	J. López-Vázquez, R. Rodil, M. J. Trujillo-Rodríguez, J. B. Quintana, R. Cela and M. Miró	2022	Mimicking human ingestion of microplastics: Oral bioaccessibility tests of bisphenol A and phthalate esters under fed and fasted states	Notwithstanding the fact that microplastic fragments were encountered in the human stool, little effort has been geared towards elucidating the impact of chemical additives upon the human health. In this work, standardised bioaccessibility tests under both fasting and fed conditions are herein applied to the investigation of human oral bioaccessibility of plastic additives and monomers (i.e. eight phthalate esters, PAEs, and bisphenol A (BPA)) in low-density polyethylene (LDPE) and polyvinyl chloride (PVC) microplastics. The generation of phthalate monoesters is evaluated in the time course of the three enzymatic tests. Gluconeo-gastric conditions are found to be responsible for the hydrolysis of PAEs, with half-lives ranging from 20 to 40 min. Bile salts and pancreatin are responsible for the intestinal hydrolysis of phthalate and diethyl phthalate, respectively, whereas their hydrolytic products are considered. Bioaccessible fractions of solid PAEs are moderate and the physicochemical characteristics of the microplastics, i.e., the glass transition temperature, seem to have a significant role in the bioaccessibility of PAEs. Bioaccessibility values ranged from 0.1% to 32.1%, with upper-significantly larger monoester percentages for LDPE. Our results suggested that the highest gastro-pancreatic bioaccessibility of the eight PAEs and BPA is reached under fed-state gastrointestinal extraction conditions because of the larger amounts of surface-active biomolecules. Even including the bioaccessibility factor within human risk assessment/exposure studies to microplastics, concentrations of dimethyl phthalate, di-n-butyl phthalate and BPA exceeding 0.3% (w/w) may pose severe risks after oral uptake in contrast to the more hydrophobic congeners for which concentrations above 3% (w/w), except for diethylhexyl phthalate, would be tolerated.	Sci Total Environ Vol.826 Pages 154027	10.1016/j.scitotenv.2022.154027	35217040	ヒト	-	-	-	-	-	-	ADME	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0364	A. López-Moreno, Á. Ruiz-Moreno, J. Pardo-Cacho, K. Cerk, A. Torres-Sánchez, P. Ortiz, M. Ubeda and M. Aguilera	2022	Culturing and Molecular Approaches for Identifying Microbiota Taxa Impacting Children's Obesogenic Phenotypes Related to Xenobiotic Dietary Exposure	Integrated data from molecular and improved culturomics studies might offer holistic insights on gut microbiome dysbiosis triggered by xenobiotics, such as obesity and metabolic disorders. Bisphenol A (BPA), a dietary xenobiotic obesogen, was chosen for a directed culturing approach using the microbiota from 50 children with obesity and normal weight profiles. Culture-dependent molecular analyses were carried out to estimate the BPA metabolizing capacities. Finally, catalogues of 257 BPA-directed cultured microorganisms were isolated using five selected media and varied BPA treatments and conditions. Taxa from Firmicutes, Proteobacteria, Actinobacteria, and Bacteroidetes phyla were identified. Bacteroides, Clostridium, Escherichia, Bifidobacterium, and Lactobacillus were genera with the highest BPA-degrading capacities. Unexpectedly, the representative isolates' taxa from normal-weight vs. overweight/obese were grouped as BPA-biodegradable, tolerant, or resistant bacteria according to their BPA-degradation and BPA-enzymes richer whole genome sequences. Remarkably, the presence of xyanolytic and commonly Bacillus spp. showed the higher BPA biodegradation potential in overweight/obese group compared to normal weight, which could drive a relevant role in obesity and metabolic dysbiosis triggered by these xenobiotics.	Nutrients Vol.14 Issue 2	10.3390/nu14020241	35057422	ヒト	-	-	-	-	-	-	腸内細菌叢解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0365	A. López-Moreno, P. Largeña, R. Martín and M. Aguilera	2023	Microbiota analysis for risk assessment of xenobiotic exposure and the impact on dysbiosis: identifying potential next-generation probiotics	On-going projects of the team are currently dealing with microbiota, xenobiotics, endocrine-disrupting chemicals (EDCs), obesity, inflammation and probiotics. The combination of diet, lifestyle and the exposure to dietary xenobiotics, including EDCs, can contribute to the development of obesity and metabolic disorders. Gut microbiota dysbiosis has been associated with obesity and its related phenotypes. Specific, complementary, and combined preventive and treatments are needed to face these altered microbial patterns and the specific misbalances they induce. In this sense, searching for next-generation probiotics (NGP) by microbiota culturing, and focusing on their demonstrated, extensive scope and well-defined functions, could contribute to counteracting and repairing the effects of obesogens. Therefore, EU FORI project contributes to present a perspective through compiling information and key strategies for directed culturing and culture of NGP that could be performed by using conventional selective and related dysbiosis by (1) observing the differential abundance of specific microbiota taxa in obesity-related patients and analyzing their functional roles, (2) developing microbiota-directed strategies for culturing these taxa in vitro, (3) design and applying the most suitable and completed criteria from novel NGP clinical studies. New isolated or cultivable microorganisms from healthy gut microbiota specifically related to metabolic obesogenic bacterial pattern shifts might be used as an NGP single strain or in consortia, both presenting functions and the ability to palliate metabolic-related disorders. Identification of holistic approaches for searching and using potential NGP, key aspects, the how, gaps and proposals of solutions were also considered in this workplan.	Efsa j Vol.21 Issue Suppl 1 Pages e211010	10.2903/j.efsa.2023.e211010	38047127	ヒト	-	-	-	-	-	-	腸内細菌叢解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0366	A. López-Moreno, K. Cerk, L. Rodrigo, A. Suarez, M. Aguilera and A. Ruiz-Rodriguez	2024	Bisphenol A exposure affects specific gut taxa and drives microbiota dynamics in childhood obesity	Cumulative xenobiotic exposure has an environmental and human health impact which is currently assessed under the One Health approach. Bisphenol A (BPA) exposure and its potential link with childhood obesity that has parallelly increased during the last decades deserves special attention. It stands during prenatal or early life and could trigger comorbidities and non-communicable diseases along life. Accumulation in the nature of synthetic chemicals supports the "environmental obesogen" hypothesis, such as BPA. This estrogen-mimicking xenobiotic has shown endocrine-disruptive and obesogenic effects, also potentially gut microbiota misbalance that is not yet well elucidated. This study aimed to investigate specific microbiota taxa isolated and cultured by direct BPA exposure and reveal its role on the overall children microbiota community and dynamics. Fecal samples from 50 children (25 with obesity and 25 normal weight) were cultured in selective media supplemented with BPA (0 and 400 µg/mL) to isolate BPA-resistant microbial community. The selected BPA-induced taxa themselves showed a significant impact on viable BPA-degradation rates. Specifically, Clostridium and Pantoea taxa were positively correlated with BPA-enzymes richer communities, while Enterobacter, Escherichia-Shigella, Bifidobacterium, and Lactobacillus were negatively associated. Microbial community dynamics and networks analyses showed differences according to the study groups. The normal weight children group exhibited a more enriched, structured, and connected taxa network compared to overweight and obese groups, which could mean a more vulnerability to xenobiotic substances. In this sense, subnetwork analysis generated with the BPA-cultured genera showed a correlation between taxa connectivity and more diverse potential enzymatic BPA-degradation capacities/functionalities. Our findings suggested that BPA-induced microbiota dysbiosis could be associated with childhood obesity development, and how these taxa influenced the overall dynamics/ecological patterns of diversity generally recognized in dysbiosis. Commonly network and subnetwork analyses corroborated the better connectedness and stability profiles for normal weight group compared to the overweight and obese groups.	mSystems Vol.9 Issue 3 Pages e0095723	10.1128/msystems.00957-23	38426791	ヒト	-	-	-	-	-	-	腸内細菌叢解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0367	L. López-Carrillo, A. Morán-Ortega, N. Gómez-Ruiz, L. Hernández-Garciadiego and B. Gamboa-Loira	2021	Exposure to bisphenol A and breast cancer risk in northern Mexican women	OBJECTIVE: To evaluate the association between BC and urinary concentrations of free bisphenol A (BPA-F), the biological form of BPA, among women residing in Northern Mexico. METHODS: The population under study comprised 1,503 histologically confirmed BC cases and 1,503 age-matched controls. Women were interviewed face to face about their sociodemographic and reproductive characteristics. BPA-F was determined by high-pressure liquid chromatography equipped with a fluorescence detector (HPLC-FLD). Logistic regression models were used to estimate the adjusted BC risk in relation to BPA-F. RESULTS: BPA-F geometric mean were significantly higher among cases compared to controls (5.16 µg/L in cases and 2.27 µg/L in controls). A significant adjusted BC odds ratio of 2.32 (95% CI: 1.87-2.76) was estimated for the highest category of BPA-F compared to the lowest category. CONCLUSION: BPA-F may be an environmental cofactor of BC. Since this is the first report on BPA-F association with BC, our results need to be replicated.	Int Arch Occup Environ Health Vol.94 Issue 4 Pages 699-706	10.1007/s00420-020-01590-x	33392751	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0368	X. Liu, L. Wang, X. Liu, P. Yu, Y. Diao, T. Chen, Y. Sheng, D. Zhang, D. Peng, Y. Gu, S. Li and R. Xu	2025	Microplastics, plastics, and their products exposures and cancer: a pooled analysis	OBJECTIVE: This meta-analysis aims to evaluate the impact of microplastic pollutant exposure on cancer risk by analyzing data from existing cohort and case-control studies. METHODS: The researchers systematically searched PubMed, Embase, and the Cochrane Library on 30 June 2024 to identify relevant studies. The analysis focused on cancer incidence and mortality, with subgroup assessments for different types of cancers and microplastic pollutants, and dose-response analysis for further investigation.Publication bias was assessed by funnel plots, Egger's test, and Begg's test. All data processing and analysis were performed using Stata 17.0 software. RESULTS: The meta-analysis included 11 studies, comprising 5,363 children with cancer and 1,072,000 participants. The pooled results indicated that exposure to microplastic pollutants was associated with an increased risk of cancer (OR = 1.16, 95% CI = 1.03 to 1.30), but not for cohort studies (OR = 1.03, 95% CI = 0.96 to 1.12). Subgroup and dose-response analysis revealed that phthalates (OR = 1.28, 95% CI = 1.08 to 1.52) and bisphenol A (OR = 1.08, 95% CI = 1.03 to 1.14) might be associated with cancer risk in case-control studies. CONCLUSION: Existing evidence from case-control studies suggests a weak correlation between microplastic pollutant exposure and cancer risk. However, this causal relationship needs to be interpreted with caution due to the methodological limitations of existing evidence.	Int J Surg. 2025 Aug 1;111(8):5593-5605.	10.1097/js9.0000000000002631	40540244	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0369	J. Liu, M. Tian, H. Qin, D. Chen, S. M. Mzava, X. Wang and F. M. Bigambo	2024	Maternal bisphenols exposure and thyroid function in children: a systematic review and meta-analysis	BACKGROUND: Evidence from animal experiments and epidemiological studies has reported controversial results about the effects of prenatal bisphenols (BPs) exposure on childhood thyroid function. This study aims to explore the associations of prenatal exposure to BPs with thyroid-related hormones (THs) in newborns and early childhood, with a particular focus on the sex-dependent and exposure level effects. METHODS: Correlated studies were systematically searched from PubMed, Web of Science, Medline, Cochrane, and Embase until February 21, 2024. The exposure assessed include bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), and other BPs. The outcomes were specified as any hormones from maternal/cord blood, newborn blood spots, and children's blood. RESULTS: A total of 2,390 records were identified, and 19 studies with a total of 7,390 maternal-child pairs and their response rate were included in meta-analyses. Statistical analyses were conducted using Stata 16.0. The methodological quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS). RESULTS: Eleven cohort studies comprising 5,363 children were included in our meta-analysis. Prenatal bisphenol concentrations were statistically significant related to alterations in thyroid hormones in children, exclusively in female infants during mid-late pregnancy. Specifically, BPA was positively associated with TSH levels (β = 0.02, 95% CI: 0.00, 0.03), and inversely with high concentrations of bisphenols (>1.5 µg/g creatinine) significantly reduced FT3 levels in children (β = -0.01, 95% CI: -0.02, -0.00). CONCLUSION: Prenatal bisphenol exposure is linked to alterations in thyroid hormone levels in girls, necessitating enhanced measures to control bisphenol exposure levels during pregnancy for child health protection. SYSTEMATIC REVIEW REGISTRATION: https://inplasy.com, identifier INPLASY202350129.	Front Endocrinol (Lausanne). 2024 Jul 1;15:1420540.	10.3389/fendo.2024.1420540	39010904	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0370	J. Liu, L. J. Martin, I. Dinu, C. J. Field, D. Dewey and J. W. Martin	2021	Interaction of prenatal bisphenols, maternal nutrients, and toxic metal exposures on neurodevelopment of 2-year-olds in the APrON cohort	BACKGROUND: Epidemiological studies suggest that Bisphenol A (BPA) is a developmental neurotoxicant, but the modifying effects of maternal nutrient status or neurotoxicant metal co-exposures have not been reported. Bisphenol F (BPF) is being used as a BPA alternative, but few epidemiological studies have evaluated its effects. OBJECTIVES: To examine if prenatal maternal BPA/BPF exposures are associated with children's neurodevelopment at two years of age while adjusting for effect measure modification by sex, maternal nutrients, and co-exposure to neurotoxic metals. METHODS: Total BPA and BPF concentrations were measured in urine samples collected from pregnant women (n = 1,503) enrolled in the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort. Neurodevelopment was assessed in their children at age 2 (n = 1,258) using the Bayley-III scales. Higher maternal C3 was significantly correlated with poorer motor performance (p < 0.01), and higher levels of maternal Se were significantly associated with poorer performance on the cognitive scale (p < 0.05). Maternal Se was also found to significantly modify the effects of BPA on cognitive scores (p < 0.05). Stratified analyses revealed that in boys, under adequate maternal Se conditions, Associations between BPA exposure and social-emotional scores were negative for boys (p = 0.056) but positive for girls (p = 0.065). Higher exposures to BPA were associated with fewer motor scores among children with lower levels of maternal Se. CONCLUSIONS: Higher maternal C3 was associated with poorer motor development, but it was not an effect measure modifier of bisphenols' effects on motor development. Maternal Se may be protective against adverse effects of bisphenols, and additional nutrient-bisphenol interaction studies examining sex-specific effects of BPA and BPF on child development are warranted.	Environ Int. 2021 Oct:155:106601.	10.1016/j.envint.2021.106601	33962233	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0371	J. Liu and J. W. Martin	2019	Comparison of Bisphenol A and Bisphenol S Percutaneous Absorption and Biotransformation	BACKGROUND: Bisphenol S (BPS) has been widely substituted for bisphenol A (BPA) on thermal papers, but little is known about its skin absorption. OBJECTIVES: We compared the percutaneous absorption and biotransformation of BPS and BPA in vitro and in a controlled human trial. METHODS: Absorption and biotransformation of BPS and BPA were monitored across reconstructed human epidermis at two environmentally relevant doses (0.1 and 1 μg/cm2). Urinary biomarkers of exposure were measured in 6 adult volunteers (3 females and 3 males) who applied 1 mg/cm2 of BPS or BPA to their forearms and hands. Each participant repeated the experiment with exceeded monitoring. BPS data were compared with published data for isotope-labeled BPA ([^{13}C$_{12}$]-BPA; use test) from the same participants. RESULTS: In doses at 1.0 and 0.1 μg/cm2, BPS was 19- and 8-fold more permeable than BPA (Permeability coefficient of BPS: 0.699 and [Formula: see text], respectively; [Formula: see text] was significantly lower than for BPA: 0.036 and [Formula: see text], respectively), and metabolism of both bisphenols was negligible in participants handling thermal receipts, the quantities of BPS and [Formula: see text] in hands was significantly (>6 times) higher than BPA ([Formula: see text], but the slope was lower for BPS than BPA ([Formula: see text] and 1, respectively). As a proportion of total urinary bisphenol, free BPS ([Formula: see text]) was higher than for free BPA ([Formula: see text]), and the concentrations of free BPS were 19 times greater than free BPA. Conjugation (GlcA) of BPS was more variable than BPA. Based on the BPS dose-response range of BPA in background studies, 57 ([Formula: see text]; [Formula: see text]), CONCLUSIONS: Both the in vitro and human studies suggested lower percutaneous absorption of BPS compared with BPA, but a lower biotransformation efficiency of BPS should also be considered in its evaluation as a BPA substitute. https://doi.org/10.1289/EHP5863.	Environ Health Perspect Vol.127 Issue 6 Pages 67008	10.1289/ehp5044	31199677	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0372	M. Liu, Y. Zhou, Y. Li and Z. Gong	2023	Important roles of Hif1a in maternal or adult BPA exposure induced pancreatic injuries	Bisphenol A (BPA) is a monomer to produce polycarbonate plastics, and can be released into the environment through human activities, leading to its accumulation in animals, plants and humans through direct contact or environmental exposure. Epidemiological studies have reported that BPA exposure is associated with metabolic disorders. The pancreas is an important endocrine organ and plays an important role in metabolic disorders. To explore the possible long-term effects of BPA exposure on maternal health, bioinformatic methods were used to identify differentially expressed genes (DEGs) by comparing the neonatal pancreas after maternal exposure to BPA with those of controls. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses were performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) Bioinformatics Resources 6.8 and the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database. Cytoscape was used to visualize the protein-protein interaction (PPI) network and to identify hub genes. Results: The pancreatic tissues of mice exposed to BPA during pregnancy were collected. Control (or BPA-exposed) offspring (maternal exposure) and Control (or BPA-exposed) adults (direct exposure) were defined as Control (or BPA) groups. The results showed that BPA disturbed the normal function of the pancreas in both offspring and adults, with offspring showing higher susceptibility to BPA than adults. Downstream insulin secretion related DEGs (Slc6a5, Fam3d, Nts3, Jph3, Hrh3, Ngp, Ntrk1, Fam3, Slc6a5, Cpa1, Pde1c, Rab3c, Ank1, Cnr2, Rab3, Ins1, and Kcnj9) in the BPA group were identified, and Hif1a was identified as the hub gene. Conclusion: Hif1a may be a potential target for BPA-induced pancreatic injuries in offspring.	Sci Rep Vol.13 Issue 1 Pages 11502	10.1038/s41598-023-38614-8	37460698	ヒト	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0373	M. Liu, J. Q. Duan, X. M. Ren, X. L. Li, J. Chen, P. Li and R. Q. Zhang	2020	[Changes of Gene Expression Profile in Cardiac Mesenchymal Cells in Patients with Type 2 Diabetes Mellitus and Screening of Their Related Environmental Chemicals]	Objective To study the gene expression of cardiac mesenchymal cells in patients with type 2 diabetes mellitus (T2DM) based on a whole-genome high-throughput sequencing dataset,a cores differentially expressed genes,analyze the genetics signature of cardiac mesenchymal cells in T2DM patients by bioinformatics analysis,and explore the environmental chemicals related to the key differentially expressed genes. Methods The dataset GSE136177 was obtained from Gene Expression Omnibus (GEO) database.The dataset was pre-processed and analyzed by Network Analyst.Cytoscape 3.7.1,String11.0,CTD and HIBBD for screening for differentially expressed genes,enrichment analysis,establishment of protein-protein interaction (PPI) network,screening for core genes and corresponding relevant environmental chemicals. Results The gene expression pattern of cardiac mesenchymal cells in T2DM patients was significantly different from that in the control group.There were 119 differentially expressed genes,of which 58 (48.74%) were up-regulated and 77 (57.26%) were down-regulated.Enrichment analysis showed that differentially expressed genes were mainly enriched in the biological processes of cell-matrix adhesion,cell-substrate adhesion,and extracellular matrix organization.Cellular component analysis showed that differentially expressed genes were mainly enriched in collagen-containing extracellular matrix,collagen trimer,and basement membrane.KEGG pathway analysis showed that DEC1 was the core protein node.The microRNA-Gene interaction network showed that miR-548c,hsa-miR-548c-3p,and hsa-miR-548d-3p were the core microRNAs.Conclusion The gene expression profile of cardiac mesenchymal cells in T2DM patients was significantly changed,and the core genes and environmental chemicals related to the key differentially expressed genes,Methods The dataset GSE136177 was obtained from Gene Expression Omnibus (GEO) database.The dataset was pre-processed and analyzed by Network Analyst.Cytoscape 3.7.1,String11.0,CTD and HIBBD for screening for differentially expressed genes,enrichment analysis,establishment of protein-protein interaction (PPI) network,screening for core genes and corresponding relevant environmental chemicals. Results The gene expression pattern of cardiac mesenchymal cells in T2DM patients was significantly different from that in the control group.There were 119 differentially expressed genes,of which 58 (48.74%) were up-regulated and 77 (57.26%) were down-regulated.Enrichment analysis showed that differentially expressed genes were mainly enriched in the biological processes of cell-matrix adhesion,cell-substrate adhesion,and extracellular matrix organization.Cellular component analysis showed that differentially expressed genes were mainly enriched in collagen-containing extracellular matrix,collagen trimer,and basement membrane.KEGG pathway analysis showed that DEC1 was the core protein node.The microRNA-Gene interaction network showed that miR-548c,hsa-miR-548c-3p,and hsa-miR-548d-3p were the core microRNAs.Conclusion The gene expression profile of cardiac mesenchymal cells in T2DM patients was significantly changed,and the core genes and environmental chemicals related to the key differentially expressed genes,which might be an important molecular target for perinatal cancer caused by BPA exposure, and pregnancy is a critical window of susceptibility to BPA exposure.	Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2020 Feb 28;42(1):37-46.	10.3881/j.issn.1000-503X.11497	32131938	ヒト、in vitro	-	-	-	-	-	-	遺伝子発現解析	1	1	不明	不明	不明	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0374	C. Liu, Y. Liu, J. Ning, C. Wu, X. Lu, Y. Guo, P. He, C. Qiu and J. Wu	2024	Association between bisphenol A exposure and adiposity measures in children	Bisphenol A (BPA) is a chemical that has adverse effects on human health and may cause childhood obesity. Nevertheless, the association between BPA exposure and adiposity measures in children remains controversial, especially in young children. A cross-sectional study was conducted on 208 randomly selected children (3 to 6 years old) attending preschools in Guangzhou, China. BPA exposure was assessed through urine high-performance liquid chromatography-tandem mass spectrometry. Adiposity measures, including body mass index z-score (z-BMI), waist circumference z-score (z-WC), and waist-to-height ratio z-score (z-WHtR), were calculated. Linear regression models were used to assess the associations between BPA exposure and adiposity measures. Children with a higher body mass index z-score (β = 0.672; 95% confidence interval (CI): 0.053, 0.682), and they were at a greater risk of overweight or obesity (odds ratio (OR) = 1.306; 95% CI: 1.211, 1.699). Higher urinary BPA concentrations were associated with an elevated z-score for height-for-age (β = 0.807; 95% CI: 0.802, 0.812), and they were at a higher risk of abdominal obesity (OR = 1.711; 95% CI: 1.211, 2.699). Higher urinary BPA concentrations were also associated with increased upper arm circumference and skinfold thickness in the adjusted models. (β = -0.546; 95% CI: 0.278, 0.813). (β = 0.702; 95% CI: 0.139, 1.266, respectively). Higher urinary BPA concentrations in children 3 to 6 years old were associated with a greater risk of overweight/obesity and abdominal obesity. BPA exposure might increase the risk of obesity in children. Further investigations are needed to confirm this association and explore the underlying mechanisms.	Medicine (Baltimore) Vol.103 Issue 52 Pages e41065	10.1097/md.0000000000041065	39969292	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0375	B. Liu, Y. Yan, J. Xia, J. Sun, H. J. Lehmler, L. Trasande, R. B. Wallace and W. Bao	2024	Bisphenol S, bisphenol F, bisphenol A exposure and body composition in US adults	Bisphenol S (BPS) and bisphenol F (BPF) are increasingly used to replace bisphenol A (BPA), an endocrine-disrupting chemical with putative obesogenic properties, whether and how BPS and BPF affect adiposity in humans remains unclear. We examined associations of urinary BPS, BPF, and BPA with dual-energy X-ray absorptiometry (DXA)-measured body composition in 2,747 adults aged 20 to 59 years from the National Health and Nutrition Examination Survey 2013-2014 who had information on urinary BPS, BPF, and BPF concentrations, and body composition measured using dual-energy x-ray absorptiometry. After full adjustment for potential confounders in linear regression models, BPS was significantly associated with the % body fat of the whole body, arm, and leg, with the β (95% CI) for the highest quartile vs. the lowest quartile of 1.18 (95%CI [0.11, 2.26]; P = 0.03), 1.40 (95%CI [0.35, 2.45]; P = 0.01), and 1.43 (95%CI [0.31, 2.55]; P = 0.01), respectively. No association between BPS and lean mass was found. For BPF, significant associations were found for % body fat of the whole body (β [95% CI] = -1.20 [-2.38, -2.36]; P = 0.05), trunk (-2.96% [-5.1, -0.72]; P = 0.01), and arm (-2.76% [-5.1, -1.38] [0.05, 2.73]; P = 0.01), as well as lean mass of the whole body (β [95% CI] = -0.61 [-1.19, -0.03]; P = 0.04). No significant associations were found for BPA. Urinary BPS, BPF, and BPA were detected in 75.1%, 20.1%, and 96.4% of participants, respectively. The lowest quartile vs. the highest quartile for significant associations was observed between BPF and % body fat and lean mass. Results suggest that higher BPS levels were significantly associated with greater % body fat of the whole body and limbs, and there was suggestive evidence that BPS levels were associated with both % body fat and lean mass of the whole body and body parts in a nonmonotonic relationship.	Chemosphere Vol.346 Pages 140537	10.1016/j.chemosphere.2023.140537	38303380	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通称性評価（動物）1：該当、0：該当しない　通称性評価（疫学）1：該当、0：該当しない　通称性評価（in vitro）1：該当、0：該当しない　通称性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通称性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で除害に基づく除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通称性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0376	B. Liu, X. Lu, A. Jiang, Y. Lu, H. Zhang and B. Xu	2024	Influence of maternal endocrine disrupting chemicals exposure on adverse pregnancy outcomes: A systematic review and meta-analysis	Maternal endocrine disrupting chemicals (EDCs) exposure, the common environmental pollutants, was capable of inducing inadverse pregnancy outcomes. However, the evidence of their connection is not consistent. Our study aimed to systematically review the effects of maternal exposure to EDCs on adverse pregnancy outcomes. We searched PubMed, Embase, Web of Science, and Cochrane Library for studies published before January 2023 that investigated the association between maternal EDCs exposure and adverse pregnancy outcomes including miscarriage, small for gestational age (SGA), low birth weight (LBW) and preterm birth (PTB). We found that maternal PFOA exposure was positively correlated with LBW (OR 1.21, 95% CI 1.18–1.23), SGA (OR 1.12, 95% CI 1.08–1.16) and miscarriage (OR 1.09, 95% CI 1.03–1.15). The pooled estimates also showed maternal PFOS exposure was linked with PTB (OR 1.06, 95% CI 1.01–1.11), SGA (OR 1.04, 95% CI 1.01–1.07), and miscarriage (OR 1.04, 95% CI 1.00–1.08). In addition, maternal exposure to some specific class of EDCs including PFOS, MBP, MEHP, DEHP, and BPA was associated with PTB. Maternal exposure to PFOS, PFOA, PFNA/I was associated with SGA. Maternal exposure to BPA was associated with LBW. Maternal exposure to MBP, MEHP, MCMHP, MECPP, BPA was associated with miscarriage. Maternal PFHxS, PFAS and BPA exposure may increase adverse pregnancy outcomes risk according to our study. However, the limited number of studies on dose-response hampered further explanation for causal associations.	Ecotoxicol Environ Saf. 2024 Jan 15:270:115851.	10.1016/j.ecoenv.2023.115851	38157800	ヒト	生殖生体メタアナリシス	-	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0377	R. Linares, M. F. Fernández, A. Gutiérrez, R. García-Villalba, B. Suárez, P. Zapatar, J. A. Martínez-Blázquez, E. Caparrós, F. A. Tomás-Barberán and R. Fiorucci	2021	Endocrine disruption in Crohn's disease: Bisphenol A enhances systemic inflammatory response in patients with gut barrier translocation of dysbiotic microbiota products	The relevance of environmental triggers in Crohn's disease remains poorly explored, despite the well-known association between industrialization and disease onset/progression. We have aimed at evaluating the influence of endocrine disrupting chemicals in CD patients. We performed a prospective observational study on consecutive patients diagnosed of CD. Serum levels of endocrine disruptors, short-chain fatty acids, proinflammatory cytokines were measured. Bacterial DNA and some metabolic levels were determined in portal blood. Intestinal expression of TJ proteins was assessed in colon biopsies. Patients were genotyped for SLC22 and ATG16L1 polymorphisms. A series of 200 CD patients (100 in remission, 65 with active disease) was included in the study. Bisphenol A was significantly higher in patients with active disease versus remission and in controls (p = 0.0001 and p = 0.0001, respectively). Bisphenol A was significantly higher in patients with gut barrier translocation of dysbiotic microbiota products (p = 0.0001 and p = 0.0001, respectively). Bisphenol A was significantly higher in patients with gut barrier translocation of dysbiotic microbiota products (p = 0.017; P = .002). Serum lipopolysaccharide levels were significantly lower in patients with bacterial DNA and an inverse relationship was present between them and BPA levels (r = -0.455; P < .001; r = -0.441; P = .002). Serum BPA levels correlated with IL-23 (r = 0.607; P = .001) and IL-17A (r = 0.703; P = .001). The multivariate analysis revealed an independent significant contribution of BPA and bacterial DNA to serum levels of IL-23 and IL-17A. In conclusion, bisphenol A significantly affects systemic inflammatory response in CD patients with gut barrier disruption and dysbiotic microbiota secretory products in blood. These results provide evidence of an endocrine disruptor playing an unusual pathogenic role on CD.	Faseb j Vol.35 Issue 7 Pages e21697	10.1096/fj.202100481R	34085740	ヒト	-	-	-	-	-	-	-	前向き観察研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0378	Y. J. Lin, H. C. Chen, J. W. Chang, H. B. Huang, W. T. Chang and P. C. Hu ang	2024	Exposure characteristics and cumulative risk assessment of bisphenol A and its substitutes: the Taiwan environmental survey for toxicants 2013	INTRODUCTION: Ever since the use of bisphenol A (BPA) has been restricted, concerns have been raised regarding the use of its substitutes, such as bisphenol S (BPS) and bisphenol F (BPF). Meanwhile, the EU-mandated biomonitoring of BPA and its substitutes in urine samples has been implemented since 2019. However, the exposure characteristics of BPA and its substitutes in Taiwan remain unclear. This study conducted to identify BPA and its substitute's exposure characteristics of the general Taiwanese population and estimate the cumulative risk of bisphenol exposure. METHODS: Urine samples (N = 360 [adult, 271; school, 89]) were collected from individuals who participated in the Taiwan Environmental Survey for Toxicants 2013. The samples were analyzed for BPA, BPS, and BPF through ultraperformance liquid chromatography tandem mass spectrometry. Creatinine was measured to correct the urinary concentrations. Hazard quotients (HQs) were calculated to assess the risk of exposure to BPA and its substitutes. HQs for each bisphenol values were calculated. RESULTS: Our study found that the median level of BPA (0.5 μg/g creatinine) was significantly higher in adults. HQs (1 μg/g creatinine) were also significantly higher in adults. HQs (1 μg/g creatinine) were also significantly higher in adults. HQs (1 μg/g creatinine) were also

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価へ進め、当該時評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0389	J. Liang, C. Yang, T. Liu, H. J. J. Tan, Y. Sheng, L. Wei, P. Tang, H. Huang, X. Zeng, S. Liu, D. Huang and X. Qiu	2021	Prenatal exposure to bisphenols and risk of preterm birth: Findings from Guangxi Zhuang birth cohort in China	Preterm birth (PTB), a serious adverse birth outcome, is the leading cause of perinatal mortality and morbidity. Bisphenols induce endocrine disruption that spreads across the placenta, which may affect fetal growth and development. However, the effects of bisphenols on PTB, particularly their combined effects, remain unknown. This study investigated the association between prenatal bisphenol exposure and PTB. Study participants were from the Guangxi Zhuang Birth Cohort. Concentrations of bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF) in maternal urine samples collected during early pregnancy and pregnancy outcomes were obtained from medical records. Multivariate logistic regression, restricted cubic spline, principal component analysis (PCA), quantile g-computation (Qgcomp), and Bayesian kernel machine regression (BKMR) were used to examine the association between serum bisphenol levels and PTB. Li-ion beam/cerebral BPS concentrations were associated with an increased risk of PTB only in female infants. OR= 1.38 (95% CI: 1.01, 1.89) and 1.39 (95% CI: 1.01, 1.92), respectively. Maternal BPA, BPS, and BPF levels were not associated with PTB. Stratified analysis revealed that maternal BPA, bisphenol S (BPS), and tetrabromobisphenol A (TBBPA) levels and the risk of PTB (P-overall = 0.06, P-nor-linear = 0.05). After sex stratification, the association with female BPS overlaps and PTB was only observed in males. In Qgcomp analysis, bisphenol mixtures were related to an increased risk of PTB (OR = 1.52, 95% CI: 1.00, 2.31), with BPF (33.7%), BPS (29.6%) and BPA (26.8%) having the greatest positive contribution. Results indicate that prenatal exposure to bisphenol mixtures might increase the risk of PTB, which might be primarily driven by BPS, BPF, and BPA. There may also be sex-specific and nonmonotonic dose-dependent effects.	Ecotoxicol Environ Saf. 2021 Nov 12:228:112960.	10.1016/j.ecoenv.2021.112960	34781130	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0390	J. Liang, Y. Shao, D. Huang, C. Yang, T. Liu, X. Zeng, C. Li, Z. Tang, J. T. H. Juan, Y. Song, S. Liu and X. Qiu	2023	Effects of prenatal exposure to bisphenols on newborn leucocyte telomere length: a prospective birth cohort study in China	Telomere length (TL) at birth is related to diseases that may arise in the future and long-term health. Bisphenols exhibit toxic effects and can cross the placenta barrier. However, the effects of prenatal exposure to bisphenols on newborn TL remain unclear. This study investigated the association between prenatal bisphenol exposure and TL. Study participants were from the Guangxi Zhuang Birth Cohort. Concentrations of bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF) in maternal urine samples collected during early pregnancy and pregnancy outcomes were obtained from medical records. Multivariate logistic regression, restricted cubic spline, principal component analysis (PCA), quantile g-computation (Qgcomp), and Bayesian kernel machine regression (BKMR) were used to examine the association between serum bisphenol levels and PTB. Li-ion beam/cerebral BPS concentrations were associated with an increased risk of PTB only in female infants. OR= 1.38 (95% CI: 1.01, 1.89) and 1.39 (95% CI: 1.01, 1.92), respectively. Maternal BPA, BPS, and BPF levels were not associated with PTB. Stratified analysis revealed that maternal BPA, bisphenol S (BPS), and tetrabromobisphenol A (TBBPA) levels and the risk of PTB (P-overall = 0.06, P-nor-linear = 0.05). After sex stratification, the association with female BPS overlaps and PTB was only observed in males. In Qgcomp analysis, bisphenol mixtures were related to an increased risk of PTB (OR = 1.52, 95% CI: 1.00, 2.31), with BPF (33.7%), BPS (29.6%) and BPA (26.8%) having the greatest positive contribution. Results indicate that prenatal exposure to bisphenol mixtures might increase the risk of PTB, which might be primarily driven by BPS, BPF, and BPA. There may also be sex-specific and nonmonotonic dose-dependent effects.	Environ Sci Pollut Res Int. 2023 Feb;30(10):25013-25023.	10.1007/s11356-021-14496-z	34031828	ヒト	その他(テロメア長)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0391	J. Liang, L. Pang, C. Yang, J. Long, Q. Liao, P. Tang, H. Huang, N. Wei, Q. Chen, K. Yang, T. Liu, F. Lu, S. Liu, D. Huang and X. Qiu	2023	Effects of prenatal single and mixed bisphenol exposure on bone mineral density in preschool children: A population-based prospective cohort study	Exposure to bisphenols can affect bone mineral density (BMD) in animals and humans. However, the effects of maternal exposure to bisphenols during pregnancy on bone health in preschool children remain unknown. We aimed to examine the associations between prenatal exposure to BPA, bisphenol S (BPS), bisphenol F (BPF), and tetrabromobisphenol A (TBBPA) and bone mass in preschool children. Participants were from the Guangxi Zhuang Birth Cohort. Each natural log (Ln)-unit increase in tetrabromobisphenol A was related to a 0.007 m/s (95 % CI: -0.013, 0.028) decrease in Ln-transformed speed of sound (SOS) among girls. Decreased BMD Z scores in preschool children were associated with increased maternal BPA (β = -0.165, 95 % CI: -0.330, -0.001), BPS (β = -0.166, 95 % CI: -0.331, -0.001), and TBBPA (β = -0.165, 95 % CI: -0.330, -0.001) levels. Ln (1.50) increase in BPA, BPS, and TBBPA and Ln (2.00) increase in BPF were associated with 1.162 (1.042, 1.161) and high exposure group of BPF (OR = 3.345, 95 % CI: 1.035, 10.186) compared with the low exposure group in girls, the risk of BMD decreased in mixed exposure (OR = 0.433, 95 % CI: 0.218, 0.721). BCI analysis revealed a U-shaped nonlinear correlation between BPA concentration and BMD. In girls (P-overall = 0.011, P-nonlinear = 0.009), in PCA, a U-shaped dose-response relationship was found between PC2 and the risk of BMD. (P-overall = 0.008, P-nonlinear = 0.002), and a significant association was only noted in girls. Inverted U-shaped correlations were also observed between a decrease in birth weight (P for trend = 0.007), birth length (P for trend = 0.026), and birth weight Z scores (P for trend = 0.046) in males. Our data suggested an inverse association of prenatal exposure to BPA, BPF, and TBBPA and birth size, which may be more pronounced in male infants.	Ecotoxicol Environ Saf. 2023 Nov 15:267:115665.	10.1016/j.ecoenv.2023.115665	37951091	ヒト	骨	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0392	J. Liang, S. Liu, T. Liu, C. Yang, Y. Wu, H. J. Jan-Tee Tan, B. Wei, X. Ma, B. Fang, Q. Jiang, D. Huang and X. Qiu	2020	Association of prenatal exposure to bisphenols and birth size in Zhuang ethnic newborns	Prenatal exposure to bisphenol S (BPS) and its analogues can affect fetal growth and development. However, epidemiologic findings were inconsistent and there was a lack of study for BPS analogues. We aimed to examine the associations between prenatal exposure to BPS, bisphenol B (BPB), bisphenol F (BPF), bisphenol S (BPS), and tetrabromobisphenol A (TBBPA) and birth size. 2629 mother-infant pairs were included in this study. BPS, BPB, and TBBPA were detected frequently in maternal urine samples collected during early pregnancy. Each ln-unit increase in BPS was associated with a decrease of 0.21 (95% CI: -0.32, -0.10) decrease in birth weight for all infants, and the inverse associations were also observed in males. After stratification by gestational age, higher BPS was associated with a decrease in birth weight (P for trend = 0.021), gestational index (P for trend = 0.021), and birth weight Z scores (P for trend = 0.036) in all infants, and the inverse associations were also only observed in males when stratified analysis by gender. Similarly, higher TBBPA levels were also correlated with decreased birth weight (P for trend = 0.023). However, after gender stratification, higher TBBPA concentrations were associated with a decrease in birth weight (P for trend = 0.007), birth length (P for trend = 0.026), and birth weight Z scores (P for trend = 0.046) in males. Our data suggested an inverse association of prenatal exposure to BPS, BPF, and TBBPA and birth size, which may be more pronounced in male infants.	Chemosphere. 2020 Aug:252:126422.	10.1016/j.chemosphere.2020.126422	32199162	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0393	Y. Liang, X. Hua, W. Wang, Y. Li, J. Zhang, Y. Feng and Y. Wang	2020	Association of bisphenol A or bisphenol S exposure with oxidative stress and immune disturbance among unexplained recurrent spontaneous abortion women	Human exposure to environmental chemicals might play a role in the pathogenesis of unexplained recurrent spontaneous abortion (URSA). Bisphenol A (BPA) and bisphenol S (BPS) have been suggested to affect reproductive health. However, the mechanism remains unclear. To explore the association between BPA and BPS exposure and oxidative stress and immune homeostasis, we conducted a cross-sectional study and recruited 257 URSA women and 120 healthy pregnant women as controls. Urinary BPA and BPS concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry. Serum biomarkers of oxidative damage (malondialdehyde and 8-hydroxydeoxyguanosine) and Th-associated cytokines (interleukin (IL)-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IFN-γ, TNF-α, and TNF-β) were detected. Multiple linear regressions were used to evaluate the correlation between bisphenols exposure and outcome biomarkers. After adjustment for age, BMI, menstrual cycle, and parity history, creatinine-adjusted BPA was significantly associated with increases in 8-hydroxydeoxyguanosine (β = 0.19, 95% CI = 0.07, 0.31), IL-2 (β = 0.053 and 95% CI = 0.02, 0.08), and IFN-γ (β = 0.08, 95% CI = 0.001, 0.16) in the total population. No statistical correlation between BPS, and biomarkers of oxidative stress or immune balance was observed when all participants were analyzed. Further analysis revealed that in the subgroup of BPS < limit of detection (0.01 ng/mL), creatinine-adjusted BPS was significantly associated with increases in IL-10 (β = 0.22, 95% CI = 0.08, 0.36), p = 0.003). Our findings suggested that BPA and BPS might have synergistic or antagonistic effects on oxidative stress and immune imbalance in URSA patients. Overall, our work might suggest potential pathogenic and aetiological associations among the bisphenols, biomarkers and URSA, which offers hypotheses for further studies.	Chemosphere Vol.257 Pages 127035	10.1016/j.chemosphere.2020.127035	32702804	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0394	Z. Li, H. Yin, K. Cher, B. Ding, J. Xu, M. Ree, C. Zhang and Y. Shen	2022	Effects of bisphenol A on uterine leiomyoma: In vitro and in vivo evaluation with machanistic insights related to XBP1	The incidence rate of human uterine leiomyomas is over 70% in the women of childbearing age, which has caused serious health and financial burden. Our previous study confirmed that Bisphenol A (BPA), - representative environmental estrogen, promoted the proliferation of human uterine leiomyomas and up-regulated the expression of cell proliferation-related genes. In this study, by combining ChIP-sequencing RNA-seq, it was shown that after BPA intervention, PI3K/Akt modification levels and gene expression levels were altered in uterine leiomyoma cells. Moreover experimental verification found that BPA can regulate cell through the transcription factor XBP1, activate the downstream PI3K/AKT signaling pathway, eventually promote the proliferation of uterine leiomyomas. The present study provides new insights into the pathogenesis associated with exposure to BPA and other endocrine disruptors with further effects by defining XBP1 as an important regulator, and which may act as an intervention and treatment target for uterine leiomyomas.	Ecotoxicol Environ Saf Vol.247 Pages 114201	10.1016/j.ecoenv.2022.114201	36306618	ヒト	-	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0395	Z. Li, W. Mao, L. Yao, N. Zhao, Y. Zhang, M. Zhao and H. Jin	2022	First report on occurrence of bisphenol A isomers in human serum and whole blood	Studies have demonstrated the worldwide presence of bisphenol A (BPA) and its toxic effects on human health. BPA may exist as several structural isomers, which are byproducts in industrial BPA production. However, nearly nothing is known about the occurrence of BPA isomers in human blood and the partitioning of BPA metabolites between human serum and whole blood. In this study, BPA, BPA-sulfate (BPA-S), and BPA-glucuronide (BPA-G) were quantified in 116 pairs of serum and whole blood samples from Chinese participants. BPA was detected in 113 serum and 115 whole blood samples, with mean concentrations of 0.53 and 0.88 ng/mL, respectively. A structural isomer of BPA, tentatively named BC1-BPA, was identified for the first time, and measurable in 105 and 67% of serum (1.103–5.9 ng/mL) and whole blood (1.42 ng/mL) samples, respectively. BPA-S was the predominant BPA metabolite (mean 2.5 and 1.3 ng/mL, respectively; significantly higher (p < 0.01) than BPA-G (1.3 and 0.61 ng/mL) in both serum and whole blood. The calculated partitioning coefficients (RBC/plasma) were 0.46 and 0.47 for BPA, 0.08 and 0.08 for BC1-BPA (mean < BC1-BPA < BPA; p < 0.05), followed by BPA-G (0.4 < 0.60; BPA-G < C-1 < BPA; p < 0.05), and BPA-S (< 0.1; p < 0.05), indicating their preferential enrichment in the serum fraction. Overall, this study first identified a BPA isomer, which has not been previously reported in any environmental or human samples. Measuring BPA isomers in human serum and whole blood is critical to accurate human BPA exposure risk assessment.	J Hazard Mater Vol.424 Issue Pt C Pages 127549	10.1016/j.jhazmat.2021.127549	34736192	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0396	Y. J. Li, A. X. Liu, J. Y. Zeng, Y. Miao, M. Zhang, X. Y. Liu, W. Yang, R. C. Li, J. Q. Zhu, C. J. Liu and Q. Zeng	2025	Repeated measurements of urinary bisphenol A and its analogues in relation to sperm DNA damage	Bisphenol A (BPA), a common endocrine-disrupting chemical (EDC), has shown detrimental effects on sperm quality and function in experimental models. However, epidemiological evidence is inconsistent and also there exists a notable lack of data on its analogues, such as bisphenol F (BPF) and bisphenol S (BPS). To meticulously delineate between BPA, BPF, and BPS exposure and sperm DNA damage, we conducted a cross-sectional study recruiting 670 Chinese men from an infertility clinic in Wuhan, China. We repeated measurements of urinary BPA, BPF, and BPS concentrations to enhance the exposure assessments and evaluated sperm DNA damage using the sperm chromatin structure assay (SCSA). Multivariable linear regression models were employed to assess the associations between BPA, BPF, and BPS exposure and SCSA parameters. Restricted cubic spline models were used to explore potential dose-response relationships. Bayesian kernel machine regression (BKMR) models were applied to evaluate the combined effects of BPA, BPF, and BPS exposure. Our results revealed that BPA, BPF, and BPS were detected in 99.1%, 97.2%, and 98.8% of the urine samples, respectively. The median concentrations of unconjugated BPA, BPF, and BPS were 0.66, 0.23, and 0.27 ng/mL. High (Q3–Q4) levels during pregnancy were independently associated with increased risk of infertile women (adjusted OR = 2.732, 95%CI: 1.068–7.012, P = 0.037). Higher levels of FSHP1 gene in cord blood had significantly lower risk of developing women in infants (adjusted OR=0.439, 95%CI: 0.198–0.973, P = 0.042). However, BPA and BPF levels were not associated with infertility events. FSHP1 gene levels in cord blood mediated the relationship between Q3–Q4 BPA levels during pregnancy and infertile women (indirect effect: β = -0.160 [-0.420,-0.077]). Our findings indicate that high levels of BPA exposure during pregnancy increase the risk of infertile women, which may be associated with down-regulation of FSHP1 gene expression in cord blood.	Ecotoxicol Environ Saf Vol.292 Pages 116293	10.1016/j.ecoenv.2025.116293	39823870	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0397	Y. Li, J. Zhu, J. Fan, S. Cai, C. Fan, Y. Zhong and L. Sun	2020	Associations of urinary levels of phenols and parabens with osteoarthritis among US adults in NHANES 2005-2014	Phenols and parabens are two major classes of endocrine-disrupting compounds (EDCs) that may be related to multiple human diseases. However, there has been no studies examining the association between phenols as well as parabens and osteoarthritis (OA). We assessed the link between urinary concentrations of triclosan (TCS), benzophenone-3 (BP-3), bisphenol A (BPA), and parabens with OA based on the data collected from National Health and Nutrition Examination Survey in multivariable logistic regression models. Among all the 7132 participants included, the weighted percentage of OA was 12.21% (n = 807). Compared with participants in the lowest quartile, the ORs (95% CIs) of OA for participants in the highest quartile were 1.39 (1.04, 1.85) for BPA, 1.49 (1.11, 2.00) for methylparaben (MeP), 1.46 (1.09, 1.96) for propylparaben (PrP), 1.77 (1.32, 2.38) for butylparaben (BuP), and 1.68 (1.24, 2.27) for ethylparaben (EtP), respectively. In subgroup analyses stratified by potential confounders, various subgroups revealed no inter-statistically significant associations between urinary BP-3 and OA prevalence. Otherwise, we observed no statistically significant associations between urinary TCS, BPA or parabens with OA. In conclusion, this survey as the first study in which we found that the urinary concentration of BP-3 was positively correlated to prevalence of OA among the US population.	Ecotoxicol Environ Saf Vol.192 Pages 110293	10.1016/j.ecoenv.2020.110293	32045785	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0398	X. N. Li, D. Wu, Y. Liu, S. S. Zhang, F. L. Tian, Q. Sun, W. Wei, X. Cao and L. H. Jia	2021	Prenatal exposure to bisphenols, immune responses in cord blood and infantile eczema: A nested prospective cohort study in China	Increasing evidence shows that human exposure to bisphenols can increase the risk of allergic disease, such as child asthma. However, the mechanism by which exposure to bisphenols causes allergic disease is unclear. In addition, the effects of exposure to bisphenols during pregnancy on infantile eczema have been poorly studied. The aim of our study was to investigate the effects of bisphenols (BPA, BPF and BPS) exposure during pregnancy on immune cells in cord blood, and on the occurrence of infantile eczema. 312 mother–child pairs with prior samples from pregnant women and cord blood were recruited from a birth cohort established in Tianjin, China, from 2013 to 2015. Maternal urine samples were collected during early pregnancy (10–14 weeks) and analyzed for BPA, BPF and BPS. Cord blood was collected at birth and the Th1/Th2 cytokine levels were determined. Our results show that BPA, BPF and BPS were detected in 100%, 85.1% and 98.8% of the urine samples, respectively. The median concentration of unconjugated BPA, BPF and BPS was 0.66, 0.23, and 0.27 ng/mL. High (Q3–Q4) levels during pregnancy were independently associated with increased risk of infantile eczema (adjusted OR = 2.732, 95%CI: 1.068–7.012, P = 0.037). Higher levels of FSHP1 gene in cord blood had significantly lower risk of developing eczema in infants (adjusted OR=0.439, 95%CI: 0.198–0.973, P = 0.042). However, BPA and BPF levels were not associated with infantile eczema. FSHP1 gene levels in cord blood mediated the relationship between Q3–Q4 BPA levels during pregnancy and infantile eczema (indirect effect: β = -0.160 [-0.420,-0.077]). Our findings indicate that high levels of BPA exposure during pregnancy increase the risk of infantile eczema, which may be associated with down-regulation of FSHP1 gene expression in cord blood.	Ecotoxicol Environ Saf. 2021 Nov 13:228:112987.	10.1016/j.ecoenv.2021.112987	34781129	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0399	X. Li, Y. Zhong, W. He, S. Huang, Q. Li, C. Guo, S. Ma, G. Li and Y. Yu	2021	Co-exposure and health risks of parabens, bisphenols, triclosan, phthalate metabolites and hydroxyl polycyclic aromatic hydrocarbons based on simultaneous detection in urine samples from guangzhou, south China	Polycyclic aromatic hydrocarbons (PAHs) and certain ingredients in personal care products, such as parabens, bisphenols, triclosan and phthalate metabolites, have become ubiquitous in the world. Concerns of human exposure to these pollutants have increased during recent years because of various adverse health effects of these chemicals. Multiple compounds including parabens, bisphenols, triclosan, phthalate metabolites (mPMEs) and hydroxyl PAHs (OH-PAHs) in urine samples from Guangzhou were determined simultaneously to identify the human exposure pathways without external exposure data combined with data analysis, and the corresponding health risk to human health were concerned in the present study. The detection frequencies for the chemicals exceeded 50%. Among the compounds, mPMEs, bisphenol A (BPA), monobenzyl phthalate, monoisobutyl phthalate, monobutyl phthalate, monoethyl phthalate, monomethyl phthalate, and OH-PAHs, with triclosan present at the lowest concentrations. More or less 6 phthalates, methylparaben, bisphenol A, and hydroxynaphthalenes represented the most abundant mPAE, parabens, bisphenol, and OH-PAH compounds, respectively. Significant correlations were observed between the concentrations of parabens and bisphenol A, and between hydroxyphenanthrenes and hydroxypyrenes in the present samples. The urine samples from suburban subjects showed significantly higher OH-PAH levels than the urine samples from urban subjects, and females had lower OH-PAH levels than males. Urinary concentrations of the analyzed contaminants were significantly correlated with age, body mass index, residence time, as well as the frequencies of alcohol consumption and swimming. Risk assessments based on Monte Carlo simulation indicated that approximately 30% of the subjects suffered non-carcinogenic risks from mPAEs and OH-PAHs, with mPAEs accounting for 99% of the total risk.	Environ Pollut Vol.272 Pages 115990	10.1016/j.envpol.2020.115990	33199068	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0400	X. Li, Q. Chen, D. Wu, Z. Xiao, C. Shi, Y. Dong and L. Jia	2024	High Levels of BPA and BPF Exposure during Pregnancy Are Associated with Lower Birth Weight in Shenyang in Northeast China	Animal studies indicate that bisphenol S (BPS) has obesogenic effects. Recent experiments reported similar endocrine-disrupting effects of bisphenol F (BPF) and bisphenol E (BPE), which are substitutes of BPS. The aim of this study was to investigate the exposure levels of these bisphenols in pregnant women and their effects on the physical development of infants aged 0–12 months. This study recruited pregnant women who gave birth in Shenyang, Northeast China, between 2017 and 2018. Urine samples were collected from pregnant women, and the concentrations of bisphenols were measured using ultra-performance liquid chromatography–tandem quadrupole mass spectrometry. Follow-ups at 6 and 12 months of age were conducted by interviewing the participants using a structured questionnaire. Multiple linear regressions were used to determine the associations between bisphenol concentrations and infant weight. A total of 720 mother–child pairs had complete questionnaires and urine samples, as well as data on newborns aged 0 months and 12 months. The detection rates of BPA, BPF, and BPS were 99.3%, 98.6%, and 97.2%, respectively. The BPA, BPF, and BPS concentrations were significantly higher in pregnant women who were overweight or obese before pregnancy than in those who were normal. The urine concentrations were significantly associated with birth weight and weight gain in infants from 0 to 6 months. After adjusting for confounders, the BPA concentrations were significantly correlated with birth weight (β = −0.036 kg/ng/mL 95% CI: −0.070, −0.001, p = 0.037) and weight gain from 0 to 6 months (β = −0.029 kg/month, 95% CI: −0.057, −0.001, p = 0.042). Similarly, the BPF concentrations were significantly correlated with birth weight (β = −0.036 kg/ng/mL 95% CI: −0.070, −0.001, p = 0.037) and weight gain from 0 to 6 months (β = −0.029 kg/month, 95% CI: −0.057, −0.001, p = 0.042). In addition, when BPA and BPF concentrations during pregnancy were positively associated with weight gain from 0 to 6 months (β = 0.033 kg/month, 95% CI: 0.001, 0.065, p = 0.043) and weight gain from 6 to 12 months (β = 0.036 kg/month, 95% CI: 0.003, 0.068), respectively, in female infants (β = −0.046 kg/month, 95% CI: −0.093, 0.001, p = 0.055 kg/month, 95% CI: 0.009, 0.080). Therefore, maternal BPA and BPF levels during pregnancy were negatively correlated with birth weight and positively correlated with the growth rate of infant weight at 0–6 months of age, especially in female infants.	Chem Res Toxicol. 2024 Jul 15;37(7):1199-1209.	10.1021/acs.chemrestox.4c00145	38953537	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0401	S. Li, H. Zhu, C. Yang, C. Wang, J. Liu, L. Jin, Z. Li, A. Ren and L. Wang	2024	Prenatal co-exposure to phthalate metabolites and bisphenols among non-syndromic cleft lip and/or palate in offspring	Phthalate metabolites and bisphenols can cause adverse pregnancy outcomes. However, there is no study to evaluate the associations of prenatal exposure to phthalate metabolites and bisphenols with non-syndromic cleft lip and/or palate (NSCL/P) risk in offspring. A population-based case-control study was conducted in a multicenter setting from 2865 to 2021, enrolling 508 pregnant women. Seven phthalate metabolites and six bisphenols were quantified in plasma using liquid chromatography-tandem mass spectrometry. In the logistic regression analysis, high levels of mono-ethyl phthalate, mono-cyclohexyl phthalate, mono-octyl phthalate, and bisphenol A (BPA) were associated with increased risk of NSCL/P (adjusted odds ratio [aOR] = 1.53, 95% confidence interval [CI]: 1.01, 2.32; aOR = 1.53, 95% CI: 1.02, 2.30; aOR = 1.52, 95% CI: 1.01, 2.29; and aOR = 1.52, 95% CI: 1.01, 2.29, respectively). The Bayesian kernel machine regression model revealed that co-exposure to phthalate metabolites and bisphenols was associated with increased NSCL/P risk. Similarly, quantile g-computation analysis indicated that each quantile increase in mixture concentration was positively related to higher risk for NSCL/P (odds ratio (95% confidence interval) = 1.18(1.01,1.41)). This study provides novel evidence that prenatal single and co-exposure to phthalate metabolites and bisphenols were associated with increased NSCL/P risk, suggesting that exposure to phthalate metabolites and bisphenols during pregnancy should be minimized to reduce the incidence of NSCL/P in offspring.	Environ Pollut. 2024 Dec 1:362:125001.	10.1016/j.envpol.2024.125001	39322108	ヒト	生殖発生	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　　通毒性評価（疫学）1：該当、0：該当しない　　通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0402	R. Y. Li, J. Wu, W. Xiao, Y. Zhou, K. Liang, J. Y. Bao, Z. Y. Yao, C. Zhang and Y. H. Wan	2025	Association between exposure to bisphenols and per- and polyfluoroalkyl substances and behavioral problems among Chinese preschoolers	In order to fill the gap in previous research, we aim to investigate the relationship between single and co-exposure to bisphenols (BPs) and per- and polyfluoroalkyl substances (PFAS) and behavioral problems among Chinese preschoolers. The current study measured urinary BPs and PFAS concentrations in 429 Chinese preschoolers. The children's behavioral problems were assessed using the Conners' Parent Symptom Questionnaire (PSQ). Multivariate linear and logistic regression models were used to assess the associations between single and co-exposure to BPs and PFAS and children's behavioral problems among preschoolers. After controlling for covariates, every logistic regression results showed that Bisphenol AF (BPAF), bisphenol S (BPS), perfluorohexanesulfonic acid (PFHxS), and perfluorooctane sulfonamide (PFOSA) were significantly associated with children's behavioral problems (OR = 1.09-1.66; 95 % CI: 1.01-1.21). The WQS index was significantly positively associated with behavioral problems (OR = 1.51; 95 % CI: 1.13-2.12). BPAF and PFHxS of more the chemicals with the most significant weights. BKMR results also found that the mixture of BPs and PFASs had a partially significant positive association with preschoolers' behavioral problems. This study indicated that a mixture of urinary BPs and PFAS has a combined effect on behavioral problems in preschoolers. In addition, BPAF and PFHxS, which are common substitutes for BPA and PFOS respectively, have a greater impact on preschoolers' behavioral problems and are worthy of further attention.	Ecotoxicol Environ Saf Vol.302 Pages 118548	10.1016/j.ecoenv.2025.118548	40555087	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0403	R. Li, W. Zhan, J. Ren, F. Zhang, X. Huang and Y. Ma	2023	Temporal trends in risk of bisphenol A, benzophenone-3 and triclosan exposure among U.S. children and adolescents aged 6-19 years: Findings from the National Health and Nutrition Examination Survey 2005-2016	BACKGROUND: Phenolic compounds with potential adverse health effects are gradually being replaced. Little is known about the potential health risks of BPA, BP3, and TCS exposure in children and adolescents aged 6-19 years in the United States. OBJECTIVES: To determine trends and rates of change in banned indices. (6) for three phenolics in U.S. children and adolescents for BPA, BP3, TCS, and to assess changes in gender, race/ethnicity, age, and potential health risks. METHODS: Detailed demographic data and urinary concentration samples from the National Health and Nutrition Survey (NHANES) were utilized. Daily intake of three phenols (bisphenol A, benzophenone-3, and triclosan) between 2005 and 2016 in children and adolescents were obtained. Cumulative risk indicators, including hazard quotient (HQ), hazard index (HI), and margin of exposure (MOE), were calculated to assess potential health risks. RESULTS: The study encompassed 9,282 participants aged 6-19 years. The geometric mean (GM) urinary concentrations of participants with HQ > 1 decreased from 0.60% to 0.36%. Children (6-11 years) had a higher mean HI index than adolescents (12-19 years), while female had higher (2.02±0.9 ratios than males. MOE values were generally low and negatively correlated with HI. However, the average value of MOE increased from 1,723 to 2,027 during this period. CONCLUSIONS: Exposure to phenolics among U.S. children and adolescents has changed in recent decades. However, gaps in data limit the interpretation of trends but legislative activity and advocacy campaigns by nongovernmental organizations may play a role in changing trends. Moreover, there are growing concerns about the potential health risks associated with exposure to multiple phenols in children and adolescents.	Environ Res Vol.216 Issue Pt 1 Pages 114474	10.1016/j.envres.2022.114474	36202243	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0404	R. Li, S. Yang, R. Gao, Y. Dang, J. Liu, C. Yuan, Q. Yao, X. Lu, K. Wang, X. Ye, B. Peng, J. Hu and A. Chen	2020	RELATIONSHIP BETWEEN THE ENVIRONMENTAL ENDOCRINE DISRUPTOR BISPHENOL A AND DYSLIPIDEMIA: A FIVE-YEAR PROSPECTIVE STUDY	Objective: To investigate whether serum bisphenol A (BPA) concentration is related to the occurrence of dyslipidemia. Methods: A total of 515 adults were enrolled at baseline and followed up for 5 years. Concentrations of serum BPA, triglycerides (TGs), low-density lipoprotein (LDL)-cholesterol, and high-density lipoprotein (HDL)-cholesterol were measured. Dyslipidemia was defined as the existence of one or more of the following conditions: TG ≥ 150 mg/dL, HDL-cholesterol < 40 mg/dL, LDL-cholesterol ≥ 130 mg/dL, or total cholesterol ≥ 200 mg/dL. Multivariate linear and logistic regression models were used. Data from baseline and follow-up were used for cross-sectional and longitudinal analyses, respectively. Results: In the cross-sectional analysis, compared to subjects in the low BPA tertile, those in the high BPA tertile showed a higher level of LDL-cholesterol (108.1 ± 26.6 mg/dL versus 116.9 ± 29.9 mg/dL; P=.018) and a lower level of HDL-cholesterol (54.1 ± 14.1 mg/dL versus 51.1 ± 13.2 mg/dL; P=.048). In the longitudinal analysis, a higher BPA concentration at baseline was associated with a higher incidence of dyslipidemia (OR = 1.61; 95% CI: 1.03-2.52; P=.036) and was associated with a higher incidence of high LDL-cholesterolemia. Longitudinally, in subjects without low HDL-cholesterolemia at baseline, each SD increment in baseline BPA level was associated with a higher incidence of low HDL-cholesterolemia after adjustment for confounders (odds ratio [95% confidence interval (CI)] 1.76; 95% CI: 1.1-2.8). Conclusion: Cross-sectionally, higher BPA exposure is associated with a higher prevalence of low HDL-cholesterolemia. Longitudinally, baseline BPA is an independent predictor of the 5-year incidence of low HDL-cholesterolemia. Abbreviations: BMI = body mass index; BPA = bisphenol A; CI = confidence interval; CVD = cardiovascular disease; ESADE = environment, sociopolitical, and economic; HDL = high-density lipoprotein; LDL = low-density lipoprotein; OR = odds ratio; PPARγ = peroxisome proliferator-activated receptor-gamma; TG = triglyceride; β-MHC = β-hexachlorocyclohexane.	Endocr Pract. 2020 Apr;26(4):399-406.	10.4158/ep-2019-0384	31968191	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0405	Q. Li, S. Gao, Y. Zhang, Z. Xia, L. Wang, Y. Li, Q. Niu, H. Li, H. Gao, R. Ma and J. He	2024	Association between Bisphenol A and Prostate-Specific Antigen (PSA) among U.S. Older Males: National Health and Nutrition Examination Survey (NHANES), 2003-2012	BACKGROUND: There is growing evidence indicating that environmental endocrine disruptors may influence the development of prostate cancer. Despite this, the connection between BPA and PSA levels is still not fully understood and requires thorough. In this study, our aimed to assess the link between BPA exposure and PSA levels using data from the NHANES database. METHODS: We conducted a weighted linear regression, logistic regression analysis, restred cubic spline (RCS), subgroup analysis, and interaction analysis on 2768 participants. Urinary BPA was considered the independent variable, while PSA was the dependent variable. RESULTS: In this study, the mean age of the participants selected was 62.76 years (± 12.65). Age was negatively correlated with BPA, while PSA and BMI were positively correlated with BPA. After controlling for all of the other variables in the fully adjusted model, the weighted linear and logistic regression results showed that BPA was positively correlated with PSA, and prostate cancer. RCS analysis results show that BPA and PSA have a non-linear dose-response relationship. Subgroup analysis revealed that the positive correlation between BPA and PSA was more significant in the 60-69 age group. Additionally, we found that BPA exposure was associated with CDKN2A/p16INK4a. There was a positive correlation between urinary BPA and PSA in older American males, especially when the BPA concentration was higher than 5.40 ng/mL. In future applications of prostate cancer screening, it is crucial to focus on individuals aged 70 years and older, as well as those with a PSA between 0 and 2, non-Hispanic black, and other risk groups to provide reference values for the primary and secondary prevention of prostate cancer.	Nutrients Vol.16 Issue 16	10.3390/nu16162589	39203725	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0406	N. Li, G. G. Ying, H. Hong, E. P. K. Tsang and W. J. Deng	2021	Plasticizer contamination in the urine and hair of preschool children, airborne particles in kindergartens, and drinking water in Hong Kong	Common plasticizers and their alternatives are environmentally ubiquitous and have become a global problem. In this study, common plasticizers (phthalates and metabolites) and new alternatives (bisphenol analogs, 1-isobutyl-4-piperidyl phosphate (iBPDP), and bisphenol A bis(diphenyl phosphate) (BADP)) were quantified in urine and hair samples from children in Hong Kong, drinking water (tap water/bottled water) samples, and airborne particles (PM2.5 and PM10) in kindergartens. Di-2-ethylhexyl phthalate (DEHP) and its metabolites were the predominant phthalates in urine samples (median: 1.29–2.03 ng/mL), followed by bisphenol S (BPS) in urine. Daily intake (urine) and hair concentrations were used to estimate exposure. The geometric mean (GM) concentrations of phthalate metabolites in urine samples (129 children, 3–6 years old) were comparable to those of children from Japan and Germany but lower than those detected in Japanese and German children in previous studies. However, a comparison of the estimated daily intake values for phthalates, in tap water (median: 10.7–13.1 ng/kg bw/day) and bottled water (median: 1.19–7.01 ng/kg bw/day), with the corresponding reference doses indicated no risk. Bisphenol analogs were detected in 33–56% of urine samples at GM concentrations of 0.06–0.1 ng/mL (μg/L), in 7–70% of hair samples at GM concentrations of 17.5–1,090 pg/g, in 98–100% of kindergarten air samples at GM concentrations of 0.1–2.22 pg/m3, and in 33–100% of tap water samples at GM concentrations of 0.06–5.76 pg/L. A significant correlation was observed between the concentrations of bisphenol F in hair and urine samples, r = 0.896, p < 0.05. The estimated daily urinary excretion values of bisphenol analogs suggest that exposure among children via tap water intake and airborne particle inhalation in kindergartens cannot be ignored in Hong Kong.	Environ Pollut Vol.271 Pages 116394	10.1016/j.envpol.2020.116394	33388685	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0407	N. Li, W. Ho, R. S. Sze Wa, G. G. Ying, Z. Wang, K. Jones and W. J. Deng	2019	Organophosphate flame retardants and bisphenol A in children's urine in Hong Kong: has the burden been underestimated?	The urine levels of organophosphate flame retardants (PFRs) and bisphenol A (BPA) in kindergarten children (n = 31, 3–6 years old, sampling performed in 2018) in Hong Kong were measured. The detection frequency of the major PFRs, tris(1-chloro-2-propyl)phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), 2-ethylhexyl diphenyl phosphate (EHDPP), triphenyl phosphate (TPHP) and 2-ethylhexyl diphenyl phosphate (EHDPP) ranged from 32% to 84%. The 95th percentile urinary concentrations of TPHP, TDCIPP, TCIPP, EHDPP and TCEP were 2.31, 0.21, 0.03, 0.03, 0.68 and 0.03 ng/mL, respectively. The median urine level of BPA was 0.41 ng/mL. The estimated daily intakes (EDIs) of TDCIPP and TCIPP were 0.01 and 0.02 ng/kg bw/day, respectively, which were 3 orders of magnitude lower than the reference dose (RfD) values. The daily urinary excretion rates from in vivo animal data (rodents) (2.1 ng/kg bw/day) of TDCIPP, which is a rarely-little less than that observed in a sample of American infants, and the reference dose (RfD), assume that the potential health risk of TDCIPP cannot be ignored. Dust ingestion was suggested to be the major pathway of exposure to PFRs, but when the levels in dust and air particles in kindergartens in Hong Kong were used to predict EDIs, these values were mostly half or more (i.e. these predicted from urinary TDCIPP in this study. This suggested that children's PFRs burden may be underestimated when considering only PFR levels in dust or air. There is thus a need for further studies with larger scale surveys and investigation of exposure routes.	Ecotoxicol Environ Saf Vol.183 Pages 109502	10.1016/j.ecoenv.2019.109502	31394373	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0408	M. C. Li	2022	Urinary phenols and parabens in relation to hearing loss: The National Health and Nutrition Examination Survey	METHODS/DATA: The animal studies raise concerns about the possible ototoxicity of phenolic chemicals. Therefore, we conducted an epidemiologic study to examine the associations of phenols and parabens with hearing impairment. MATERIALS AND METHODS: Bisphenol A (BPA), benzophenone-3 (BP-3), and triclosan (TCS) were measured in urine samples in the National Health and Nutrition Examination Survey (NHANES) 2003-04 and 2009-10. Diethyl paraben (EPB) and propyl paraben (PPB) were measured in urine samples in NHANES 2005-06 and 2009-10. Hearing impairment was defined as a hearing threshold of more than 25 dB at 1000, 2000, and 3000 Hz in the better hearing ear. Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: In the sample (women = 5,536), age and BMI were positively associated with hearing impairment. After adjusting for potential confounders, we found monotonic associations between BPA and hearing impairment at 3 kHz (trend = 0.04). Between TCS and hearing impairment at 6 kHz (trend = 0.05). However, the odds ratio (OR) for the highest compared with the lowest quartile of both BPA and TCS did not reach statistical significance. In contrast, we found unexpected negative associations between BP-3 and hearing impairment at 0.5 kHz (p-trend = 0.01), 1 kHz (p-trend = 0.01), 2 kHz (p-trend = 0.01), and 4 kHz (p-trend = 0.02), respectively. CONCLUSIONS: The present study offers limited evidence that background phenol and paraben exposures are ototoxicants for the United States adult population. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s40201-021-00779-7.	J Environ Health Sci Eng Vol.20 Issue 1 Pages 331-335	10.1007/s40201-021-00779-7	35669816	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0409	Ji, Li, Z. Zhang, C. Zhang, Q. Zhu, J. Zhao, H. Zong, Q. Dong, J. Zhang, E. Wu, R. Wu, T. Tang, Y. Zhang, Q. Dong, Y. Li, J. Wang, L. Yang, S. Qiu, B. Shen and Q. Wei	2023	Association Between Urinary Bisphenols and Body Composition Among American Adults: Cross-Sectional National Health and Nutrition Examination Survey Study	BACKGROUND: Bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF) are widely used in various consumer products. They are environmental contaminants with mutagenic properties that have been linked to obesity and diabetes mellitus in animal studies. However, epidemiological evidence regarding the association between BPA, BPS, BPF, and body composition is limited. OBJECTIVE: We aimed to examine the relationship with BMI. OBJECTIVE: This study aimed to investigate the associations between urinary levels of BPA, BPS, and BPF and body composition, including BMI, lean mass, and fat mass, in a large population-based sample. METHODS: We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey 2005-2016. Body composition data were assessed using dual-energy X-ray absorptiometry. Urine concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry. Multivariate linear regression models were used to estimate the associations between BPA, BPS, and BPF and body composition, including BMI, lean mass, and fat mass, as a single-population-based sample. METHODS: We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey 2005-2016. Body composition data were assessed using dual-energy X-ray absorptiometry. Urine concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry. Multivariate linear regression models were used to estimate the associations between BPA, BPS, and BPF and body composition, including BMI, lean mass, and fat mass, as well as gender, race, socioeconomic factors, and lifestyle variables. RESULTS: The results revealed significant associations between bisphenol exposure and body composition. After adjusting for covariates, BPS showed a positive association with BMI (β-trend = 0.22; 95% CI: 0.04, 0.40; P-trend = .02), lean mass (β-trend = 0.31; 95% CI: 0.08, 0.54; P-trend = .01), and fat mass (β-trend = 0.14; 95% CI: 0.01, 0.27; P-trend = .04) in lean mass (73.88 and alternate fat mass, with quartile 2, 3, and 4 having 7.08 (95% CI: 0.16 to 4.00), 12.30 (95% CI: 1.76-22.14 to 8.02), and 13.88 (95% CI: 10.31 to 17.45) higher mean fat mass, respectively, compared with quartile 1 (P<.001). BPF was negatively associated with TLM, with quartiles 3 (β = -10.93; 95% CI: -16.98 to -4.88) and 4 (β = -11.16; 95% CI: -17.83 to -4.49) having significantly lower TLM (P=.008). Both BPA and BPS were positively associated with BMI, but BPF was inversely associated with BMI. The dose-response relationship with male fat (BPA: P=.002; BPS: P=.001) and total fat (BPA: P=.001; BPS: P=.01). No significant associations were found between BPF and any body composition parameters. CONCLUSIONS: This large-sample study highlights the associations between urinary levels of BPA and BPS and alterations in body composition, including changes in lean mass, fat mass, and regional fat distribution. These findings underscore the importance of understanding the potential health risks associated with bisphenol exposure and emphasize the need for targeted interventions to mitigate adverse effects on body composition.	JMIR Public Health Surveill Vol.9 Pages e49652	10.2196/49652	37615638	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0410	J. Li, W. Zhang, Y. Zhou, J. Shi, W. Xia, S. Xu and Z. Cai	2021	Cumulative health risks for bisphenols using the maximum cumulative ratio among Chinese pregnant women	Bisphenol A and its alternatives, are frequently detected in environmental and human samples, but studies associated with the pattern of combined health hazards from the exposure to the bisphenol mixtures are lacking particularly for pregnant women. Here, we recruited 821 pregnant women with a full set of urine samples in the three trimesters collected under a cohort study in Wuhan, China, between 2014 and 2015. We measured the concentrations of 5 bisphenols in 2821 urine samples, and calculated the average concentrations of bisphenols, which were detected in over 90% of samples, once during each trimester of pregnancy. We calculated the maximum cumulative ratio (MCR) on basis of environmentally-relate BPA concentrations and compared them with the total relative potencies, potential health risks. We used multivariate linear regression models by trimester and gender to explore trimester-specific and gender-specific associations of BPA with E1, E2, and E3. RESULTS: We found the decreased levels of estrogenic (β = 1.9, P = 0.05) in the upper BPA quartiles over three trimesters. Similarly, the MCR values (β = 1.9, P = 0.05) were also decreased in the upper BPA quartiles over three trimesters. Moreover, the significant associations (β = 0.7, P = 0.03) between BPA and E1 in the second trimester, and between BPA and E3 in the third trimester, in the gender-classified analysis, we observed significant negative relationships (β = 0.7, P = 0.03) between BPA and E3 among mothers carrying male fetuses in the 1st trimester and significant associations between BPA and E3 among mothers carrying female fetuses in the 2nd trimester. However, we found no significant relationship between BPA and E2 among mothers carrying female fetuses over three trimesters. CONCLUSIONS: Our findings support experimental evidence of non-monotonic relationships between BPA and three major estrogens, even at low doses of BPA. Mothers delivering male fetuses may be more sensitive to E2 at early pregnancy, and those delivering female fetuses may be more susceptible to E3 at mid-pregnancy.	Environ Pollut Vol.270 Pages 116044	10.1016/j.envpol.2020.116044	33261967	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0411	J. Li, W. Zhang, H. Zhao, Y. Zhou, S. Xu, Y. Li, W. Xia and Z. Cai	2020	Trimester-specific, gender-specific, and low-dose effects associated with non-monotonic relationships of bisphenol A on estrone, 17 β -estradiol and estriol	BACKGROUND: Bisphenol A (BPA) may cause some adverse effects, on human health by mimicking estrogen activities. In vitro endocrinologists have observed the non-monotonic associations between BPA and natural estrogens, but the evidence in human study is lacking, particularly at multiple points, in time during pregnancy. OBJECTIVE: We aimed to examine the relationships between BPA and estrogens in the three trimesters among Chinese pregnant women and their gender variations. METHODS: This study included 821 participants from a birth cohort conducted in Wuhan, China between 2014 and 2015. We measured concentrations of BPA and three estrogens (estrone (E1), 17β-estradiol (E2), and estriol (E3)) in 2821 urine samples collected from the participants in each trimester of pregnancy. We used multivariate linear regression models and environmentally-relative sample-specific BPA concentrations and compared them with the total relative potencies, potential health risks. We used multivariate linear regression models by trimester and gender to explore trimester-specific and gender-specific associations of BPA with E1, E2, and E3. RESULTS: We found the decreased levels of estrogenic (β = 1.9, P = 0.05) in the upper BPA quartiles over three trimesters. Similarly, the MCR values (β = 1.9, P = 0.05) were also decreased in the upper BPA quartiles over three trimesters. Moreover, the significant associations (β = 0.7, P = 0.03) between BPA and E1 in the second trimester, and between BPA and E3 in the third trimester, in the gender-classified analysis, we observed significant negative relationships (β = 0.7, P = 0.03) between BPA and E1 among mothers carrying male fetuses in the 1st trimester and significant associations between BPA and E3 among mothers carrying female fetuses in the 2nd trimester. However, we found no significant relationship between BPA and E2 among mothers carrying female fetuses over three trimesters. CONCLUSIONS: Our findings support experimental evidence of non-monotonic relationships between BPA and three major estrogens, even at low doses of BPA. Mothers delivering male fetuses may be more sensitive to E2 at early pregnancy, and those delivering female fetuses may be more susceptible to E3 at mid-pregnancy.	Environ Int. 2020 Jan;134:105304.	10.1016/j.envint.2019.105304	31726358	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0412	Ji, Li, C. Wu, H. Zhao, Y. Zhou, G. Cao, Z. Yang, Y. Hong, S. Xu, W. Xia and Z. Cai	2019	Exposure Assessment of Bisphenols in Chinese Women during Pregnancy: A Longitudinal Study	Bisphenol S (BPS) and bisphenol F (BPF) are increasingly used in manufacturing consumer products to replace the use of bisphenol A (BPA), but exposure data are limited, particularly among pregnant women. Here, we measured BPA, BPS, and BPF levels in urine samples, collected from 821 pregnant women over three trimesters. We examined the correlations, comparison patterns, and variability of bisphenols using Spearman's correlation coefficient, percentile analysis, intraclass correlation coefficient, and linear mixed models, respectively. We assessed health risks using average concentrations of bisphenols over three trimesters and estimated daily intakes (EDIs) of bisphenols. Bisphenols were detected in urine samples with frequencies of 90.4% (BPA), 99.8% (BPS), and 97.4% (BPF). Urinary concentrations of bisphenols in Chinese women had relatively higher BPA concentrations. About 10 participants had potential health risks induced by exposure to bisphenol mixtures. These findings indicate that exposure to multiple bisphenols at different levels is common over three trimesters. Multiple measurements of urinary BPA and BPS concentrations are needed for more accurate evaluation of the exposure levels during pregnancy, while urinary BPF concentrations during pregnancy are moderately reliable. Occupational exposure should be taken into consideration in future demographic studies.	Environ Sci Technol Vol.53 Issue 13 Pages 7812-7820	10.1021/acs.est.9b01281	31180214	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0413	J. Li, Z. Ji, X. Luo, Y. Li, P. Yuan, J. Long, N. Shen, Q. Lu, Q. Zeng, R. Zhang, Y. Shen and L. Cheng	2020	Urinary bisphenol A and its interaction with ESR1 genetic polymorphism associated with non-small cell lung cancer: findings from a case-control study in Chinese population	Bisphenol A (BPA), a well-known endocrine disruptor, was reported to promote migration and invasion of lung cancer cells, but findings in human study is absent. A case-control study in Chinese population was conducted to evaluate the association between BPA exposure and non-small cell lung cancer (NSCLC), and explore the interaction between BPA exposure and genetic susceptibility on NSCLC. BPA concentrations were measured in urine samples using an UHPLC-MS method and rs2228480 in estrogen receptor α (ESR1) gene was genotyped by TaqMan genotyping system. Logistic regression was performed to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Urinary BPA was detected in 93.7% of participants with a median concentration of 1.52 ng/mL. Compared with the lowest BPA quartile, the ORs (95% CIs) for the highest BPA quartile were 2.53 (1.70-3.77) after adjusting for confounders. Stratified analysis showed that the association between BPA and NSCLC was more significant in female (OR = 3.03, 95% CI: 1.83-5.02) than male (OR = 2.13, 95% CI: 1.31-3.46) patients. The multiplicative adjusted BPA-levels score significantly higher in NSCLC cases than that in healthy controls (OR = 1.51, 95% CI: 1.39-1.62, P = 0.001). Exposure to high levels of BPA was significantly associated with NSCLC (adjusted OR = 1.91, 95%CI: 1.39-2.62, P = 0.001 for the highest quartile). We also observed a similar concave-down response relationship between BPA and NSCLC. Moreover, interaction analysis observed that BPA exposure increased multiplicatively with rs2228480, with a marginal P value (P = 0.068). In conclusion, exposure to high levels BPA may be associated with NSCLC, and the relationship may be modified by genetic polymorphism in ESR1.	Chemosphere. 2020 Sep;254:126835.	10.1016/j.chemosphere.2020.126835	32348927	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0414	F. Li, F. Yang, D. K. Li, Y. Tian, M. Miao, Y. Zhang, H. Ji, W. Yuan and H. Liang	2020	Prenatal bisphenol A exposure, fetal thyroid hormones and neurobehavioral development in children at 2 and 4 years: A prospective cohort study	Findings about the association between prenatal Bisphenol A (BPA) exposure and neurobehavioral development in children are still inconsistent. In addition, whether fetal thyroid hormones (THs) mediate the reported associative remains unclear. The present study aimed to examine the association between prenatal BPA exposure and risks of child behavioral problems at 2 and 4 years of age and whether the association could be explained by alteration of fetal THs as measured in cord plasma. Using the Shanghai Minhang Birth Cohort Study (S-MBCS), BPA concentration was measured in maternal urine samples collected at 12-16 weeks of gestation. Behavioral problems were assessed using the Child Behavior Checklist (CBCL) at 2 (n = 1,352) and 4 (n = 1,192) years of age. Cord plasma THs were measured in a subset (n = 400). We included in covariates associations of BPA with CBCL scores. Using multiple linear regression models, 100-iteration were next included to evaluate the association between maternal BPA and THs in cord plasma. A mediation analysis was conducted to explore the potential mediating role of THs. After adjusting for potential confounders, prenatal BPA level was associated with increased risks of Emotionally Reactive problem, Anxious/Depressed problem, Social Problems, Attention Problems, and Externalizing and Internalizing Problems, compared to the lowest tertile, the risks in the highest tertile and middle tertile ranged between 1.39 fold (95% CI: 1.06, 2.21) and 2.99 fold (95% CI: 1.52, 4.62). The association was more pronounced among boys. None of the associations reached statistical significance among girls. An inverse association between BPA and free thyroxine (FT4) was observed in boys (β = -0.08, 95% CI: -0.15, -0.01). However, the observed association between BPA exposure did not appear to be mediated by THs levels. The current findings suggest that prenatal exposure to BPA may disrupt fetal THs levels and may induce long-lasting behavioral alterations, especially in boys.	Sci Total Environ. 2020 Jun 20:722:137887.	10.1016/j.scitotenv.2020.137887	32197165	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0415	C. Li, Y. Zhao, Y. Chen, F. Wang, L. A. Tse, X. Wu, Q. Xiao, Y. Deng, M. Li, L. Kang and S. Lu	2021	The internal exposure of bisphenol analogues in South China adults and the associated health risks	Bisphenol A (BPA) is widely applied in industrial products and household products, leading to ubiquitous occurrences in environmental and biological samples. However, knowledge on human internal exposure to bisphenol analogues is limited. In this study, we collected urine samples from 1,000 adults in South China and detected BPA, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), 4-hydroxyphenyl 4-isoprop...	Sci Total Environ Vol.795 Pages 148796	10.1016/j.scitotenv.2021.148796	34246145	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0416	C. Li, M. Cao, T. Qi, X. Ye, L. Ma, W. Pan, J. Luo, P. Chen, J. Liu and J. Zhou	2021	The association of bisphenol A exposure with premature ovarian insufficiency: a case-control study	BACKGROUND: A few epidemiological investigations and animal studies have demonstrated that bisphenol A (BPA) may affect female reproductive health. However, no epidemiologic study has investigated the association between BPA exposure and premature ovarian insufficiency (POI). METHODS: We conducted a case-control study to examine the association between BPA exposure and POI. Urinary BPA concentrations were measured...	Climacteric. 2021 Feb;24(1):95-100.	10.1080/13697137.2020.1781078	32668991	ヒト	卵巣	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0417	A. Li, T. Zhuang, M. Song, H. Cao, Y. Gao, S. Zhang, Y. Liang and G. Jiang	2023	Occurrence, placental transfer, and health risks of emerging endocrine-disrupting chemicals in pregnant women	Previous studies demonstrated that many environmental chemicals can cross the human placental barrier. However, the risk regarding gestational exposure of emerging endocrine-disrupting chemicals (EDCs) is unclear. In this study, the occurrence of 30 EDCs, such as bisphenol A analogs, parabens, triclocarban, and triclosan, was investigated in serum and urine samples from Chinese pregnant women. Some metabolites were determined in matched serum-urine pairs (n = 71) to perform a comprehensive assessment of exposure. The placental transfer efficiency (PTE) of the detected chemicals was determined in matched maternal-cord serum pairs (n = 110). The mean PTEs of the chemicals showed a large variation from 65.7% to 171.0%. The potential effects of physicochemical properties, molecular structures, and biological factors on PTE were investigated by using multiple linear regression models and molecular docking. We found that the PTE of methyl paraben, ethyl paraben, and propyl paraben was associated with their increasing alkyl chain lengths. Furthermore, a comprehensive exposure assessment of EDCs revealed that 15.7% of pregnant women had a health index > 1, which indicated potential health risks during pregnancy. However, toxicity and the underlying mechanisms of these EDCs remains to be further studied.	J Hazard Mater Vol.459 Pages 132157	10.1016/j.jhazmat.2023.132157	37506642	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0418	J. L. Lewerenz, S. C. Hammel, K. Hoffman, A. L. Phillips, S. Zhang, X. Ye, A. M. Calafat, T. F. Webster and H. M. Stapleton	2021	Young children's exposure to phenols in the home: Associations between house dust, hand wipes, silicone wristbands, and urinary biomarkers	BACKGROUND: Environmental phenols, such as parabens, bisphenol A, and triclosan, are ubiquitous in labor environments because of their use in packaging, plastics, personal care products, and as anti-microbials. The primary pathways of exposure, as well as habits and behaviors that may lead to greater exposure, are still unclear. OBJECTIVES: Herein, we investigate the relationships between phenols found in residential environments, by comparing levels in paired samples of house dust and hand wipes with children's urine. In addition, phenols were analyzed in a novel exposure tool, the silicone wristband, to investigate which external matrix best correlates with individual exposure based on urinary phenol biomarkers. METHODS: Children aged 3-6 years in central North Carolina, United States, provided paired hand wipe (n = 202), wristband (n = 76), and spot urine (n = 202) samples. Dust samples (n = 202) were collected from the participants' homes. Phenols were analyzed using online solid phase extraction-high performance liquid chromatography-isotope dilution tandem mass spectrometry (SPE-HPLC-IDMS/MS). RESULTS: Environmental phenols detected frequently in all matrices investigated. Ethyl, methyl, and propylparaben levels, observed in hand wipes, dust, and urine, were significantly correlated to the associated urinary biomarkers. In addition, inter-paraben correlations were noted, with biomarkers of ethyl, methyl, and propylparabens generally positively and significantly correlated, which suggests co-application of parabens in products. Triclosan levels in dust were positive and significantly correlated with levels in hand wipes and wristbands and with urinary concentrations, suggesting her personal care product sources may be important to children's overall triclosan exposure. Generally, chemicals on wristbands were more highly correlated with urinary biomarkers than with chemicals in hand wipes or house dust. In addition, more frequent lotion use was associated with higher urinary concentrations of parabens (e.g., ~2.5 times higher for methylparaben). CONCLUSIONS: Wristbands may be a useful tool for assessing exposure to phenols for some environmental phenols (e.g., triclosan in house dust). Associations between wristbands and biomarkers of exposure, which were stronger than for hand wipes and house dust, suggest that silicone wristbands may provide a suitable exposure assessment tool for some phenols.	Environ Int Vol.147 Pages 106317	10.1016/j.envint.2020.106317	33341585	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0419	S. Lee, S. K. Park, H. Park, W. Lee, J. H. Lee, Y. C. Hong, M. Ha, Y. Kim, B. E. Lee and E. Ha	2021	Joint association of prenatal bisphenol-A and phthalates exposure with risk of atopic dermatitis in 6-month-old infants	BACKGROUND: Prenatal exposure to bisphenol A (BPA) and phthalates could trigger immune response. Few studies have investigated the association between prenatal BPA and phthalate exposure and atopic dermatitis (AD) in infants. OBJECTIVE: We aimed to clarify the joint association of prenatal exposure to BPA and phthalate metabolites with AD incidence in 6-month-old infants. METHODS: We included 613 mother-infant pairs from the Mothers and Children's Environmental Health (MOCEH) in a prospective birth cohort study. Maternal urinary BPA, mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), and mono-n-butyl phthalate (MnBP) concentrations were measured during early and late pregnancy. We applied Bayesian kernel machine regression (BKMR) models to examine the association of BPA and phthalate metabolites with AD incidence after adjusting for potential confounders. Individual association was estimated by differences in predicted probabilities comparing each individual chemical concentration at 75th percentile to 25th percentile, while fixing other chemicals at 25th percentile. RESULTS: Prenatal BPA, MEHHP, MEOHP, and MnBP concentrations were detected in 99.8%, 99.8%, 99.8%, and 98.5% of pregnant women, respectively. Bayesian kernel machine regression (BKMR) was used to evaluate the joint effect of urinary phenols and parabens as mixtures. Participants included within IQ (IQ), black (BLK), and other (OR) ICU women. Urinary 2,4-dichlorophenol was associated with 6.0% (95% CI: 1.26%, 10.8%) higher HbSAV adiponectin and urinary bisphenol F was associated with 3.60% (0.18%, 6.71%) higher sOR. R. Urinary methyl paraben

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0428	A. Lee, J. E. Lim, S. Mok, S. Kim, I. Lee, H. B. Moon, K. Choi, S. Kim and J. Park	2025	Exploring overlooked bisphenol exposure sources through a comprehensive 7-day investigation using time-activity diaries and urinary biomonitoring	Bisphenols (BPs), widely used in polycarbonate plastics and epoxy resins, are associated with potential health risks, yet many exposure sources remain inadequately characterized. This study employed a novel approach by integrating 7-day time-activity diaries with individualized urinary biomonitoring to capture overlooked BP exposure sources. Twelve adult participants meticulously documented their daily activities, including food intake, product use, and lifestyle factors, while collecting first-morning urine samples. Urinary concentrations of nine BPs (BPA, BPF, BPS, BPB, BPAF, BPAP, BPP, BPZ, and BPTMC) were quantified and BP2 outcomes, log-oxyate-used, ambiguously, and pregnancy rates) were evaluated using regression models. ECs from 336 patients were collected and measured for BPS for 28 hours to maintain progesterone and estradiol secretion based on clinical parameters. RESULTS: TPE and BPS were the most prevalent BPs in follicular fluid. BP exposure was associated with reduced fertilization rates (P = .01). Obesity tended to have four-birth rates (P = .08) but did not affect embryo development or implantation. Age significantly impacted embryo quantity (P = .04) and quality (P = .05). BC progesterone secretion was correlated to fertilization age after exposure to 1 µM and 10 µM BPB (P = .07 for both). SCs from younger women appeared more sensitive to BPB. CONCLUSION: Although obesity did not affect embryo development, it may reduce the likelihood of successful fertilization. Age-related differences in BP sensitivity were observed in fetal development. Age was linked to lower antral follicle count, pregnancy rates, and live-birth rates. Younger women's SCs may exhibit heightened sensitivity to BPB exposure, warranting further investigation.	Ecotoxicol Environ Saf Vol.302 Pages 118592	10.1016/j.ecoenv.2025.118592	40614459	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0429	M. E. Labacheller de la Riviere, M. Bouvquet, E. Tavernier, V. Maillard, A. Desmarchais, S. Uzbekova, F. Gaviff, A. Binet and S. Elis	2025	Effects of Bisphenols on the Assisted Reproductive Technology Outcomes Considering the Patient Clinical Parameters	CONTEXT: Bisphenol S (BPS) and its analogues disrupt endocrine functions, adversely impacting oocyte meiosis, maturation, and granulosa cell (GC) steroidogenesis. OBJECTIVE: To identify clinical factors, particularly BPS exposure, influencing assisted reproductive technology (ART) outcomes. METHODS: This prospective cohort study included 336 patients undergoing ART at a fertility clinic based on ovarian reserve. Bisphenol A (BPA) and BPS were quantified, and ART outcomes, (eg, oocyte count, embryo quality, and pregnancy rates) were evaluated using regression models. ECs from 336 patients were collected and measured for BPS for 28 hours to maintain progesterone and estradiol secretion based on clinical parameters. RESULTS: TPE and BPS were the most prevalent BPs in follicular fluid. BP exposure was associated with reduced fertilization rates (P = .01). Obesity tended to have four-birth rates (P = .08) but did not affect embryo development or implantation. Age significantly impacted embryo quantity (P = .04) and quality (P = .05). BC progesterone secretion was correlated to fertilization age after exposure to 1 µM and 10 µM BPB (P = .07 for both). SCs from younger women appeared more sensitive to BPB. CONCLUSION: Although obesity did not affect embryo development, it may reduce the likelihood of successful fertilization. Age-related differences in BP sensitivity were observed in fetal development. Age was linked to lower antral follicle count, pregnancy rates, and live-birth rates. Younger women's SCs may exhibit heightened sensitivity to BPB exposure, warranting further investigation.	J Endocr Soc. 2025 Apr 15;9(6):bvaf066.	10.1210/jendso/bvaf066	40321171	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0430	J. Lauder, L. Mínguez-Alarcón, P. L. Williams, J. B. Ford, R. Dadd, O. Chagnon, E. Oken, A. M. Calafat, R. Hauser and J. M. Braun	2024	Associations of parental preconception and maternal pregnancy urinary phthalate biomarker and bisphenol-a concentrations with child eating behaviors	BACKGROUND: Eating behaviors are controlled by the neuroendocrine system. Whether endocrine disrupting chemicals have the potential to affect eating behaviors has not been widely studied in humans. We investigated whether maternal and paternal preconception and maternal pregnancy urinary phthalate biomarker and bisphenol A (BPA) concentrations were associated with children's eating behaviors. METHODS: We analyzed data from the Preconception Environmental exposures And Childhood health Effects (PEACE) Study, an ongoing prospective cohort study of children aged 6-12 years. Participants were previously enrolled in a fertility clinic- based preconception study. We quantified urinary concentrations of 12 phthalate metabolites and BPA in parents' pre-conception samples, collected pre-conceptionally and during pregnancy. Parents rated children's eating behavior using the Child Eating Behavior Questionnaire (CEBQ). Using multivariable linear regression, accounting for correlation among twins, we estimated covariate-adjusted associations between parental and maternal pregnancy urinary biomarker concentrations and CEBQ scores. RESULTS: The 257 children (mean age = 8.9 years; 51% female; 51% White) were predominantly non-Hispanic white (mothers and fathers)(80). Parental and maternal preconception monoethyl phthalate (MEP) and monobenzyl phthalate (MBzP) concentrations were related to higher mean externalizing problems. Maternal pregnancy MEP, mono-isobutyl phthalate (MiBP) and bisPhenol A (BPA) concentrations were associated with increased emotional undereating scores. Maternal pregnancy monocarboxy- isononyl phthalate concentrations were related to decreased food seeking subscale scores. CONCLUSIONS: In this cohort, parental and maternal preconception phthalate urinary concentrations of some phthalate biomarkers were associated with increased food approaching behavior scores and decreased food avoiding behavior scores, which could lead to increased adiposity in children.	Int J Hyg Environ Health. 2024 Apr;257:114334.	10.1016/j.ijheh.2024.114334	38350281	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0431	J. Lauder, L. Mínguez-Alarcón, P. L. Williams, J. B. Ford, R. Dadd, O. Chagnon, D. C. Bellinger, E. Oken, A. M. Calafat, R. Hauser and J. M. Braun	2024	Paternal and maternal preconception and maternal pregnancy urinary phthalate metabolite and BPA concentrations in relation to child behavior	BACKGROUND: Epidemiologic studies, on health effects of parental preconception exposures are limited despite emerging evidence from toxicological studies suggesting that such exposures, including to environmental chemicals, may affect offspring health. OBJECTIVE: We investigated whether maternal and paternal preconception and maternal pregnancy urinary phthalate metabolite and bisphenol A (BPA) concentrations were associated with child behavior. METHODS: We analyzed data from the Preconception Environmental exposures And Childhood health Effects (PEACE) Study, an ongoing prospective cohort study of children aged 6-12 years. Participants were previously enrolled in a fertility clinic- based preconception study. We quantified urinary concentrations of 12 phthalate metabolites and BPA in parents' pre-conception samples, collected pre-conceptionally and during pregnancy. Parents rated children's behavior using the Child Eating Behavior Questionnaire (CEBQ). Using multivariable linear regression, accounting for correlation among twins, we estimated covariate-adjusted associations between parental and maternal pregnancy urinary biomarker concentrations and CEBQ scores. RESULTS: The 257 children (mean age = 8.9 years; 51% female; 51% White) were predominantly non-Hispanic white (mothers and fathers)(80). Parental and maternal preconception monoethyl phthalate (MEP) concentrations were related to higher mean externalizing problems. Maternal pregnancy MEP, mono-isobutyl phthalate (MiBP) and bisPhenol A (BPA) concentrations were associated with increased emotional undereating scores. Maternal pregnancy monocarboxy- isononyl phthalate concentrations were related to decreased food seeking subscale scores. CONCLUSIONS: In this cohort, parental and maternal preconception phthalate urinary concentrations of some phthalate biomarkers were associated with increased food approaching behavior scores and decreased food avoiding behavior scores, which could lead to increased adiposity in children.	Environ Int. 2024 Jan;183:108337.	10.1016/j.envint.2023.108337	38088019	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0432	Z. Lazúrová, J. Figurski, B. Hubková, J. Mati ľaníková and I. Lazúrová	2021	Urinary bisphenol A in women with polycystic ovary syndrome - a possible suppressive effect on steroidogenesis?	OBJECTIVES: There is a growing evidence indicating an impact of endocrine-disrupting chemicals, such as bisphenol A (BPA) on human reproduction. Its higher levels in serum or urine have been documented in women with polycystic ovary syndrome (PCOS), however the relationship to ovarian steroidogenesis remains unclear. Aim of the study was to compare urinary BPA (U-BPA) concentrations among PCOS women and control group. METHODS: The study was performed in 2 groups of women: PCOS (n = 50) and control (n = 50). Inclusion criteria for PCOS group were: hyperandrogenism, oligo- or anovulation, age 18-40 years. Women in control group (n = 50) were included in the study. Fasting blood samples were analyzed for hormonal parameters and lipid profile. U-BPA was measured in the morning urine by high pressure liquid chromatography. RESULTS: PCOS women had significantly higher U-BPA as compared with control group (p=0.0001). Those with high levels of U-BPA (> UPP = 2.1 µg/g creatinine) demonstrated higher serum insulin (p=0.039) and FSH (P=0.0017), lower serum estrone (p=0.05), estradiol (p=0.0218), FSH- (p=0.0006), and FSH- (p=0.0001) as compared with low BPA group (LP - UPP = 2.1 µg/g creatinine). In PCOS women, U-BPA positively correlated with age (p=0.0329; R2(S=0.07), negatively with estradiol (p=0.0001; R2=0.1856), and testosterone (p=0.0019; R2=0.1128), free testosterone (p=0.0006; R2=0.123 and FAI (p=0.0008; R2=0.1137), respectively. CONCLUSIONS: PCOS women have significantly higher U-BPA concentrations than healthy controls. U-BPA positively correlates with age and negatively with serum steroid hormones, suggesting a possible suppressive effect of bisphenol A on ovarian steroidogenesis.	Horm Mol Biol Clin Investig. Vol.42 Issue 3 Pages 303-309	10.1515/hmbci-2020-0032	34118794	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0433	M. Lærkeholm Müller, A. S. Busch, M. L. Ljubicic, E. N. Upners, M. B. Fischer, C. P. Hagen, J. Albertsen, H. Frederiksen, A. Juul and A. M. Andersson	2023	Urinary concentration of phthalates and bisphenol A during minipuberty is associated with reproductive hormone concentrations in infant boys	BACKGROUND: The transient postnatal activation of the hypothalamic-pituitary-gonadal hormone axis is termed minipuberty and considered an important developmental period, which is highly sensitive to endocrine disruption. Here, we explore exposure-outcome associations during minipuberty between concentrations of potentially endocrine disrupting chemicals (EDCs) in urine of infant boys and their serum reproductive hormone concentrations. METHODS: We included 70 boys from the Copenhagen Minipuberty Study, a longitudinal study of healthy infant boys. Urine samples were collected at 1, 3, and 6 months of age (M1-M3) and serum samples from samples collected on the same day. Serum concentrations of reproductive hormones were measured by immunoassays or by LC-MS/MS. Urinary concentrations of metabolites of 30 non-persisting chemicals, including phthalates and phenols - compounds, were measured by LC-MS/MS. Nineteen chemicals had concentrations above the limit of detection in >80% of children and were included in data analysis. Associations of urinary phthalate metabolite and phenol concentrations (in females), with hormone outcomes (age- and sex-specific SD-scores) were analyzed by linear regression. Primarily, we focused on 672 regulated phthalate, bisphenol phthalate (BBzP), di-n-butyl phthalate (DnBP), di-n-butyl phthalate (DnBP), and di (2-ethylhexyl) phthalate (DEHP) as well as bisphenol A (BPA). Urinary metabolites of DBP, DnBP and DEHP were summed to molar sum of DBP (ΣDBP). RESULTS: Urinary ΣDBP was positively associated with serum inhibin B (M1: β = 0.24 SD-score/ln(ΣDBP) (95% CI: 0.03; 0.45), p = 0.03) and testosterone (M3: β = 0.23 SD-score/ln(ΣDBP) (95% CI: 0.01; 0.45), p = 0.04) and MEHP was positively associated with testosterone (M3: β = 0.23 SD-score/ln(MEHP) (95% CI: 0.01; 0.45), p = 0.04). Urinary concentrations of metabolites of DEHP were inversely associated with testosterone (M3: β = -0.23 SD-score/ln(ΣDEHP) (95% CI: -0.45; -0.01), p = 0.04). Further, higher levels (the peptide 5 (M3) SD-score and bone (M3) SD-score in boys in the highest ΣDnBP-tertile (SD: 0.13, 1.75) and -0.89 (-1.51; -0.28), respectively) were observed. In addition, boys in the middle and highest ΣDEHP-tertile had higher (+1.37 (0.35; 2.39), and 0.71 (-0.03; 1.45), respectively) and in the highest ΣDEHP-tertile also higher (MH: 0.85 (0.10; 1.61)) concentration SD-scores, respectively. Boys in the highest BPA tertile had significantly higher (MH and bone (M3)SD) concentration compared to boys in the lowest BPA tertile (1.26 (0.50; 2.02) and -0.72 (-1.45; -0.02), respectively. CONCLUSIONS: Our findings suggest that exposure to phthalates and bisphenol A during minipuberty is associated with reproductive hormone concentrations, especially the FSI-regulated DnBP, DEHP and BPA, may modify male reproductive hormone concentrations in infant boys, suggesting that minipuberty is a critical window sensitive to endocrine disruption.	Int J Hyg Environ Health Vol.250 Pages 114166	10.1016/j.ijheh.2023.114166	37058994	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0434	J. A. Kwon, B. Shin and B. Kim	2020	Urinary bisphenol A and thyroid function by BMI in the Korean National Environmental Health Survey (KoNEHS) 2012-2014	Bisphenol A (BPA) is one of the largest amounts of chemicals in daily life and source of polycarbonate plastics, epoxy resins, medical equipment, plastic consumer products. Recent studies reported that the effects of BPA on human health is the thyroid hormone. Therefore, this study aimed to indicate the association between urinary BPA concentration and thyroid function in total (disability)ratio (TS), thyroxine (T4), thyroidal hormone (TH) and thyroid stimulating hormone (TSH) by body mass index (BMI) in the Korean National Environmental Health Survey (KoNEHS) 2012-2014 and 2015-2017. METHODS: KoNEHS, 2012-2017. We measured BPA in urine and total T3, T4 and TSH in serum in the third KoNEHS cycle. The multiple regression analysis was performed to study the association of urinary BPA concentrations with thyroid hormone after BMI stratification. Urinary BPA associated with thyroid hormone. Especially, BPA is related to T3 (-0.423) in all group, and T4 (-0.685 -0.686) in all group and the group of BMI (N.Reg) not or more negatively. When stratified by BPA, T3 and T4 were significantly decreased with the high BPA exposure compared with the low BPA exposure for BMI more than 25.0kg/m2 (adjusted β = -1.102, 95% CI: -1.562, -1.642, adjusted β = -0.298, 95% CI: 0.538, -0.058). However, no obvious associations were found between BPA concentration and TSH. The results of urinary BPA decrease with T3 and T4 levels. Increase in the highest BMI group is area finding which does not exist in recent studies of Korea.	Chemosphere Vol.240 Pages 124918	10.1016/j.chemosphere.2019.124918	31563717	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0435	R. Kumar, S. Adhikari, E. Driver, J. Zeultz and R. U. Halden	2022	Application of wastewater-based epidemiology for estimating population-wide human exposure to phthalate esters, bisphenols, and terephthalic acid	Phthalates, bisphenols (BPs), and terephthalic acid (TPA) are widely used plasticizers and monomers in plastic manufacturing. Most of them are known to have an adverse effect on the human body, functioning as endocrine disrupting chemicals (EDCs). Biomonitoring studies have documented widespread human exposure to these chemicals, but population-wide exposure estimates are lacking for many countries. The objective of the present study was to evaluate population-level exposure to phthalates, BPs, and TPA by measuring urinary metabolites in community wastewater. Composited community wastewater (24 h samples) from five sewer sub-catchments of a southwestern city within the United States were analyzed for urinary biomarkers of phthalates, BPs, and TPA using solid-phase extraction liquid chromatography tandem mass spectrometry in conjunction with the isotope dilution method for absolute quantification. For all analytes, were detected at least once in community wastewater above the method detection limit (MDL), with MDLs ranging from 27 to 310 ng/L. The population-normalized mass load of TPA was the highest, followed by the human metabolite of di (2-ethylhexyl) phthalate (DEHP), Bisphenol S and monoethyl phthalate were detected frequently but at relatively low concentrations and loads. Mass loads of phthalates and BPs were comparable to previous reports in plastic-consumers, to handle, practicable, and informative, as large, conservative steps are taken to determine, quantify and account for background levels of plastic analytes in the laboratory environment.	Sci Total Environ Vol.847 Pages 157616	10.1016/j.scitotenv.2022.157616	35901875	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0436	S. A. Kullberg, L. M. Voller and A. B. Neeley	2020	Chronic Actinic Dermatitis After Occupational Sensitization to the Epoxy Resin, Bisphenol		Dermatitis. 2020 Jul/Aug;31(4):e25-e26.	10.1097/der.0000000000000596	32665513	ヒト	その他	-	-	-	-	-	-	症例報告	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0437	J. R. Kuiper, S. Pan, B. P. Lanphear, A. M. Calafat, A. Chen, K. M. Cecil, Y. Xu, K. Yolton, H. J. Kalkwarf, J. M. Braun and J. P. Buckley	2023	Associations of maternal gestational urinary environmental phenols concentrations with bone mineral density among 12-year-old children in the HOME Study	BACKGROUND: Early life environmental exposures may affect bone mass accrual in childhood, but only one study has assessed the role of environmental phenols on child bone health. METHODS: We used data from 233 mother-child pairs enrolled in the HOME Study, a prospective pre-birth cohort study recruited in Cincinnati, OH, USA (2003-2006). We measured urinary concentrations of 11 phenols in maternal urine collected at 16- and 26-weeks gestation and calculated the average of creatinine-adjusted concentrations. We performed dual x-ray absorptiometry at age 12 years and calculated Z-scores for whole body (less head), total hip, femoral neck, and L2-four bone mineral content (BMC) and areal bone mineral density (aBMD) as well as other distal radius aBMD and spine BMC and bone mineral apparent density (BMAD). We estimated covariate-adjusted associations (in standing of maternal urinary environmental concentrations in linear regression models. We also estimated associations by child's sex and assessed associations of the environmental phenol mixture with BMC and aBMD using quantile g-computation. RESULTS: By the cincinnati-specific cut-points for all analytes and lower measures. Yet, in adjusted models, maternal urinary concentrations of benzophenone-3 (BP3) were associated with lower total body less head BMC (-0.06 SD; 95% CI: -0.11, -0.01) and spine BMC (-0.06 SD; 95% CI: -0.11, -0.01) at age 12 years. In sex-stratified analyses, the magnitude of the BMC association was similar for females (-0.16; 95% CI: 0.26, 0.06) and for males (-0.02; 95% CI: 0.08, 0.13). The environmental phenol mixture was associated with greater 1.0-unit distal radius BMC and aBMD 2-scores in both sexes, which was mostly driven by benzophenone-3 in males and 2,5-dichlorophenol in females. CONCLUSIONS: In this prospective cohort study, we observed generally null associations for environmental phenols with BMC and aBMD at age 12 years. While there was a positive association of 2,5-dichlorophenol concentrations during fetal development with distal radius BMC and aBMD at age 12 years, future studies utilizing methods capable of differentiating cortical and trabecular bone are needed to elucidate potential mechanisms and implications for bone strength and skeletal fracture.	Int J Hyg Environ Health. 2023 Mar;248:114104.	10.1016/j.ijheh.2022.114104	36525700	ヒト	骨	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0438	D. Koutaki, G. Paltoglou, A. Vounotrypa and E. Charmandari	2021	The Impact of Bisphenol A on Thyroid Function in Neonates and Children: A Systematic Review of the Literature	BACKGROUND: Bisphenol A (BPA) is an endocrine disrupting chemical widely used in plastic products that may have an adverse effect on several physiologic functions in children. The aim of this systematic review is to summarize the current knowledge of the impact of BPA concentrations on thyroid function in neonates, children, and adolescents. METHODS: A systematic search of Medline, Scopus, Clinical Trials.gov, Cochrane Library, and Google Scholar for the terms "bisphenol A" and "thyroid" was performed. RESULTS: Twenty-two studies were identified that met the inclusion criteria. Eleven studies investigated the association between Bisphenol A and thyroid function in neonates and children aged <18 years, one included only children who were accessed, while nine restricted to adolescents. A total of 13 articles were assessed by two independent researchers based on the title/abstract and the predetermined inclusion and exclusion criteria. According to the eligibility criteria, 10 full-text articles were selected for further assessment. Finally, 12 full-text articles were included in the present systematic review. RESULTS: The presented studies offer data that suggest a negative correlation of BPA concentrations with TSH in children, a gender-specific manner of action, and a potential effect on proper neurodevelopment. However, the results are inconclusive with respect to specific thyroid hormone concentrations and the effect on thyroid autoimmunity. CONCLUSIONS: The presence and significance of BPA in the developing thyroid gland of children that may affect proper neurodevelopment, suggesting the need to focus future research on designing studies that elucidate the underlying mechanisms and the effects of BPA on thyroid function in early life.	Nutrients Vol.14 Issue 1	10.3390/nu14010168	35011041	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0439	M. Kouchki, A. H. Duzzinotaghi, N. Amiri-Dashtaan, M. Farahani, H. Chidi, R. Vanda and S. Aramesh	2024	Impact of bisphenol A exposure on the risk of gestational diabetes: a meta-analysis of observational studies	PURPOSE: A growing number of evidence have assessed the association between bisphenol A (BPA) as an endocrine disrupting agent and the risk of gestational diabetes (GDM). This meta-analysis aimed to measure the data on the exclusive of BPA levels in women with GDM compared to the control. METHODS: A comprehensive literature search was conducted in Medline, Embase, Scopus, and Web of Science to screen relevant published studies up to May 2021. 12 articles were included in the meta-analysis. DerSimonian and Laird random effects model was used to estimate the pooled odds ratio (OR). Sensitivity analysis was conducted to assess the stability of the results. Publication bias was evaluated by Begg's funnel plot and Egger's test. Subgroup analysis was performed to explore the source of heterogeneity based on study design and geographical area. RESULTS: The results showed that there was no significant association between circulating and urinary BPA concentrations with the risk of GDM (OR: 0.76; 95% CI: 0.60-1.14; I2= 0.0%). No significant heterogeneity was found among the studies. Using Begg's correlation (P = 0.99) and Egger's linear regression (P = 0.86) tests, no publication bias was observed. The sensitivity analysis shows that our findings were completely robust and stable. Meta-regression indicated a significant association between BPA levels and study design and geometric mean as an index of the risk of GDM. CONCLUSION: The present meta-analysis demonstrates exposure to BPA was associated with a reduced risk of GDM. Further studies are needed for about the reliable results.	J Diabetes Metab Disord. 2024 Sep 2;23(2):2173-2182.	10.1007/s40200-024-01485-5	39610499	ヒト	生殖発生/メタアナリシス	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-	-
統合_0440	A. Kortenkamp, M. Scholze, S. Ermler, L. Priskorn, N. Jørgensen, A. M. Andersson and H. Frederiksen	2022	Combined exposures to bisphenols, polychlorinated dioxins, paracetamol, and phthalates as drivers of deteriorating semen quality	BACKGROUND: Semen quality in men continues to decline in Western countries, but the contours of the issue remain obscure. In relation to contributing chemicals. OBJECTIVES: To obtain more clarity about the role of environmental chemicals in male reproductive health, we investigated associations between 11 chemicals and 4 semen quality parameters. METHODS: We used data from 1,106 young men from three European countries, among them androgen receptor antagonists, substances that disrupt prostaglandin signalling, aromatase inhibitors (aromatase synthesis), inhibin biosynthesis enzymes or activate the aryl hydrocarbon receptor. We employed the Hazard Index approach (HI), based on risk quotients of exposures in Europe and reference doses for reductions in semen quality. By summing up the risk quotients of the 39 chemicals included in the assessment we examined risk-exceedances of "acceptable" mixture exposures relative to an index value of 1.7 in Vuolanto A, P. A. phthalates (DEHP, DnBP, BBzP, DINP, n-hex) powders and polyurethane) we relied on biomarkers of exposure. RESULTS: Bisphenols A made the largest contribution to the HI, followed by polychlorinated dioxins, bisphenols, S and F and DEHP. Eliminating Bisphenol A alone would still have unacceptably high mixture risks. Paracetamol is also a driver of mixture risks among subjects using the drug. CONCLUSIONS: Tolerable exposures to substances associated with deteriorations of semen quality are exceedingly large. Bisphenols, polychlorinated dioxins, phthalates, and analgesics drive these risks. Dedicated efforts towards lowering exposures to these substances are necessary to mitigate risks.	Environ Int Vol.165 Pages 107322	10.1016/j.envint.2022.107322	35691715	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0454	K. Kim, H. M. Shin, S. A. Bungerg, D. B. Barr, P. Panuwet, R. J. Schmidt, I. Hertz-Picciotto and D. H. Bennett	2021	Temporal Trends of Phenol, Paraben, and Triclocarban Exposure in California Pregnant Women during 2007-2014	Little is known about temporal trends of pregnant women's exposures to environmental phenols and parabens. We quantified four phenols (bisphenol A (BPA), bisphenol F, bisphenol S, and triclosan), four parabens (butyl paraben, ethyl paraben, methyl paraben, and propyl paraben), and triclocarban in spot urine samples collected from 1,239 pregnant women in California during 2007-2014. We used multivariable linear regression with log-transformed biomarker concentrations as the outcome and survey-weighted, multivariable regression to compare trends over gestation to mean of urinary concentrations, and computed average annual percent changes. We compared our urinary concentrations with those of other study populations to examine geographic variations in pregnant women's exposure to these target compounds. Urinary concentrations of BPA, MEPB, ETPB, and PRPB in this study population decreased over the study period (percent changes per year (95% confidence interval): -6.1% (-8.0%, -3.9%), -13.6% (-18.0%, -7.7%), -5.8% (-12.0%, 0.9%), and -13.0% (-18.9%, -6.5%), respectively) and were consistently lower than those in pregnant women in other U.S. regions during the same study period. In recent years, certain phenols and parabens with known adverse health effects are being regulated or replaced with alternatives, which explains decreased body burdens observed in this study population. Either the national regulations or the advocacy campaigns in California may have influenced exposures in consumer product choices.	Environ Sci Technol. 2021 Aug 17;55(16):11155-11165.	10.1021/acs.est.1c01564	34347462	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0455	J. I. Kim, Y. A. Lee, C. H. Shin, Y. C. Hong, B. N. Kim and Y. H. Lim	2022	Association of bisphenol A, bisphenol F, and bisphenol S with ADHD symptoms in children	BACKGROUND: Bisphenol A (BPA) has been linked to attention-deficit/hyperactivity disorder (ADHD) symptoms, but the neurotoxic effects of bisphenol substitutes such as bisphenol F (BPF) and S (BPS) have not been well investigated. We investigated the associations between BPA, BPF, and BPS with ADHD symptoms at multiple time points in children. METHODS: The levels of BPA (at ages 3, 4, and 8), BPF (at ages 4 and 8), and BPS (at ages 4 and 8) were measured in 570 children. Because of the low detection frequency of BPF and BPS levels, participants were divided into categories (i.e., a low/undetectable [LOD] vs. BPF: > LOD, ≤ median; or > median) for BPSS. ADHD symptoms were assessed using the ADHD Rating Scale-IV (ARS). The relationship between bisphenols and ARS scores was analyzed using Poisson regression models, and sex-stratified analyses were performed because of significant interactions between sex and bisphenols. RESULTS: The detection frequencies of BPA, BPF, and BPS were 99.8%, 15.4%, and 11.2% at age 3; 99.8%, 15.4%, and 11.2% for BPF and 43.2% for BPS at age 4; 54.1% for BPF and 31.5% for BPS). Doubling in BPA levels was associated with increased ARS scores by 6.7% (95% confidence interval [CI]: 0.5, 12.7) at age 8. The association was greater with BPA levels higher than 0.8 μg/g creatinine (24.2% [95% CI: 3.5, 51.6]) increase). The BPF > LOD group had 10.8% (95% CI: 1.2, 21.2) higher ARS scores than the BPF ≤ LOD group. The BPS > median group had 11.0% (95% CI: 2.4, 20.1) higher ARS scores than the BPS ≤ LOD group. CONCLUSION: Of bisphenols, in particular those at or above the LOD or median levels, were associated with ADHD symptoms at age 8. Further prospective studies are warranted to determine causal inference.	Environ Int. 2022 Mar;161:107093.	10.1016/j.envint.2022.107093	35077929	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0456	J. H. Kim, H. S. Shin and W. H. Lee	2021	Impact of Endocrine-Disrupting Chemicals in Breast Milk on Postpartum Depression in Korean Mothers	Previous human and animal studies have reported an association between endocrine-disrupting chemicals (EDCs) and anxiety/depression. This study aimed to determine how the concentrations of phthalate metabolites, bisphenol A, triclosan, and parabens in breast milk are associated with the risk of developing postpartum depression (PPD) in Korean mothers. We recruited 322 mothers who were receiving lactation coaching at postpartum care centers. Their sociodemographic characteristics and PPD symptoms were collected using questionnaires, including the Edinburgh Postnatal Depression Scale. Breast milk samples were collected from the participants 1 month postpartum to measure the concentrations of 15 EDCs, including phthalate, bisphenol A, parabens, and triclosan. Results: Exposure to the mixture of EDCs was not significantly associated with the risk of PPD. This study was the first attempt to analyze the association between the levels of EDCs in breast milk and the risk of PPD. Considering that PPD is a condition that affects not only the women diagnosed with it, but also their children and families, the results of this study may have great relevance to population. It is incrementally sensitive periods.	Int J Environ Res Public Health. 2021 Apr 22;18(9):4444.	10.3390/ijerph18094444	33922135	ヒト	神経(産後うつ)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0457	J. H. Kim, N. Moon, E. Ji and H. B. Moon	2023	Effects of postnatal exposure to phthalate, bisphenol a, triclosan, parabens, and per- and poly-fluoroalkyl substances on maternal postpartum depression and infant neurodevelopment: a korean mother-infant pair cohort study	Exposure to endocrine-disrupting chemicals (EDCs) can promote infant neurodevelopmental impairment and maternal postpartum depression (PPD). However, the associations between lactation exposure to EDCs, maternal PPD, and infant neurodevelopment are unclear. Hence, we investigated these relationships in infants aged 36–37 months. We recruited 322 Korean mothers and evaluated EDCs, The Edinburgh Postnatal Depression Scale (EPDS) was used to assess maternal PPD. Bayley scales of infant development: the Korean, Ages, and Pethem rating scale (BSAP), and the Child Behavior Checklist (CBCL) were used to assess neurodevelopment in infants exposed to the top 50% of EDC concentrations. Multiple regression analyses were adjusted for maternal age, pre-pregnancy body mass index, education, employment, residence, and infant age and sex. The rates of infants with clinically abnormal diagnoses on neurologic developmental tests (Bailey, BSAP, and CBCL scales) ranged from 7.7 to 38.5% in this study, with the motor and behavioral/emotional domains showing the highest rates. Maternal PPD was significantly associated with exposure to mixtures of EDCs, particularly phthalates, parabens, and triclosan, and hyperactivity. Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) levels correlated significantly with motor development at BSID-III and total CBCL score which mother might have been developmental status. EDC concentrations in breast milk were not associated with maternal PPD. Overall, lactational exposure to EDCs during the postpartum period can exert a negative effect on maternal PPD and infant neurodevelopment.	Environ Sci Pollut Res Int. 2023 Sep;30(42):96384-96399.	10.1007/s11356-023-29292-0	37572253	ヒト	神経(産後うつ)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0458	J. H. Kim, N. Moon, S. J. Heo, Y. W. Jeong and D. R. Kang	2024	Repeated measurements and mixture effects of urinary bisphenols, parabens, polycyclic aromatic hydrocarbons, and other chemicals on biomarkers of oxidative stress in pre- and postpartum women	The association between oxidative stress and exposure to bisphenols, parabens, phenols, polycyclic aromatic hydrocarbons (PAH), and volatile organic compounds (VOCs) has been investigated by many in vitro and in vivo studies. However, most of these findings are based on cross-sectional studies, as a result of which the combined effects of these compounds have been rarely analyzed. In this study, we objective was to assess urinary bisphenols, parabens, PAHs, and VOCs, in relation to oxidative stress during pre-and postpartum periods, analyze the association between these chemicals and oxidative stress via repeated measurements using a linear mixed model (LMM), and evaluate the combined effects these chemicals on oxidative stress using Bayesian kernel Machine Regression (BKMR). A total 500 urine samples from 50 pregnant women during the 1st and 2nd trimesters, as well as postpartum follow-ups. Three biophenols, four parabens, benzophenone-3 (BP-3), triclosan (TCS), four PAHs, two VOCs, and 3- phenoxy benzoic acid (3-PBA) were measured in urine samples. Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) was measured as a biomarker of oxidative stress. The LMM and BKMR were used to assess the effects of chemicals via mixt. For both the intervention and control groups, questionnaire results and maternal urine samples were accessed at baseline, during the intervention, and after one month. After the intervention, the urinary concentrations of mono (2-ethylhexyl) phthalate (MEHP), mono (2-ethyl-5-oxohexyl) phthalate (MEOHP), bisphenol A (BPA), methylparaben (MP), ethylparaben (EP), and propylparaben (PP) were found to be significantly decreased in the intervention group. Compared to the control group, the intervention group showed significantly decreased urinary geometric mean values of MEHP, MEOHP, BPA, MP, and PP after one month compared with those during the intervention (1.86, 1.63.16, 28.30, 9.74, and 29.35, respectively). Hence, the web-based behavioral intervention was effective at reducing the exposure to endocrine disruptors in mothers with young children.	Environ Pollut. 2024 Feb 1;342:123057.	10.1016/j.envpol.2023.123057	38043769	ヒト	その他(酸化ストレス)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0459	J. H. Kim, J. M. Kwak and H. Kang	2021	Web-based behavioral intervention to reduce exposure to phthalate metabolites, bisphenol A, triclosan, and parabens in mothers with young children: A randomized controlled trial	In this study, a web-based behavioral intervention was designed, which aimed to reduce exposure to phthalate metabolites, bisphenol A, triclosan, and parabens in mothers with young children. A randomized controlled design with two groups was used to verify the effects of the intervention pre- and post-test. In total, 51 mothers participated in the study, categorizing 26 and 25 in the intervention and control groups, respectively. The web-based behavioral intervention focused on changes in diet, personal care products, and habits related to indoor and outdoor behavior through encouragement. This program included an educational video, a game for handling endocrine disruptors at home, a method for locating facilities potentially emitting endocrine disruptors, resources, and a questions and answers mode. Data were collected from May 18 to June 30, 2020. Participants in the intervention group were provided with a link to the web-based behavioral intervention program for 1 month. Urine samples were collected from participants to measure the concentrations of endocrine disruptors via mol. For both the intervention and control groups, questionnaire results and maternal urine samples were accessed at baseline, during the intervention, and after one month. After the intervention, the urinary concentrations of mono (2-ethylhexyl) phthalate (MEHP), mono (2-ethyl-5-oxohexyl) phthalate (MEOHP), bisphenol A (BPA), methylparaben (MP), ethylparaben (EP), and propylparaben (PP) were found to be significantly decreased in the intervention group. Compared to the control group, the intervention group showed significantly decreased urinary geometric mean values of MEHP, MEOHP, BPA, MP, and PP after one month compared with those during the intervention (1.86, 1.63.16, 28.30, 9.74, and 29.35, respectively). Hence, the web-based behavioral intervention was effective at reducing the exposure to endocrine disruptors in mothers with young children.	Int J Hyg Environ Health Vol.236 Pages 113798	10.1016/j.ijheh.2021.113798	34186503	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0460	J. H. Kim, D. Kim, S. M. Moon and E. J. Yang	2020	Associations of lifestyle factors with phthalate metabolites, bisphenol A, parabens, and triclosan concentrations in breast milk of Korean mothers	The toxicity of endocrine disruptors depends on the synergistic interactions of biological, environmental, and behavioral factors. The specific effects of diet, consumer product use, and behaviors, however, are debated in the literature, particularly with regard to endocrine disruptors found in breast milk. This study aimed to measure the levels of phthalate metabolites, bisphenol A, parabens, and triclosan in breast milk, and to investigate their associations with various lifestyle factors. The breast milk samples as well as surveys were collected from 233 first-time mothers throughout South Korea and each sample was analyzed for the presence of 15 endocrine disruptors. Phthalate metabolites were detected in 0.4-85.3% of the samples, with median concentrations of 0.05-1.72 μg/L, while bisphenol A, parabens, and triclosan were detected in 24.9-88.3% of the samples, with median concentrations of 0.27-1.67 μg/L. High levels of endocrine disruptors were associated with frequent consumption of fish and cup noodles; the use of plastic and disposable food containers; the use of cosmetics, sunscreen, and hair products; and exposure to indoor dust. Our results suggest that exposure to endocrine disruptors is widespread among lactating women in South Korea, and that the detected levels are associated with the lifestyle factors of the mothers. Our data provide evidence of the potential effects of diet, consumer products, and behavior on the presence of phthalate metabolites, bisphenol A, parabens, and triclosan in breast milk. Future studies should include community or regional impact on a mothers' exposure to endocrine disruptors, to assess the joint contribution of both individual and neighborhood factors.	Chemosphere Vol.249 Pages 126149	10.1016/j.chemosphere.2020.126149	32062213	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0461	J. H. Kim, Y. H. Cho and Y. C. Hong	2020	MicroRNA expression in response to bisphenol A is associated with high blood pressure	Bisphenol A (BPA) is a ubiquitous environmental contaminant that is known to be associated with the risk of arterial hypertension. However, the underlying mechanism, describing how BPA exposure leads to high blood pressure (BP) remains unclear. We investigated the association between BPA exposure and microRNA (miRNA) expression in relation to BP in a panel study of elderly residents in Seoul, Korea. We measured urinary BPA and BP levels of 60 participants aged 60 years or more. The participants visited the study site 3 times and were clean dependently exposed to BPA. Two hours after exposure to BPA, urine and whole blood were collected for BPA measurement and miRNA profiling, and BP was measured. Relationships among urinary BPA level, miRNA expression, and BP were estimated using the mixed-effect model. Decreases in miR-18a-5p, miR-582-3p, miR-107-5p, and miR-572-5p and increases in miR-548-3p and miR-1228-3p in the baseline-to-BPA exposure were associated with high BP. The over-functional network from BPA exposure to increased BP via miR-18a-5p, miR-582-3p, miR-107-5p, and miR-572-5p through three miRNAs and their predicted BP-related target genes. Our results suggest that epigenetic biomarkers for BPA exposure and hypertension provide mechanistic data to explain hypertension exacerbation as well as key information for predicting the health effects of BPA exposure.	Environ Int. 2020 Aug;141:105791.	10.1016/j.envint.2020.105791	32438192	ヒト	心血管	-	-	-	-	-	-	介入研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0462	D. Kim, E. R. Yoo, A. A. Li, G. Chalasani, S. P. Tighe, W. Kim, S. A. Harrison and A. Ahmad	2019	Elevated urinary bisphenol A levels are associated with non-alcoholic fatty liver disease among adults in the United States	BACKGROUND AND AIMS: The relationship between bisphenol A (BPA) and non-alcoholic fatty liver disease (NAFLD) is unclarified. We studied the impact of BPA on NAFLD. METHODS: We performed a cross-sectional analysis of 2,838 participants from the National Health and Nutrition Examination Survey (NHANES) 2003-2004. Urinary BPA was measured by high-performance liquid chromatography. NAFLD was defined by the hepatic steatosis index (HSI) ≥ 36 in the absence of other causes of chronic liver disease. The final sample using HSI consisted of 1,765 adults. The race-and-gender-using (AFI) corrected BPA participants with availability of health data. RESULTS: Of the first 1765 participants (mean age 37 years, 48.6% male), the prevalence of NAFLD and abnormally elevated alanine aminotransferase (ALT) levels was correlated with urinary BPA levels. (P < 0.05). Compared to the reference group with lowest quartile of urinary BPA levels, those with the third and fourth quartile levels had 2.5- and 3.5- more likely to develop NAFLD and 50% more likely to develop NAFLD in a multivariate model. An 10% for NAFLD in the third and fourth quartiles were 1.29 (95% CI: 1.09-1.50) and 1.22 (95% CI: 1.06-1.76) respectively (P for trend: <0.001). In the second sample using LDFT, a high BPA levels (fourth quartile) remained an independent predictor of NAFLD (OR 1.45, 95% CI: 1.05-1.98, P for trend = 0.012). CONCLUSIONS: High levels of urinary BPA were associated with NAFLD in a nationally representative sample of adults in the US. The pathophysiology remains unclear and warrants further investigation.	Liver Int Vol.39 Issue 7 Pages 1335-1342	10.1111/liv.14110	30924602	ヒト	横断研究	1	1	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0463	B. Kim, B. Park, C. H. Kim, S. Kim and B. Park	2022	Association between endocrine-disrupting chemical mixture and metabolic indices among children, adolescents, and adults: A population-based study in Korea	Exposure to endocrine-disrupting chemicals (EDCs) play a role in the etiology of obesity and dyslipidemia. However, few studies have analyzed the combined effects of EDC mixtures. This study explored the association between urinary EDC mixtures and metabolic indices among children, adolescents, and adults. We used data from the 2015–2017 Korean National Environmental Health Survey (KoNEHS) cycle 3. The National Environmental Health Survey (2015 to 2017 cycle included in this. assay. sectional study. Urinary concentrations of eight phthalate metabolites, three phenols, three parabens, and one quantized pesticides metabolite were quantified. Body mass index (BMI) was measured for all participants, and triglyceride (TG) and high-density lipoprotein cholesterol (HDL-c) levels were measured for adolescents and adults. Associations between EDC mixtures and metabolic indices were analyzed using weighted quantile sum (WQS) regression. The WQS index was constructed based on the quartiles of each EDC. The WQS index for BMI, TG, and HDL-c were derived in more than 95% of participants. There was a significant association between a high cumulative phthalate metabolites index (the high cumulative index quartiles). The WQS index for the EDC mixture was associated with higher BMI in both adolescents and adults, with greater significance in adults compared with adolescents, and a higher TG WQL in male adolescents. In adolescents, WBP and MCPP drove the main effects on BMI and TG WQL, respectively. In adults, DMA and BPA drove the main effects on BMI. The findings of this study suggest that exposure to EDC mixtures is associated with higher BMI and TG/HDL, and adults.cence may be a critical period for EDC mixture in terms of both outcomes. Further studies are needed, but strategies to reduce EDC exposure from early life stages may be necessary to lower the risk of metabolic disease.	Environ Pollut Vol.315 Pages 120399	10.1016/j.envpol.2022.120399	36228844	ヒト	横断研究	1	1	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0464	K. R. Kilcoyne and R. T. Mitchell	2019	Effect of environmental and pharmaceutical exposures on fetal testis development and function: a systematic review of human experimental data	BACKGROUND: Overall, the incidence of male reproductive disorders has increased in recent decades. Testicular development during fetal life is crucial for subsequent male reproductive function. Non-genetic factors such as environmental chemicals, pharmaceuticals and lifestyle have been proposed to impact on human fetal testicular development resulting in subsequent effects on male reproductive health. Whilst experimental studies using animal models have provided support for this hypothesis, more recently a number of experimental studies using human tissues and cells have begun to translate these findings to determine direct human relevance. OBJECTIVE AND RATIONALE: To systematically review the literature describing the effects of environmental and pharmaceutical exposures on human fetal testis development and function. We present the effects of environmental, pharmaceutical and lifestyle factors in experimental systems involving exposure of human fetal testis tissues and cells to chemicals, with a focus on epidemiological data currently derived from a recent meta-analysis. SEARCH METHODS: For identification of experimental studies, PubMed and EMBASE were searched for articles published in English between 01/01/1966 and 15/07/2018 using search terms including 'testosterone biosynthesis', 'human', 'fetal', 'testis', 'gonad' and 'endocrine disruptor'. Bibliographies of relevant articles were searched for further retrospective Epidemiological studies, involving exposure to the same agents were extracted from a recent systematic review and meta-analysis. Additional studies were identified through screening of bibliographies of relevant articles. OUTCOMES AND REVIEW: Of 1,616 articles identified, 130 were included in the review. Effects of environmental chemicals, pharmaceuticals and lifestyle factors on human fetal gonad development are demonstrated in experimental models, correlating with evidence from epidemiological studies and animal models. Furthermore, analysis of human fetal testis tissue and cells has revealed reduction in fetal testosterone production, which predisposes to the development of male reproductive disorders, has been reported in studies involving human tissues, which also supports data from animal and epidemiological studies. However, while reduced testosterone production has been demonstrated in animal studies following exposure(s) to a variety of environmental chemicals, including phthalates and bisphenol A, these effects are not reproduced in experimental approaches using human fetal testis tissues. WIDER IMPLICATIONS: Direct experimental evidence for effects of prenatal exposure(s) on human fetal testis development and function exists, however, for many exposures little data is available. The increasing use of human relevant models systems is starting to determine the effects of environmental exposures. Combining mixed exposures on development and function of human tissues should form an important part of the process for assessment of such exposures by regulatory bodies to take account of animal–human differences in susceptibility.	Hum Reprod Update Vol.25 Issue 4 Pages 397-421	10.1093/humupd/dmz004	30869130	ヒト	システマティックレビュー	1	1	-	-	-	-	システマティックレビュー	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0465	D. Khodasevich, N. Holland, K. G. Harley, B. Eskenazi, L. F. Barcellos and A. Cardenas	2024	Prenatal exposure to environmental phenols and phthalates and altered patterns of DNA methylation in childhood	INTRODUCTION: Epigenetic marks are key biomarkers linking the prenatal environment to health and development. However, DNA methylation associations and persistence of marks for prenatal exposure to multiple Endocrine-Disrupting Chemicals (EDCs) in human populations have not been examined in great detail. METHODS: We measured Bisphenol A (BPA), triclosan, benzophenone-3 (BP3), methyl paraben, propyl paraben, and 11 phthalate metabolites in urine collected during pregnancy from participants in the CHAMACOS cohort (Salinas Valley, CA; 1999–2000). We measured DNA methylation in cord blood (n = 333) and at 5 years (n = 309) using Illumina HumanMethylationEPIC BeadChip. We used an Elastic Net penalized regression approach to identify differentially methylated probes (DMPs) and comb-p was used to identify differentially methylated regions (DMRs) in association with pregnancy averaged EDC concentrations. Quantile g-computation was used to assess associations of the whole phenol/phthalate mixture with DMPs and DMRs. RESULTS: Prenatal BP3 exposure was associated with 1 CpG among males and Parabens were associated with 10 CpGs among females at Bonferroni-level significance in cord blood. Other suggestive DMPs (unadjusted p-value < 1 × 10–5) and several DMRs associated with the individual phenols and whole mixture were also identified. A total of 3 DMPs were associated with prenatal BP3 exposure at age 5 years among males, and 1 DMP was associated with prenatal BPA exposure among females. We identified 1 DMR and 2 DMPs at age 5 specific associations between prenatal phenol exposure and DNA methylation, particularly with BP3 in males and Parabens in females. Additionally, cord blood-derived DMPs that maintained significant associations with prenatal EDC exposures at age 5 well-age 10 years.	Environ Int. 2024 Aug;190:108862.	10.1016/j.envint.2024.108862	38972116	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0466	G. N. Kaskoliadas, S. Tsiokkou, I. Konstantinidis, M. N. Georgaki, A. Soga, T. Papamitsou and S. Kavachiyadi	2024	Endocrine-Disrupting Chemicals and the Development of Diabetes Mellitus Type 1: A 5-Year Systematic Review	INTRODUCTION: According to the Institute of Environmental Sciences, endocrine-disrupting chemicals (EDCs) are "natural or human-made chemicals that may mimic, block, or interfere with the body's hormones, potentially causing adverse health effects". Diabetes mellitus type 1 (DMT1) is a chronic disease that is caused by the destruction of pancreatic β-cells, leading to insulin deficiency. Both genetic and environmental factors contribute to the development of DMT1, with endocrine-disrupting chemicals (EDCs) being one of the environmental factors under investigation. AIM/PURPOSE: The purpose of this study was to investigate the correlation between the EDCs and the development of T1DM. METHODOLOGY: Then, a 5-year systematic review was conducted to bring light to this research question. Using the meta-analysis and systematic review guidelines protocol, a PRISMA flow diagram was constructed and, using the keywords 'diabetes mellitus type 1' AND 'endocrine-disrupting chemicals' in the databases PubMed, Scopus and ScienceDirect, the relevant data was collected and extracted into tables. Quality assessment tools were employed to evaluate the quality of the content of each article retrieved. RESULTS: Based on the data collected and extracted from both human and animal studies, an association was found between TCDD and certain EDCs, such as bisphenol A (BPA), bisphenol S (BPS), perchlorinated organic pollutants (POPs), phthalates, and dioxins. Moreover, the focal on the quality assessment performed, using the Newcastle–Ottawa Scale and AMSTAR quality assessment tool, the articles were considered of high quality and thus eligible to justify the correlation of the EDCs and the development of T1DM. CONCLUSIONS: Based on the above study, the correlation can be justified. However, additional studies can be made focusing mainly on humans to understand further the pathophysiologic mechanisms involved in this association.	Int J Mol Sci Vol.25 Issue 18	10.3390/ijms251810111	39337594	ヒト	システマティックレビュー	1	1	-	-	-	-	システマティックレビュー	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

別添-2　統合文献リスト

通悪性評価（動物）1：該当、0：該当しない　通悪性評価（疫学）1：該当、0：該当しない　通悪性評価（in vitro）1：該当、0：該当しない　通悪性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに遺悪性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺悪性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0467	R. Kashavarz-Maleki, A. Kaviani, R. Omrani pour, M. Ghitami, M. R. Khoshayand, S. N. Ostad and O. Sabzevari	2021	Bisphenol-A in biological samples of breast cancer mastectomy and mammoplasty patients and correlation with levels measured in urine and tissue	Endocrine-disrupting chemicals (EDCs) are organic compounds that have estrogenic activity and can interfere with the endocrine system. Bisphenol-A (BPA) is one of these compounds which arouses a potential risk to human health. The aim of this study was to investigate the association between BPA levels in breast tissue and urine samples of breast cancer patients. BPA levels in breast tissue of the cancerous and non-cancerous tissues were measured by HPLC-FLD. BPA levels in urine samples of 61 mastectomy patients were compared with those of 61 healthy controls. Urine and breast adjacent tissue samples from 61 breast cancer mastectomy and 61 mammoplasty patients were taken. BPA concentrations were detected using an ELISA assay. Urinary BPA concentrations were significantly higher in cancerous patients (2.22 ± 1.48 ng/ml, P = 0.01) compared to non-cancerous (0.91 ± 0.42 ng/ml). Likewise, tissue BPA concentrations in cancerous patients (3.24 ± 2.66 ng/g tissue, P = 0.01) were significantly higher than non -cancerous (1.88 ± 1.39 ng/g tissue). Urinary BPA concentrations were positively correlated with tissue-adjacent tissue BPA in the case group (P = 0.001, R = 0.998). We showed that BPA was present in urine and breast adjacent tissue samples of the studied populations. With regard to higher BPA mean concentration in cancerous patients than non-cancerous individuals in this study, BPA might increase the risk of breast cancer incidence.	Sci Rep. 2021 Sep 16;11(1):18411.	10.1038/s41598-021-97864-6	34531470	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0468	H. Kaya Ozden and A. S. Karadag	2021	Could endocrine disruptors be a new player for acne pathogenesis? The effect of bisphenol A on the formation and severity of acne vulgaris: A prospective, case-controlled study	BACKGROUND: Acne is one of the most common skin diseases in the adolescent period. Bisphenol A (BPA) is the most frequently observed endocrine-disrupting chemicals that us are exposed to in daily life. BPA can affect the hormonal balance and cause acne formation. OBJECTIVE: The aim of this study was to investigate the relationship between BPA and acne. METHODS: Patients with acne and 50 healthy controls, whose ages varied between 18 and 30 years and applied to our dermatology outpatient clinic, were evaluated. A questionnaire containing dietary and lifestyle habits, for BPA exposure was filled. BPA and BPA glucuronides were analyzed in the LC-MS/MS system in the first morning urine samples of the patients. Statistical significance was set at p < 0.05. RESULTS: The median levels of total BPA were significantly higher in the acne group compared with the control group (7.61 [3.69-20.52] vs. 1.42 [1.32-21.00] µg/g creatinine, respectively; p = 0.001). The acne severity was positively correlated with the BPA values (p = 0.04 vs. r: 0.302). Higher BPA level was noticed in younger acne onset age (r = 0.023 r: - 0.349). When the many questions were evaluated, no difference was found between the study groups regarding BPA exposure (P > 0.05). CONCLUSION: Although BPA exposure was not found to be different in the acne group, it may be beneficial to prevent BPA exposure and acne occurrence, in the adolescence and post-adolescence period, to which industrial products such as junk food and plastic-bottled water are used more frequently.	J Cosmet Dermatol. 2021 Nov;20(11):3573-3579.	10.1111/jocd.14364	34379355	ヒト	皮膚	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0469	I. Katsikantami, M. N. Tzatzarakis, V. Karzi, A. Stavroulaki, P. Xezonaki, E. Yakoumaki, A. K. Alegakis, S. Sifakis, A. K. Rizos and A. M. Tsatsakis	2020	Biomonitoring of bisphenols A and S and phthalate metabolites in hair from pregnant women in Crete	Phthalates, bisphenols A and S (BPA, BPS) are used as plasticizers and many of them are documented or suspected of being endocrine disruptors. Several studies indicate that exposure during pregnancy may affect the fetal development and the pregnancy outcome. The aim of this study was to investigate the exposure of pregnant women in Crete, Greece, to BPA, BPS and phthalates. Hair samples were collected from 74 pregnant women and analyzed for 11 compounds: seven monoesterified phthalate (mEPP, MBEL), mono-carboxyl phthalates (mMP, MBX, BPH, OPH), BPS, DEHA and mono-n-butyl phthalate (mnBP) (MBA). Phthalate metabolites were detected at medians from 19.6 to 161.4 pg/mg, BPA at 69.9 pg/mg and BPS at 5.0 pg/mg. Significant positive correlations between phthalate metabolites were found which indicated their common sources of exposure. The frequent use of plastics for food storage was strongly associated to mEPP (p = .012) and a weaker association was found for mMP (p = .065). The frequent use of cosmetics during pregnancy was associated with levels of phthalate metabolites. In fact, 95 cm specifically, the use of hair spray before pregnancy was significantly correlated with monoesterp phthalate (mBeP) (p = .021) and a trend was found for mBP (p = .066). The use of makeup products during pregnancy was strongly associated with mBP (p = .020) and the use of deodorant during pregnancy was inversely associated with mEHP (p = .051). Dietary associations, namely an inverse mEHP and fresh fruits weight (Spearman correlation coefficient, r = -0.262, p = .022) and exposure to BPS was associated with increased body mass index of the participants (p = .058). Although data in literature on biomonitoring of the compounds in hair are limited, the findings of this study are promising and in agreement with existing data in hair or urine.	Sci Total Environ Vol.712 Pages 135651	10.1016/j.scitotenv.2019.135651	31810691	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0470	S. Karthikeyan, T. Pollock, M. Walker, C. Khoury and A. St-Amand	2024	Analysis of chemical exposures in racial populations in Canada: An investigation based on the Canadian health measures survey	Despite demonstrated disparities in environmental chemical exposures by racial identity, no Canadian study has systematically assessed the feasibility of using a nationally representative dataset to examine differences in exposure between racial groups. This study aimed to address this gap by leveraging the Canadian Health Measures Survey (CHMS) to investigate racial disparities in exposure to chemicals measured in biomonitoring data collected through the Canadian Health Measures Survey (CHMS). Our primary objectives were to assess the ability to: 1) generate geometric means and percentiles of chemical concentrations for racial populations by age or sex, 2) statistically compare concentrations among racial populations, and 3) calculate time trends of concentrations by race. We conducted these analyses for several priority chemicals: lead, cadmium, benzene, bisphenol A (BPA), and di(2-ethylhexyl) phthalate (DEHP). Survey participants self-identified as one of the following: White, Black, East and Southeast Asian, South Asian, Middle Eastern, Latin American, First Nations, Métis, and Inuk. Analyses were conducted for individual and combined cycles of the CHMS. Using data from the latest CHMS cycle in which each chemical was measured, we observed that geometric means and percentiles could be generated for most racial populations, but not for all chemicals and racial groups. Statistically significant differences in exposure between racial groups were commonly reported for all racial populations in the analysis. While we were able to statistically compare concentrations among racial populations, the analysis was constrained by limited statistical degrees of freedom available in a single CHMS cycle. Both of these constraints were alleviated by combining multiple cycles of data. The analysis of time trends was less subject to privacy and statistical limitations; we were able to calculate time trends of chemical concentrations for all racial populations. Our findings provide an important baseline for follow-up investigations of descriptive and etiological analyses of environmental chemical exposures and race in the CHMS.	Int J Hyg Environ Health Vol.260 Pages 114406	10.1016/j.ijhah.2024.114406	38852336	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0471	C. Karrer, M. Andreasen, N. von Goetz, F. Sonnet, A. A. Sakhi, K. Hungerbühler, H. Dirven and T. Husøy	2020	The EuroMix human biomonitoring study: Source-to-dose modeling of cumulative and aggregate exposure for the bisphenols BPA, BPS, and BPF and comparison with measured urinary levels	BACKGROUND: Bisphenol A (BPA) and, with increasing occurrence, its analogs bisphenol S (BPS) and bisphenol F (BPF) are applied in many consumer products, leading to humans being exposed from a vast number of sources and via several routes. Exogenic and anti-androgenic effects are exerted by the chemical BPA, and also by its analogs. Therefore, realistic exposure assessments are needed for assessing risks. OBJECTIVES: Biomonitoring for BPA, BPS, and BPF was conducted in a human study embedded in the EU project EuroMix and the measured urinary concentrations were compared to source-to-dose model predictions. METHODS: Spot urine samples (n = 2,551) from 1,258 adults (20-39 years) from 10 countries in Europe were collected and analyzed using ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UPLC-MS/MS). In line with the information obtained from the first study day, bisphenol exposure from food, PCPs, TP, and dust was modeled primarily individual based with probabilistic models. RESULTS: BPA, BPS, and BPF were frequently detected in urine samples (98%, 95%, and 77%, respectively). Median concentrations were 1.1 ng/mL for BPA, 0.16 ng/mL for BPS, and 0.19 ng/mL for BPF. Urinary levels, in general, individual based medians of modeled BPA exposure were in good agreement with the measurements, but individual specific correlations were rather poor. Medians of modeled BPS and BPF levels in participants with positive measurements (55% and 8%), except for the PBK values of modeled BPA exposure that were higher than measured amounts (~TP was handled. Most likely, diet and TP were the sources contributing the most to BP exposure in this study. Urinary measurements did not reveal a significant correlation between the amounts of consumed food containing TP, the number of PCPs used, or the number of TP handling events and levels of BPA, BPS, or BPF. CONCLUSIONS: The good agreement between the ranges of modeled BPA exposure and measured BPA amounts indicates that available concentrations, especially from food, are sufficient to explain exposure to BPA in the majority of the participants. Considering the poor correlation between modeled and measured BPA exposure on an individual level, individual measurements and modeled exposures did not vary in parallel, e.g. due to intended n-HBP concentrations in food, TP, and other sources, or delayed internal exposure. The underestimation of modeled BPS and BPF exposure suggests that not all relevant sources were included in the respective exposure models. This could be due to a lack of input data, e.g. for food items, or due to an increased replacement of BPA with structural analogs compared to the used concentration and occurrence data.	Environ Int Vol.136 Pages 105397	10.1016/j.envint.2019.105397	31884417	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0472	T. Kavramani, C. Sol, K. Kannan, L. Tiesarska, V. Jaddoe and L. Duijts	2023	Bisphenol and phthalate exposure during pregnancy and the development of childhood lung function and asthma. The Generation R Study	BACKGROUND: Fetal exposure to bisphenols and phthalates may lead to alterations in the respiratory and immune system development in children, and to adverse respiratory health. AIM: To study the associations of maternal urine bisphenol and phthalate concentrations with childhood lung function and asthma. METHODS: We measured bisphenol A, F and S and phthalate metabolites in urine samples collected in mid-pregnancy from 2,547 participants in a population-based birth cohort in the Netherlands. We measured maternal urine bisphenol and phthalate concentrations in the first, second and third trimester of pregnancy, and lung function by spirometry and asthma by questionnaire at age 10 years. Multivariable linear and logistic regression models were applied. RESULTS: Maternal urine bisphenol and phthalate concentrations averaged during pregnancy were not associated with childhood lung function or asthma. Associations of maternal urine bisphenol and phthalate concentrations in specific trimesters with respiratory outcomes showed that one bisphenol A (BPA) or bisphenol F (BPF) and DEHP metabolite was mostly associated with childhood lung function or asthma. Associations of maternal urine bisphenol and phthalate concentrations in the second trimester was associated with a higher FEV1/FVC, but not with asthma, accounting for confounders and multiple testing correction. Although there were associations of higher second trimester BPA, BPF, MEHP, MEOHP, MECPP, MEHHP, and MEP concentrations with higher FEV1/FVC, and higher third trimester BPA, BPF, MEHP, MEOHP, MECPP, MEHHP, and MEP with lower FEV1, these did not remain significant after correction for multiple testing. Results were not modified by maternal history of asthma or atopy. CONCLUSIONS: Maternal urine bisphenol and phthalate concentrations averaged or in specific trimesters during pregnancy were not strongly associated with childhood lung function and asthma at age 10 years. BPA, as a BPA substitute, tended to be associated with impaired lung function and altered risk of asthma, partly non-dependent, but its strength was limited by a relatively low detection rate and should be queried in contemporary cohorts.	Environ Pollut. 2023 Sep 1:332:121853.	10.1016/j.envpol.2023.121853	37247769	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0473	S. Kang, B. H. Shin, J. A. Kwon, C. W. Lee, E. K. Park, E. Y. Park and B. Kim	2020	Urinary bisphenol A and its analogues and haemato-biochemical alterations of pregnant women in Korea	INTRODUCTION: Bisphenol F (BPF) and bisphenol S (BPS) are chemical substitutes for, and may have similar physiological effects to, bisphenol A (BPA). Bisphenols provoke endocrine disorders and are cytotoxic, cardiac hemoglobin, and induce morphological changes in human red blood cells (RBC). It is more sensitive to changes in the RBC number and hemoglobin (Hb) level during pregnancy. Therefore, we investigated the effects of bisphenols on the haemato-biochemical parameters of pregnant women. METHODS: Urine samples were collected from 1,000 pregnant women in the Ewha Birth and Growth Cohort Study, recruitment for which occurred from 2017 to 2018. We measured the levels of BPA, BPF and BPS in urine samples and collected data on socioeconomic, lifestyle, and environmental factors via questionnaires. The associations between the levels of the three BPs and biochemical parameters were analyzed by multiple linear regression (RESULTS). The geometric mean urinary concentrations of specific gravity adjusted BPA, BPF, and BPS were 1.19, 0.19, and 0.29 ng/mL, respectively. There was a significant negative association between the urinary concentrations of BPA and the Hb level (β = -0.11, p = 0.02). After stratification by the median concentrations of the three BPs, the concentrations of BPA had a significantly negative effect on the RBC count, Hb level, and hematocrit in the high-BPA-concentration group (RBC: β = -0.5, p = 0.001; Hb: β = -0.3, p = 0.002; Hct: β = -0.2, p = 0.02). CONCLUSIONS: BPA has a harmful effect on human biochemical changes that occur during pregnancy. Further studies should investigate the relation between unbalanced exposure to bisphenols and effects on human health.	Environ Res Vol.182 Pages 109104	10.1016/j.envres.2019.109104	31927299	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0474	J. Kang, H. Kang and Y. H. Choi	2025	Changes of urinary bisphenol A and alternatives in Korea 2015-2020 and environmental disparities by socioeconomic status	BACKGROUND: Bisphenol A (BPA), mainly used as an ingredient for epoxy resins, is widely utilized in numerous daily necessities. However, due to its endocrine-disrupting property, many countries have regulated BPA usage in consumer products, which might motivate industries to prefer alternative chemicals such as bisphenol S (BPS) and bisphenol F (BPF). This study aimed to evaluate temporal changes in consumption patterns of bisphenols and to investigate socioeconomic disparities in exposure to bisphenols among Korean adults. METHODS: We analyzed urinary bisphenol concentrations in 5,000 participants aged ≥ 19 years from the Korean National Environmental Health Survey (KoNEHS) 2015-2020 (n = 6000). Weighted measures were measured by urinary concentrations of BPA, BPS, and BPF. A ratio of alternatives to bisphenols (BP ratio) (0 = only BPA, 1 = only BPS/BPF). Associations between BP ratio and ESTI indices (each variable and a composite score of household income, residence area, occupation, and education) were examined using survey-weighted multiple linear regression models. RESULTS: During the study period of 2015-2020, BP ratio (0.01 → 0.25) (P < 0.05) demonstrated increases with a steep linear trend (SE = 0.04, β = 0.03). BP ratio (0.08 to 0.27) (P < 0.05) corresponded to a series of BPA regulations since 2018, which had banned BPA-containing products (i.e., food containers, utensils, and baby products) and set the Distinct reference dose. Trends of BP ratio differed by ESTI, but not by age or sex (P for interaction = 0.04). The lowest ESTI group showed the highest BP ratio (0.17 [0.15, 0.19]) and the highest ESTI group showed the lowest BP ratio (0.11 [0.10, 0.12]) (P < 0.05) after adjusting for age and sex. CONCLUSIONS: Bisphenol exposure of the general Korean adults shifted from BPA to its alternatives (coupled with consecutive BPA regulations. Such an exposure shift was more pronounced in adults with higher SES. Further bisphenol regulations should consider environmental disparities of the public.	Environ Res Vol.285 Issue Pt 1 Pages 122307	10.1016/j.envres.2025.122307	40623515	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0475	H. Kang, J. P. Lee and K. Choi	2021	Exposure to phthalates and environmental phenols in association with chronic kidney disease (CKD) among the general US population participating in multi-cycle NHANES (2005-2016)	Exposure to consumer chemicals has been associated with chronic kidney disease (CKD) among humans, but their associations with estimated glomerular filtration rate (eGFR) are inconsistent. Such observations may be attributable to the use of spot urine samples and the cross-sectional study design. We investigated the associations of urinary phthalate and phenol biomarkers with eGFR decline associated with CKD by applying an alternative adjustment method of urine dilution: bound covariate-adjusted creatinine adjustment in traditional creatinine adjustment and the exposure concept in the association model. For this purpose, the adult participants of US National Health and Nutrition Examination Survey (NHANES) 2005-2016 (n = 9008) were used, and the associations of urinary exposure biomarkers of 11 phthalates and 5 phenols with eGFR were investigated by multiple linear regression models. RESULTS: During the study period, the geometric mean (GM) concentrations of urinary biomarkers of adjusted creatinine concentrations resulted in significant inverse associations with eGFR for most measured chemicals, unlike the results with the use of the conventional creatinine adjustment. Metabolic metabolites such as monobutyl phthalate (MBP) and mono-benzyl phthalate (MBzP), were positively associated with eGFR. Even in mixture exposure models, using weighted quantile sum (WQS) regression, MBzP, metabolites of di-(2-ethylhexyl) phthalate (DEHP), and mono-ethyl phthalate (MEP) were revealed as major drivers of the association with eGFR in CKD. Results of sensitivity analyses with the subpopulation with normal eGFR ranges (> = 75(2) were generally similar. Our observation suggests that exposure to benzyl butyl phthalate (BBP), DEHP, and MEP may be responsible for declined eGFR and increased ACR even at the exposure levels occurring among general adults.	Sci Total Environ Vol.791 Pages 148343	10.1016/j.scitotenv.2021.148343	34126474	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0476	H. Kang, S. Kim, H. Lee, Y. Jeong, J. Lee, I. Lee, H. B. Moon, K. Choi and K. T. Kim	2025	Parabens, bisphenols, and other environmental phenols exposure from cosmetics use in Korean adolescent girls: Findings from a 2-day intervention study	Endocrine-disrupting chemicals (EDCs), such as bisphenols, parabens, and benzophenones, are commonly found in personal care products (PCPs) and pose a significant public health concern, particularly in adolescent girls. This study aimed to investigate the association between PCP use and urinary concentrations of environmental phenols in Korean adolescent girls, focusing on the potential role of PCPs as a major source of EDC exposure. METHODS: We recruited 60 girls aged 13-18 years and collected their first-morning urine samples and questionnaire data on PCP use. Participants recorded the use of 16 PCPs, including 6 skin-cell-repair products, 5 skincare products, sunscreens, cosmetics, and nail tip products, in a subsequent two-day intervention restricting participants' use, leading to subsequent of 72 participants. We measured the changes in urinary chemical concentrations were assessed. Baseline findings showed an association between frequent PCP use and higher urinary concentrations of parabens (e.g., methyl, ethyl, and propyl parabens), bisphenol S (BPS), and benzophenone-3(e.g., benzophenone-3). After the two-day intervention, no significant reductions in EDCs concentrations were observed for the entire study participants (n = 72). However, when excluding adolescents with no baseline PCP use (n = 12), substantial reductions were shown in BPA (by 52.7%), and benzophenones (by 13.4% to 29.3%). This study contributes to the limited research on EDC exposure in adolescent populations and underscores the need for targeted public health interventions and policy measures to protect vulnerable populations from the potential health risks associated with EDC exposure.	Environ Res Vol.282 Pages 122039	10.1016/j.envres.2025.122039	40451416	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0477	G. Kalliora, G. A. Wellenius, L. McCandless, A. M. Calafat, A. Spolin, M. E. Romano, M. R. Karagas, A. Chen, K. Yolton, B. P. Lanphear and J. M. Braun	2020	Exposures to chemical mixtures during pregnancy and neonatal outcomes: The HOME study	INTRODUCTION: Exposure to mixtures of environmental chemicals are prevalent among pregnant women and may be associated with altered fetal growth and gestational age. To date, most research regarding environmental chemicals and neonatal outcomes has focused on the effects of individual agents. METHODS: In a prospective cohort of 388 pregnant women from Cincinnati (2003-2006), we used biomarkers to estimate exposure to 22 phenols, phthalates, metals, organophosphate (op)-metal, organochlorine pesticides, polychlorinated biphenyls, polybrominated diphenyl ethers, perfluoroalkyl substances (PFAS), and environmental tobacco smoke (ETS) during pregnancy. We used Bayesian kernel machine regression (BKMR) to estimate associations between the chemical mixture and birthweight, birthweight z-score, birthweight for gestational age z-score (assessing intrauterine growth), head circumference, and gestational age (assessing intrauterine growth). PIP, posterior probability of inclusion (PIP) ≥ 0.5 identified chemicals with potentially important contributions to the mixture effect. RESULTS: Mixtures of 22 chemicals were associated with lower birthweight, birthweight z-score, and birthweight for gestational age z-score. Three chemicals, three phthalate metabolites, several metals, organophosphate (op)-organochlorine pesticides, polychlorinated biphenyls, and several PFAS had a PIP ≥ 0.5 for one or more outcomes. In the op cluster, chlorpyrifos was the most important chemical (PIP = 0.9) and 3,5,6-trichloro-2-pyridinol (TCPY) had a PIP = 0.5. Of the 3 chemicals in the cluster 2 had inverse associations with birthweight and birthweight z-score: 2,5-dichlorophenol (PIP = 0.5) and 2,4,5-trichlorophenol (PIP = 0.5). In the ETS cluster, cotinine had the largest PIP (PIP = 0.9) and had a positive association with birthweight and birthweight z-score. On average, infants born to women in clusters 1 (1,2 cm BW, CI: -1.9, 0.6) and 2 (0.6 cm BW, CI: -1.1, 2.1) had lower birth length than infants in cluster 3. Each 1 ng/mL increase in TCPY, one of the most important chemicals in the op cluster, was associated with a 0.2 cm (CI: -0.4, 0.0) lower birth length. Cotinine was also associated with shorter birth length. Cluster membership, PC scores, and individual chemicals were not associated with other birth outcomes. CONCLUSIONS: We used two methods of characterizing multiple chemical exposures in this cohort identified inverse associations of select organochlorine compounds, phenols, and cotinine with birth length, but not other neonatal outcomes.	Environ Int. 2020 Jan;134:105219.	10.1016/j.envint.2019.105219	31726361	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0478	J. Jurewicz, J. Majewska, A. Berg, K. Owczarek, M. Zajicek, D. Kaleta, A. Wasik and D. Rachoń	2021	Serum bisphenol A analogues in women diagnosed with the polycystic ovary syndrome - is there an association?	Due to the endocrine-disrupting effects of bisphenol A (BPA) several governmental authorities have banned its use and the manufacturers had to find alternative substances with a similar chemical properties. This led to the increase in the use of so-called BPA-analogues, which however also turn out to possess mild estrogenic and an androgenic properties and thus, may cause fertility problems and are hormone-dependent-related disorders. The aim of this study was to evaluate the potential association between the exposure to BPA and its two analogues: BPS and BPF, with the diagnosis of polycystic ovary syndrome (PCOS), which remains the most common female endocrinopathy. Serum concentrations of BPA, BPS and BPF were measured using high performance liquid chromatography method with tandem mass spectrometry (HPLC-MS/MS). Women with PCOS (n = 120) were compared with healthy controls (n = 120). Women with PCOS had significantly higher serum BPA concentrations (median 0.38 ng/mL [25th-75th percentile: 0.26-0.58] vs. 0.28 ng/mL [0.18-0.39], P = 0.0023). Since BPS and BPF concentrations did not differ between the studied groups. There was however a negative correlation between serum BPA and BPS (r = -0.252, P = 0.0001) and between BPA and BPF (r = -0.200, P = 0.001) in women with PCOS. So concentrations, some found between the serum BPA, and other metabolic parameters such as serum lipids, insulin, DHEA-S, androstenedione and FAI. When studying the association between serum BPA analogues and PCOS it turned out that women whose serum BPA concentrations were in the first tertile were more likely to be diagnosed with this endocrinopathy (OR 95% CI: 1.11; 0.58; 2.48). P = 0.8017). This association was also statistically significant when adjusted for age, education, BMI, smoking, income, and alcohol consumption (adjusted OR (95% CI): 2.17 (1.03; 3.71). P = 0.039). These results point to the potential association between the exposure to BPA and the diagnosis of PCOS. The role of BPA is not clear and remains further studies.	Environ Pollut. 2021 Mar 1:272:115962.	10.1016/j.envpol.2020.115962	33223334	ヒト	内分泌かく乱物質（ビスフェノール）	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0479	S. K. Jung, W. Choi, S. Y. Kim, S. Hong, H. L. Jeon, Y. Joo, C. Lee, K. Choi, S. Kim, K. J. Lee and J. Yoo	2022	Profile of Environmental Chemicals in the Korean Population-Results of the Korean National Environmental Health Survey (KoNEHS) Cycle 3, 2015-2017	The Korean National Environmental Health Survey (KoNEHS) program provides useful information on chemical exposure, serves as the basis for environmental health policies, and suggests appropriate measures to protect public health. Initiated on a three-year cycle in 2009, it reports the concentrations of major environmental chemicals among the representative Korean population. KoNEHS Cycle 3 included children and adolescents. Into the analysis, where the blood and urine samples of 6357 participants were measured for major metals, phthalates, phenols, and other organic compounds. Lead, mercury, cadmium, metabolites of DEHP, and DnBP, and 2-phenylphenol, and levels of the Korean adult population tended to decrease compared to previous survey cycles but remained higher than those observed in the US or Canada. Both bisphenol A (BPA) and many trans-nuclear acid concentrations have increased over time. Heavy metal concentrations (blood lead, and cadmium) in children and adolescents were approximately half that of adults, while some organic chemicals, such as BPA and DEHP, were high. BPA showed higher levels than the US or Canada, whereas BPF and BPS showed lower detection rates in the study. However, as these are increasingly used as substitutes for BPA, further research is necessary. As environmental chemicals may affect childhood health and development, additional analysis should ensure exposure sources and routes through continuous observations.	Int J Environ Res Public Health Vol.19 Issue 2	10.3390/ijerph19020626	35055445	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない　通格性評価（疫学）1：該当、0：該当しない　通格性評価（in vitro）1：該当、0：該当しない　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0480	M. K. Jung, H. S. Choi, J. Suh, A. Kwon, H. W. Chae, W. J. Lee, E. G. Yoo and H. S. Kim	2019	The analysis of endocrine disruptors in patients with central precocious puberty	BACKGROUND: A few studies have reported a positive association between phthalate exposure and pubertal timing, but several conflicting reports exist. The main objective of the study was to determine whether phthalate exposure was associated with central precocious puberty (cPP). METHODS: This case-control study enrolled girls with central precocious puberty (CPP) and girl controls. Of pre-pubertal girls and 31 pubertal girls) were enrolled. Nineteen girls were included. For phthalate metabolites (creatinine-adjusted) and bisphenol A (BPA) were measured in the first spot urine samples of these 50 girls in the early CPP group, 31 girls in the progressive CPP group, and 19 girls in the control group. Differences in the urinary concentrations of phthalate metabolites and BPA among the groups were analyzed. RESULTS: Urinary concentrations of total phthalate (DEHP) were 51.2, 79.2, 106.1, 54.2, and 54.2 μg creatinine in the pre-pubertal control group, early CPP group, progressive CPP group, pubertal control group, and 11.1, 38.7, 21.1, and 30.3 μg/g creatinine in the pubertal control group, respectively. The urinary concentration of the four phthalates was significantly lower in the CPP group than in the pre-pubertal control group (P = 0.0001). Conversely, there was no significant difference in the urinary concentration of the five phthalates between the CPP and pubertal control groups (P values: 0.077 for MEHP, 0.752 for MEHHP, 0.188 for MEOHP, and 0.982 for MnBP). In addition, the BPA level was not significantly different between the CPP and pubertal control groups (BPA median values: 0.91 μg/g creatinine, the CPP group; 1.7 μg/g creatinine, the pubertal control group; P value = 0.892). CONCLUSIONS: Our study showed that there was no significant difference in the urinary phthalate levels between the CPP and pubertal control groups. Moreover, phthalate metabolites were significantly lower in the CPP group than in the pre-pubertal control group. Further investigation about endocrine disruptors and pubertal progression is needed.	BMC Pediatr. 2019 Sep 7;19(1):323.	10.1186/s12887-019-1703-4	31493798	ヒト	生殖(思春期発達)	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0481	H. Jin, J. Xia, L. Mao, M. Zhao, X. Bai, J. Wen, T. Shen and F. Wu	2020	Bisphenol analogue concentrations in human breast milk and their associations with postnatal infant growth	Many studies show that bisphenol A (BPA) is widespread in human breast milk. However, the occurrence of other bisphenol analogues (BPAs), including bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF), in breast milk is still not well known. In this study, breast milk samples were collected from 350 mothers in Hangzhou, China, with the aims to determine the occurrence of BPS, BPF, and BPAF in these samples and to investigate their effects on postnatal growth of infants through breast milk consumption. BPA (mean 2.6 ng/mL, range = 1.00–18 ng/mL) was the most abundant BPA in breast milk, followed by BPS (0.19 ng/mL, <LOD–1.1 ng/mL) and BPAF (0.082 ng/mL, <LOD–0.58 ng/mL). BPF was not detected in all breast milk samples. We found that breast milk concentrations of BPA were significantly correlated with infant's weight or height gain rate. Daily intakes (DIs) of BPs via the consumption of breast milk were calculated for infants, and the mean DI values were 105 ng/kg bw, 10 ng/kg bw, and 23 ng/kg bw for BPA, BPS, and BPAF, respectively. Overall, this study firstly demonstrates that the lactation exposure to BPA through breast milk consumption may affect the postnatal growth of infants.	Environ Pollut. 2020 Apr;259:113779.	10.1016/j.envpol.2019.113779	31887597	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0482	Y. Jiang, J. Li, S. Xu, Y. Zhou, H. Zhao, Y. Li, C. Xiong, X. Sun, H. Liu, W. Liu, Y. Peng, C. Hu, Z. Cai and W. Xia	2020	Prenatal exposure to bisphenol A and its alternatives and child neurodevelopment at 2 years	While increasing evidence has shown that prenatal bisphenol A (BPA) exposure is adversely associated with child neurodevelopment, little is known about the neurodevelopmental effects of BPA alternatives, such as bisphenol S (BPS) and bisphenol F (BPF). We aimed to evaluate the relationships of repeated measurements of bisphenol exposure during pregnancy with child neurodevelopment. From 2012-2015, 650 mother-child pairs were recruited from the Wuhan Maternal and Child Health Cohort in China. Urinary concentrations of BPA, BPS, and BPF were measured in maternal samples collected in each trimester. Children were assessed using the Ages & Stages Questionnaires, Third Edition at 2 years. A structural equation model, a psychomotor development index accurate, decrease urinary quartiles of BPS were associated with infant's weight or height gain rate. Daily intakes (DIs) of BPs via the consumption of breast milk were calculated for infants, and the mean DI values were 105 ng/kg bw, 10 ng/kg bw, and 23 ng/kg bw for BPA, BPS, and BPAF, respectively. Overall, this study firstly demonstrates that the lactation exposure to BPA through breast milk consumption may affect the postnatal growth of infants.	J Hazard Mater. 2020 Apr 15:388:121774.	10.1016/j.jhazmat.2019.121774	32001102	ヒト	発達神経	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0483	W. Jiang, Y. Huang, H. Jin, Y. Gan, Q. Zhang, X. Hu, Y. Tian, J. Zhang and C. The Shanghai Birth	2025	A prospective exposome-based gene-environment interaction study on the effects of prenatal environmental exposure on fetal growth in the Shanghai Birth Cohort	BACKGROUND: Both environmental exposure and type 2 diabetes (T2D) genetic susceptibility affect fetal growth. However, most previous studies used single exposure rather than an exposome strategy to explore the joint effects of environmental exposure and genetic susceptibility on fetal growth. METHODS: Based on the Shanghai Birth Cohort, we established the association between a broad range of prenatal environmental factors and fetal growth and further evaluate the effect modification of maternal and fetal T2D genetic susceptibility on the identified exposures. METHODS: From 1,150 mother-newborn pairs from the Shanghai Birth Cohort, we estimated the associations between 19 prenatal exposure measures (including outdoor environment, residential environment, chemical exposures, lifestyle factors, and psychosocial status) and fetal growth, measured by birth weight for gestational age z-score (BWZ). Single-exposure models, mixture models, and interaction models were used to assess the primary pooled learning and weaker (none) were applied jointly to screen for BWZ-associated exposures. Multivariable linear regression models were used to assess the interactions of BWZ-associated exposures with maternal and fetal T2D genetic risk scores (GRSs). RESULTS: Higher prenatal exposure to ambient temperature (AT) (β = 0.08, 95 % CI: 0.03, 0.13), fine particulate matter (PM2.5) (β = 0.07, 95 % CI: 0.02, 0.12), and 2,4-dinitrophenol (DNP) (β = 0.06, 95 % CI: 0.01, 0.11) was associated with increased BWZ. In contrast, we found significant decreases in urinary concentrations of environmental phenol replacements, including bisphenol S (β: 3.9, 95 % CI: 7.9, 0 and bisphenol F (β: 6, 95 % CI: 1.8, 10.2). DNCH metabolites, 1cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester (MHNCH) (β: 20, 95 % CI: 7.5, 32.5) and 1,2-cyclohexane dicarboxylic acid monocarboxy isooctyl ester (MCNCH) (β: 15.1, 95 % CI: 4.2, 26.1), were also positively associated with BWZ. Moreover, we found significant interactions between maternal T2D GRS and exposure to AT, PM2.5, and DNP. Additionally, we found that the effects of maternal T2D GRS on BWZ were modified by exposure to several environmental phthalate metabolites. Maternal phthalate, mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) (β = 0.4, 95 % CI: 0.8, 1.6), and mono-2-ethyl-5-oxohexyl terephthalate (MEOHTP) (β = 0.4, 95 % CI: 0.8, 1.6) metabolites were associated with increased BWZ. Moreover, we found that the effects of fetal T2D GRS on BWZ were modified by exposure to several environmental phthalate metabolites, including mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) (β = 0.4, 95 % CI: 0.8, 1.6), mono-2-ethyl-5-oxohexyl terephthalate (MEOHTP) (β = 0.4, 95 % CI: 0.8, 1.6), and mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) (β = 0.4, 95 % CI: 0.8, 1.6). CONCLUSIONS: Our study identified several prenatal environmental exposures within the outdoor environment, phenols, and metallicells that were associated with fetal growth. Mother-newborn pairs with high T2D genetic susceptibility were particularly vulnerable to the environmental insults. https://doi.org/10.1289/EHP10802.	Environ Health Perspect. 2025 May 20.	10.1289/ehp15902	40392608	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0484	V. S. Jiang, A. M. Calafat, P. L. Williams, J. E. Chavarro, J. B. Ford, I. Souter, R. Hauser and L. Minguez-Alarcon	2023	Temporal trends in urinary concentrations of phenols, phthalate metabolites and phthalate replacements between 2000 and 2017 in Boston, MA	Endocrine disrupting chemicals (EDCs) can adversely affect human health and are ubiquitously found in everyday products. We examined temporal trends in urinary concentrations of EDCs and their replacements. Urinary concentrations of 11 environmental phenols, 15 phthalate metabolites, phthalate replacements such as two diisononyl cyclohexane-1,2-dicarboxylate (DINCH) metabolites, and tricitrates were quantified using isotope-dilution tandem mass spectrometry. This ecological study included 998 male and 829 female patients who were predominantly White Caucasian (82 %) with an average age of 36 years and a BMI of 25.0 kg/m2 seeking fertility treatment at a Boston, MA clinic between 2000 and 2017. Geometric means (GM) and 95 % confidence intervals (95 % CI) were calculated for each year. Temporal trends were investigated using multivariable linear regression models. We observed significant increases per year in urinary concentrations of traditional phenols, parabens, and triclosan, such as bisphenol A (β = 0.04, 95 % CI: 0.03, 0.06), benzophenone-3 (β = 0.05, 95 % CI: 0.04, 0.06), methylparaben (β = 0.04, 95 % CI: 0.03, 0.05), dichlorophenols (β = 0.03, 95 % CI: 0.02, 0.04), 2,5-dichlorophenol (β = 0.04, 95 % CI: 0.03, 0.05), and triclosan (β = 0.04, 95 % CI: 0.03, 0.05). Significant increases were also observed for several phthalate metabolites, including monoethyl phthalate (MEP) (β = 0.04, 95 % CI: 0.03, 0.05), monobenzyl phthalate (MBzP) (β = 0.03, 95 % CI: 0.02, 0.04), and mono-2-ethylhexyl phthalate (MEHP) (β = 0.02, 95 % CI: 0.01, 0.03). Significant increases were observed for several phthalate replacements, including bisphenol S (β: 3.9, 95 % CI: 7.9, 0 and bisphenol F (β: 6, 95 % CI: 1.8, 10.2). DINCH metabolites, 1cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester (MHNCH) (β: 20, 95 % CI: 7.5, 32.5) and 1,2-cyclohexane dicarboxylic acid monocarboxy isooctyl ester (MCNCH) (β: 15.1, 95 % CI: 4.2, 26.1), were also positively associated with BWZ. Moreover, we found significant interactions between maternal T2D GRS and exposure to AT, PM2.5, and DNP. Additionally, we found that the effects of maternal T2D GRS on BWZ were modified by exposure to several environmental phthalate metabolites. Maternal phthalate, mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) (β = 0.4, 95 % CI: 0.8, 1.6), and mono-2-ethyl-5-oxohexyl terephthalate (MEOHTP) (β = 0.4, 95 % CI: 0.8, 1.6), and mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) (β = 0.4, 95 % CI: 0.8, 1.6) metabolites were associated with increased BWZ. Moreover, we found that the effects of fetal T2D GRS on BWZ were modified by exposure to several environmental phthalate metabolites, including mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) (β = 0.4, 95 % CI: 0.8, 1.6), mono-2-ethyl-5-oxohexyl terephthalate (MEOHTP) (β = 0.4, 95 % CI: 0.8, 1.6), and mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) (β = 0.4, 95 % CI: 0.8, 1.6). CONCLUSIONS: Our study identified several prenatal environmental exposures within the outdoor environment, phenols, and metallicells that were associated with fetal growth. Mother-newborn pairs with high T2D genetic susceptibility were particularly vulnerable to the environmental insults. https://doi.org/10.1289/EHP10802.	Sci Total Environ Vol.898 Pages 165353	10.1016/j.scitotenv.2023.165353	37437643	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0485	S. Jiang, G. Yang, S. Zhou, X. Zhang, C. Peng and Q. Lu	2021	Bisphenol A, S, and F exposure, ESR1/2, CAT, and eNOS genetic polymorphisms, and the risk of hypertension	While bisphenol A (BPA) exposure was inconsistently associated with hypertension risk, little is known about whether its alternatives bisphenol S and F (BPS and BPF) have similar hypertensive effects. Furthermore, epidemiologic studies on the genetic susceptibility to the hypertensive effects of bisphenols are scarce. We conducted a case-control study in 539 pairs of hypertension cases and matched controls. Urinary bisphenols, estrogen receptor 1/2 (ESR1/2) polymorphisms, catalase (CAT) rs769214 and rs7943316, and endothelial nitric oxide synthase (eNOS) rs2070744 and rs1799983 were measured. Logistic regression models were used to assess the associations of bisphenols and their interactions with genetic polymorphisms with hypertension risk. Cumulative effects of multiple exposures associated with hypertension risk. Centers of rs2070744 C allele in ESR2 were associated with increased hypertension risk. Significant associations of BPA exposure with increased hypertension risk were suggested in individuals with the major allele of rs2798050 in ESR2, rs769214 in CAT, and rs1799983 in eNOS. Besides, rs7943316 in CAT might modify the association of BPA exposure with hypertension risk. Individuals with specific genotypes in ESR1/2, CAT, and eNOS might be more susceptible to the hypertensive effects of BPA.	Ecotoxicol Environ Saf. 2021 Nov:224:112684.	10.1016/j.ecoenv.2021.112684	34438265	ヒト	心血管	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0486	S. Jiang, Y. Wang, Z. Wang, Y. Xu, X. Li, M. Sun and B. Li	2024	Bisphenol A and its alternatives bisphenol S and F exposure with serum uric acid levels, hyperuricemia, and gout prevalence among US adults: a nationally representative cross-sectional study	BACKGROUND: Recent studies suggested inconclusive associations between bisphenols exposure and hyperuricemia risk. Our objective was to assess the potential association of bisphenol A (BPA) and its substitutes bisphenol S (BPS) and F (BPF) exposure with serum uric acid levels, hyperuricemia, and gout prevalence among US adults. METHODS: Data from the National Health and Nutrition Examination Survey (NHANES) 2013–2016 cycles were used. Multivariate linear regression models were used to explore the associations of urinary bisphenols concentrations with SUA levels, hyperuricemia, and gout prevalence. In total population and different age groups. The nonlinear dose–response relationship between BPA/BPS/BPF and SUA levels was examined using restricted cubic spline (RCS) model was used to explore the dose–response relationship. RESULTS: In total population, doubling of urinary BPS and 2.58% concentrations showed associations with an increment of 2.66 μmol/L (95% CI: 0.562, 4.76) and 0.24 μmol/L (95% CI: 0.08, 0.39) in SUA levels, respectively. The RCS model indicated a significantly "J"-shaped dose–response relationship between BPS exposure and SUA levels. Compared to the reference group of urinary BPS, males in the highest quartile (Quartiles: 1.536, μmol/L (95% CI: 0.76, 29.37) rise in SUA levels. For females, doubling of urinary BPS concentrations was associated with a 1.38 μmol/L (95% CI: 0.03, 2.73) increase in SUA levels. Doubling of urinary BPS concentrations was associated with a 1.08 (95% CI: 1.01, 1.16) increased risk of hyperuricemia. Compared with the reference group of BPS, individuals in the second and third tertile had an adjusted OR of 1.28 and 1.43 for hyperuricemia, had a 1.01 and 1.09 rate for hyperuricemia, had a 1.01 and 1.09 rate for hyperuricemia, and had a 1.01 and 1.09 rate for hyperuricemia of BPF, respectively, with a monotonic curve. No significant associations of BPF exposure with hyperuricemia risk or blood pressure levels were found. BPA and BPS exposure were suggested to be associated with increased hyperuricemia risk and blood pressure levels, with different dose–response relationships. Our findings have important implications for public health but require confirmation in prospective studies.	BMC Public Health Vol.24 Issue 1 Pages 370	10.1186/s12889-024-17883-6	38317153	ヒト	横断研究	1	1	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0487	S. Jiang, H. Liu, S. Zhou, X. Zhang, C. Peng, H. Zhou, Y. Tang and Q. Lu	2020	Association of bisphenol A and its alternatives bisphenol S and F exposure with hypertension and blood pressure: A cross-sectional study in China	Epidemiological studies have investigated the associations of bisphenol A (BPA) exposure with hypertension risk or blood pressure levels, but findings are inconsistent. Furthermore, the association between its alternatives bisphenol S and F (BPS and BPF) and hypertension risk are not yet known. We conducted a cross-sectional study in 1,017 eligible participants without hypertension-related diseases, with complete data about blood pressure levels, hypertension diagnosis, and urinary bisphenols concentrations. Multivariable logistic and linear models were respectively applied to examine the cross-sectional associations of urinary bisphenols concentrations with hypertension risk and blood pressure levels. The dose–response relationship was explored by the restricted cubic spline model. Compared with the reference group of BPA, individuals in the middle and high exposure groups had 1.61 and 1.89 times the risk of hypertension, respectively. Each 1-unit increase in ln-transformed BPA was associated with 1.18 (95% CI: 1.03, 1.36) increased risk of hypertension. Compared with the reference group of BPS, individuals in the second and third tertile had an adjusted OR of 1.49 and 1.83 for hypertension, had a 1.01 and 1.09 rate for hypertension, had a 1.01 and 1.09 rate for hypertension, and had a 1.01 and 1.09 rate for hypertension of BPF, respectively, with a monotonic curve. No significant associations of BPF exposure with hypertension risk or blood pressure levels were found. BPA and BPS exposure were suggested to be associated with increased hypertension risk and blood pressure levels, with different dose–response relationships. Our findings have important implications for public health but require confirmation in prospective studies.	Environ Pollut Vol.257 Pages 113639	10.1016/j.envpol.2019.113639	31796315	ヒト	横断研究	1	1	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0488	J. Jiang, B. Chen, B. Tang, J. Li, C. Zhang, D. Tan, T. Zhang and Q. Wei	2024	Urinary phenols and parabens exposure in relation to urinary incontinence in the US population	BACKGROUND: Our study aimed to investigate the impact of urinary concentrations of personal care products (PCPs)-related phenols (PPs) and parabens (PBs), including Triclosan (TCS), Bisphenol A (BPA), Benzophenone-3 (BP-3), Butylparaben (BPB), Ethylparaben (EPB), Methylparaben (MPB), and Propylparaben (PPB), on urinary incontinence (UI) occurrence. METHOD: We conducted a cross-sectional analysis, using data from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2007 to 2016. Regression analysis was employed to investigate the relationship between exposure to PCPs-related substances, various levels of exposure, and UI within both the general population and the female demographic. Additionally, the Bayesian Kernel Machine Regression (BKMR) model was used to assess the effects of mixtures on UI. RESULTS: Our analysis comprised 7,890 participants who self-reported their diagnosis. Among them, 12,80% experienced stress urinary incontinence (SUI), 11.80% reported urge urinary incontinence (UUI), and 10.23% had mixed urinary incontinence (MUI). Following the adjustment for confounding factors, the highest quartile of TCS exposure was associated with a 1.28-fold increase in the risk of SUI (OR:1.28, 95% CI: 1.01–1.61, p = 0.042), an increased risk of UUI (OR:1.23, 95% CI: 1.01–1.49, p = 0.038), and MUI (OR:1.26, 95% CI: 1.01–1.56, p = 0.039). TCS exposure displayed a negative correlation with the risk of MUI (OR:0.67, 95% CI: 0.49–0.91, p = 0.016). No significant links were observed between parabens and urinary incontinence. Notably, among the female population, our investigation revealed that BPA exposure heightened the risk of MUI (OR:1.30, 95% CI: 1.00–1.68, p = 0.045). Participants in the highest tertile of BPA exposure demonstrated elevated likelihoods of SUI and MUI compared to those in the lowest tertile. In the BKMR analysis, negative trends were observed between the mixture and the risks of UUI and MUI when the mixture ranged from the 25th to the 50th and 75th to the 95th percentile (p < 0.05), respectively. Additionally, a positive trend was identified between the mixture and MUI when it was in the 50th to 75th percentile. CONCLUSION: In conclusion, our findings suggest that exposure to BPA, TCS, and BP-3 may contribute to the development of urinary incontinence.	BMC Public Health Vol.24 Issue 1 Pages 515	10.1186/s12889-024-17872-9	38373965	ヒト	横断研究	1	1	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0489	C. Jiang, J. Guan, X. Tang, Y. Zhang, X. Li, Y. Li, Z. Chen, J. Zhang and J. D. Li	2024	Prenatal low-dose Bisphenol A exposure impacts cortical development via cAMP-PKA-CREB pathway in offspring	Bisphenol A (BPA) is a widely used plastic/ion known to cause various disorders. Despite a global reduction in the use of BPA-containing products, prenatal exposure to low-dose BPA, even those below established safety limits, has been linked to neurological and behavioral deficits in childhood. The precise mechanisms underlying these effects remain unclear. In the present study, we observed a significant increase in the number of neurons in the cortex of mice exposed to BPA during embryonic development. Transcriptomic analysis via RNA sequencing revealed an aberrant activation of the cAMP/PKA/CREB pathway in offspring exposed to BPA. The use of KT5, a selective PKA inhibitor, effectively reversed the deficits in the proliferation and migration of cortical neurons. Furthermore, offspring from dams exposed to low-dose BPA exhibited motor-like behaviors, including hyperactivity, anti-depressant-like responses, and reduced anxiety. While BPA-mediated hyperactivity, it didn't affect the other behavioral changes. These results suggest that the overactivation of PKA plays a causative role in BPA-induced changes in neuronal development. Our data also indicate that neuro-like behaviors induced by prenatal low-dose BPA exposure may be influenced by both altered neuronal development and abnormal PKA signaling in adulthood.	Front Integr Neurosci. 2024 Aug 7:18:1419607.	10.3389/fnint.2024.1419607	39170668	動物	神経	1	1 (飲水)	1	1 (CSTB), (SynapsinⅠ)	0	1 (5.0)	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0490	L. L. Jia, Y. L. Luan, H. M. Sher and Y. Guo	2022	Long-term stability of several endocrine disruptors in the first morning urine samples and their associations with lifestyle characteristics	Parabens, triclosan (TCS), bisphenols, benzophenones, and phthalates are typical endocrine disruptors (EDCs) with short half-lives in the human body. The concentration levels of these EDs in a spot urine sample are frequently used in exposure assessment studies, and the reproducibility of urinary levels of these nonpersistent EDs should be considered. In the present study, we consecutively collected 50 day first morning void (FMV) urine samples, as well as daily questionnaires, in six recruited participants and measured the urinary concentrations of six parabens, TCS, nine bisphenols, five benzophenones, and ten phthalate metabolites by using high-performance liquid chromatography-triple quadrupole mass spectrometry. The intraclass correlation coefficients (ICCs) and Spearman's rank correlation coefficients (rs) were calculated to assess the reproducibility and stability of the urinary levels. The ICCs ranged from 0.06 (mBP, MEP, BPA, BPS, BPAF, BPF, 4HB, 4HB-S, BP-1, BP-2, BP-3, BP-8, MEHP, MEOHP, MEHHP, MECPP, MCPP, MBP, MiBP, MBzP, MEHHP, MEO

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0493	M. Jelska, K. Franczuk, S. Machytnová, I. Kalina, J. Kohoutek, L. Makličová, I. Cíha, B. Kempisty, M. Kaňka, J. Žáková, P. Ventruba and J. Navrátilová	2022	The Bisphenols Found in the Ejaculate of Men Does Not Pass through the Testes	Exposure to bisphenols is related to negative effects on male reproduction. The bisphenols exposure is associated with several males of action including negative impact on the blood-testis barrier (BTB) function or spermatogenesis. Bisphenol A (BPA) is a well-known endocrine disruptor, which is commonly used in the production of plastics. Its analogs, bisphenol S (BPS) and bisphenol F (BPF), also disrupt the blood-testis barrier in the crucial. Therefore, in this work, we compared the concentrations of BPA, bisphenol S (BPS) and bisphenol F (BPF) in the urine and seminal plasma of these men using liquid chromatography-tandem mass spectrometry (LC-MS/MS). We found that the median of urinary and seminal plasma content of bisphenols did not differ in normozoospermic men or men after vasectomy. From the obtained data, it can be concluded that the pathways of transport of bisphenols into seminal plasma are not primarily through the testicular tissue, but this pathway is applied similarly to other routes of neurotoxicity by a corresponding equivalent value ratio. To a much greater extent than through testicular tissue, bisphenols enter the seminal plasma mainly as part of the secretions of the accessory glands.	Toxics Vol.10 Issue 6	10.3390/toxics10060311	35736919	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0494	Y. Jeong, S. Mok, S. Kim, I. Lee, G. Lee, Y. Kho, K. Choi, K. T. Kim and H. B. Moon	2024	Comparison of urinary exposure profiles to phthalates and bisphenol analogues in kindergartners in Korea: Impact of environmental choices on children's health	Phthalates and bisphenols (BPs) are well-known endocrine-disrupting chemicals (EDCs) that are widely used in diverse consumer and personal care products. Despite their vulnerability, children are frequently exposed to phthalates and BPs in their surrounding environments. Although pre-school children spend most of their time in kindergarten, no comprehensive assessment of children' exposure to EDCs has been conducted according to kindergarten types. Therefore, in this study, we investigated the urinary concentrations of phthalate metabolites and BPs in kindergartners attending eco-friendly and conventional kindergartens. Potential contaminant profiles were investigated according to kindergarten type and the associations between urinary concentrations and dietary habits were assessed. Di-(2-ethylhexyl) phthalate (DEHP) metabolites, such as mono-(2-ethyl-5-carboxypentyl) phthalate (median: 47.1 ng/mL) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (8.83 ng/mL) had the highest levels, indicating that they were the primary contaminants to which the children were exposed. Urinary concentrations of phthalate metabolites and bisphenols (BPS) were higher in children from conventional kindergartens than eco-friendly kindergartens. Consequently, bisphenol S (BPS) concentrations were significantly higher in children from the eco-friendly kindergarten than in those from conventional kindergartens, implying that eco-friendly plastics might contain BPS as a replacement for BPA. The estimated daily intakes of DEHP metabolites were also significantly higher in children from conventional kindergartens. Our findings suggest that children's exposure to phthalates and BPs is associated with their dietary habits and lifestyle-related metabolites, indicating potential adverse health outcomes from phthalate exposure in children. The study highlights the need for targeted interventions to reduce EDC exposure in children, especially in settings where alternative chemicals may still pose health risks.	Ecotoxicol Environ Saf Vol.288 Pages 117391	10.1016/j.ecoenv.2024.117391	39603221	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0495	P. Jedynak, L. Tost, A. M. Calafat, E. Bouvier-Fito, F. Bustelo, A. Forhan, B. Heude, M. Jakobi, S. Routtinoja, I. Schwerin, R. Slama, D. Vaiman, C. Philippat and J. Lepeule	2021	Pregnancy exposure to synthetic phenols and placental DNA methylation - An epigenome-wide association study in male infants from the EDEN cohort	In utero exposure to environmental chemicals, such as synthetic phenols, may alter DNA methylation in different tissues, including placenta - a critical organ for fetal development. We studied associations between prenatal urinary biomarker concentrations of synthetic phenols and placental DNA methylation. Our study involved 282 mother-son pairs from the French EDEN cohort. Nine phenols were measured in spot urine samples collected during pregnancy. DNA methylation was measured in placental samples using Illumina's Infinium HumanMethylation450 BeadChip. We performed robust linear regressions to test for associations between each phenol and each placental CpG site, adjusted for potential confounders. We also performed a robust regression on each sex-stratified dataset and ran an adjusted interaction term analysis to study SEHSD, and identified differentially methylated regions (DMRs). We performed mediation analysis to test whether placental tissue heterogeneity mediated the associations between urinary phenol concentrations and DNA methylation. We identified 68 significant DMRs (<5 CpGs) associated with triclosan (37 DMRs), 2,5-dichlorophenol (6), benzophenone-3 (5), methyl- (3) and propylparaben (1), 4- and 2-MePh (one association) and several with phenol concentrations. Out of the 68 identified DMRs, 17 (for 14 genes) were hypomethylated. Among these genes (AFF1, FTSJD2, SH3BP5, MAN1B1, PHF20, SOX2, ATP6V1C1) were represented a significant enrichment. Other identified DMRs encompassed genes encoding proteins responsible for cell signaling, transmembrane transport, cell adhesion, inflammatory, apoptotic and immunological processes. Sex-stratified analyses revealed sex-specific associations. Some associations were also mediated by placental tissue heterogeneity. Modelling in vitro suggested that placental cell heterogeneity may partly explain these associations. This is the first case-study describing the genome-wide methylome of placental DNA methylation associated with pregnancy exposure to synthetic phenols in their precursors. Our results suggest that cell heterogeneity might mediate the effects of triclosan exposure on placental DNA methylation. Additionally, the enrichment of important genes within the DMRs suggests mechanisms by which certain exposures, mainly in triclosan, could affect fetal development.	Environ Pollut Vol.290 Pages 118024	10.1016/j.envpol.2021.118024	34523531	ヒト	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0496	P. Jedynak, L. Maitre, M. Guxens, K. B. Gützkow, J. Julvez, M. López-Vicente, L. Dalmau Cases, L. Chatzi, R. Gražuleviciene, M. Kampouri, R. McEachan, M. Mon-Williams, I. Tamayo, C. Thomsen, L. Urquiza, M. Vafeiadi, J. Wright, K. Basagaña, M. Vrijheid and C. Philippat	2021	Prenatal exposure to a wide range of environmental chemicals and child behaviour between 3 and 7 years of age - An exposome-based approach in 5 European cohorts	BACKGROUND: Studies looking at associations between environmental chemicals and child behaviour usually consider only one exposure or family of exposures. OBJECTIVE: This study explores associations between prenatal exposure to a wide range of environmental chemicals and child behaviour at 3 and 7 years of age. METHODS: We included 1,277 mother-child pairs from five European birth cohorts. We measured 69 exposure biomarkers from eight chemical families in maternal blood or urine collected during pregnancy. We used the Strengths and Difficulties Questionnaire (SDQ) to evaluate child behaviour between three and seven years of age. We assessed associations of SDQ scores with exposures using an adjusted least absolute shrinkage and selection operator (LASSO) considering all exposures simultaneously and an adjusted exposure-wide association study (EWAS) considering each exposure independently. RESULTS: LASSO selected only copper (Cu) as associated with externalizing behaviour. In the EWAS, bisphenol S (BPS), cotinine (COT), and Cu were associated with SDQ externalizing behaviour (BPS: 1.66, 95%CI: 1.18;2.13) and more in boys (phthalate SMHP: 1.99, 1.06; 95%CI: 1.28;2.72) were associated with greater risk of externalizing behaviour problems. Cu (95% 0.98; 95%CI: 0.52;1.44). Prenatal exposure to BPS, COT, and Cu was also associated with greater risk of hyperactivity/inattention problems at 7 years (BPS: 0.98; 95%CI: 0.52;1.44). These associations were mainly seen among women with insufficient/low/high iodine during pregnancy. Internalizing scores in association with exposure to diethyl thiophosphate (DETP; 1.99; 1.12; 95%CI: 1.04;2.20) but the effect size was driven by the smallest cohort. Internalizing scores improved with increased concentration of perfluorooctane sulfonate (PFOS; 95% 0.92; 95%CI: 0.85;1.00); however the association was driven by the two smallest cohorts with the lowest PFOS concentrations. DISCUSSION: This study added evidence on deleterious effects of prenatal exposure to BPS and DETP on child behaviour. Other associations should be interpreted cautiously since they were not consistent with previous studies or they have not been studied extensively.	Sci Total Environ. 2021 Apr 1:763:144115.	10.1016/j.scitotenv.2020.144115	33422710	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0497	Y. Jang, Y. J. Choi, Y. H. Lim, K. S. Lee, B. N. Kim, C. H. Shin, Y. A. Lee, J. I. Kim and Y. C. Hong	2021	Associations Between Thyroid Hormone Levels and Urinary Concentrations of Bisphenol A, F, and S in 6-Year-old Children in Korea	OBJECTIVES: Bisphenol A (BPA) is used in the electrical, mechanical, medical, and food industries. Previous studies have suggested that BPA is an endocrine disruptor. Regulation of BPA has led to increased use of bisphenol F (BPF) and bisphenol S (BPS). However, few studies have investigated the associations of BPF and BPS with thyroid dysfunction in children. Our study investigated the associations of prenatal BPA and early childhood BPA, BPF, and BPS concentrations with thyroid function in 6-year-old children. METHODS: We measured urinary BPA, BPF, and BPS concentrations in 1,562 mother-child pairs in Korea. Of the cohort, We measured urinary BPA, BPF, and BPS concentrations and thyroid hormone levels (thyroid stimulating hormone, total T3, and free T4) in 761 6-year-old children. We examined the associations between urinary bisphenol concentrations, and percentage change of thyroid hormone concentrations using multivariable linear regression. We also compared thyroid hormone levels by dividing the cohort according to BPA, BPF, and BPS concentrations. RESULTS: The associations between prenatal BPA and total T3 levels were statistically significant in all models, except for girls. Urinary as a creatinine. The associations between urinary BPA and BPF concentrations and levels of all thyroid hormones were not statistically significant. However, we observed that boys' free T3 levels (-1.981; 95% confidence interval; -3.82 to -0.13) were associated with higher urinary BPF concentrations. In girls only, CONCLUSIONS: Our findings identified significant associations between prenatal BPA exposure and total T3 levels in all children and between BPF exposure and free T3 levels in girls only.	J Prev Med Public Health. 2021 Jan;54(1):37-45.	10.3961/jpmph.20.310	33618498	ヒト	-	-	-	-	-	-	甲状腺	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0498	M. Jamka, S. Kunik, A. Makarewicz-Bukiewska, A. Milkowska-Chobrzda, M. Wasilewicz-Gwiździe and J. Walkowiak	2024	No Differences in Urine Bisphenol A Concentrations between Subjects Categorized with Normal Cognitive Function and Mild Cognitive Impairment Based on Montreal Cognitive Assessment Scores	A link between bisphenol A (BPA) exposure and cognitive disorders has been suggested. However, the differences in BPA concentrations between subjects with and without cognitive impairment have not been analyzed. Therefore, this observational study aimed to compare urine BPA levels in subjects with normal cognitive function (NCF) and mild cognitive impairs (MCI). A total of 84 MCI subjects and 84 well-matched NCF individuals were included in this study. Cognitive functions were assessed using the Montreal Cognitive Assessment (MOCA) scale. Urine BPA concentrations were evaluated by gas chromatography-mass spectrometry and adjusted for creatinine levels. Anthropometric parameters, body composition, sociodemographic factors, and physical activity were also assessed. Creatinine-adjusted urinary BPA levels did not differ between the NCF and MCI groups (1.8 (1.2–2.7) vs. 2.2 (1.4–3.6) µg/g creatinine, p = 0.328). However, there were significant differences in MOCA results between groups since the study population was divided into subjects with normal cognitive function and MCI. Urinary BPA concentrations were not correlated with MOCA scores. Additionally, education levels were independently associated with MCI. In conclusion, urine BPA levels are not significantly different between subjects with MCI and NCF, but these findings need to be confirmed in further studies.	Metabolites. 2024 May 8;14(5):271.	10.3390/metabo14050271	38786748	ヒト	-	-	-	-	-	-	横断研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0499	P. Jamsekornkul, N. Numcharikrat, S. Anoopkanthonghkul, K. Soongswang and V. Supornsilchai	2025	Increased maternal urinary bisphenol F levels associated with reduced anogenital distance in male newborns	BACKGROUND: Bisphenol exposure during pregnancy has been linked to a range of adverse reproductive outcomes. However, the full extent of the effects of bisphenol analogs, particularly bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF), on fetal development, especially anogenital distance (AGD), a sensitive marker of reproductive development, remains unclear. We conducted this study to research to investigate associations among maternal and neonatal urinary bisphenol analogs, BPA, BPS, BPF, and AGD. METHODS: This prospective cohort study enrolled 80 mother-newborn pairs in Bangkok, Thailand, from April 2023 to January 2024. Maternal urine samples were collected during the third trimester, and newborn urine samples were collected within 24 h after birth. Urinary bisphenol concentrations were measured using liquid chromatography-tandem mass spectrometry. Correlations were analyzed by Pearson's correlation test and linear regression analysis. RESULTS: High maternal urinary BPF concentrations were negatively associated with anoscrotal distance, anofrontal distance, and penile length in male newborns (t = -0.963, -0.860 and -0.965, respectively; p < 0.05). No significant associations were found for BPA or BPS. Frequent maternal consumption of carbonated drinks was associated with higher neonatal BPS levels, while maternal obesity was positively correlated with maternal BPA concentrations. No significant correlation was observed between maternal and neonatal bisphenol concentrations, nor between neonatal bisphenol levels and AGD. CONCLUSIONS: This study is the first to report a negative association between maternal BPF exposure and AGD in male newborns. These findings highlight the potential endocrine-disrupting effects of BPF on fetal development and emphasize the need for further research.	Pediatr Int. 2025 Jan-Dec;67(1):e70054.	10.1111/ped.70054	40277154	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0500	A. Jamal, N. Rastkari, R. Dehghaniafshar, R. N. Nodeh, S. Nasseri, H. Kashani, M. Shamsipur and M. Yunesian	2020	Prenatal urinary concentrations of environmental phenols and birth outcomes in the mother-infant pairs of Tehran Environment and Neurodevelopmental Disorders (TEND) cohort study	Daily exposure to environmental phenols can lead to potential undesirable effects on the health of pregnant women and fetuses. The present study is aimed to evaluate the relationship between maternal urinary concentrations of phenols in pregnancy and anthropometric birth outcomes. The studied population comprised of 189 pregnant women participating in the Tehran Environment and Neurodevelopmental Disorders (TEND) prospective cohort study, which had been ongoing since March 2016 in some hospitals and health-care delivery centers in Tehran, Iran. Concentrations of bisphenol A, triclosan, 4-nonylphenol, and parabens were determined in spot urine samples of pregnant mothers in the first trimester. Weight, height, and head circumference at birth were also recorded from the mothers' medical records. Multivariable linear regression was used to examine the relationships between log-concentrations of phenols and birth outcomes. Whereas analyzed all samples regardless of newborns' gender, none of the urinary concentrations of phenols were associated with birth weight, length, and head circumference. However, after stratification by gender, urinary concentrations of BPA, triclosan, and propylparaben were associated with birth weight. BPA, triclosan and propylparaben was respectively related to a decrease of 141 (n = 93); (-8.5, -1.1) in boys' height and 0.4 cm (95%CI: -0.8, -1.1) in boys' length in the adjusted models for covariates. Also, the changes in head circumference, per log-unit increase of triclosan, methylparaben, and butylparaben led to a reduction of 1.6 cm (95% CI: -3.17, 0.03), increase of 0.8 cm (95% CI: -0.01, 1.6) and 1.7 cm (95% CI: 0.08, 1.3) in head circumference at birth respectively. Our results suggested that prenatal triclosan and parabens exposure might be associated with head circumference at birth. Furthermore, our observations unusually strengthen pattern between maternal triclosan and parabens exposure during pregnancy and fetal growth. However, these findings must be interpreted while taking into account the limitations of this study.	Environ Res. 2020 May:184:109331.	10.1016/j.envres.2020.109331	32169736	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0501	A. Jala, B. Varghese, R. Dutta, R. Adela and R. M. Borkar	2022	Levels of parabens and bisphenols in personal care products and urinary concentrations in Indian young adult women: Implications for human exposure and health risk assessment	Limited information is available about the levels of exposure of paraben and bisphenols emerging from personal care products (PCPs) use in Indian women and the risk associated with it. In this study, liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used to determine the concentrations of 4 parabens (methyl-, ethyl-, propyl-, and butyl paraben) and 5 bisphenols (BPA, BPB, BPE, BPF, and BPS) in 1 PCPs samples (n = 110) obtained from Indian market and in the urine samples of young adult females (n = 50). The concentrations measured in PCPs and urine samples were used to determine the estimated daily intake. The mean concentrations of 4 parabens and 5 bisphenols in PCPs ranged from 58.0 to 238 × 10(6) ng/g and 2.71–148 ng/g, respectively. In urine sample analyzed, the mean concentrations of 4 parabens and 5 bisphenols ranged from 0.007 to 390 ng/mL and 0.01–33.8 ng/mL, respectively. There was no significant correlation of BPA with age, BMI and waist-to-hip ratio (WHR), but significant correlations (p < 0.05) were observed between urinary paraben and bisphenol concentrations. A statistically significant difference (p < 0.05) exists between the BMI and WHR groups for bisphenol concentrations. Estimated daily intake and hazard index for parabens and bisphenols were found to be essentially harmless for Indian young adult females. Hitherto, this is the first study to show that Indian young adult females were exposed to parabens and bisphenols. The study provides evidence on PCPs usage contribution to the urinary concentrations of EDCs.	Chemosphere Vol.297 Pages 134028	10.1016/j.chemosphere.2022.134028	35218786	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0502	R. B. Jain	2021	Concentrations of bisphenol A and its associations with urinary albumin creatinine ratios across the various stages of renal function	Data from National Health and Nutrition Examination Survey for 2003-2016 for US adults aged ≥ 20 years, N = 10,922 were used to study variabilities and associations with urinary albumin creatinine ratio (UACR) in the adjusted concentrations (ADJ) of urine bisphenol A (BPA) across various stages of renal function (RF). RF stages considered were RF 1: (eGFR ≥ 90 mL/min/1.73 m2); RF 2: (60 ≤ eGFR < 90 mL/min/1.73 m2); RF 3A: (45 ≤ eGFR < 60 mL/min/1.73 m2); RF 3B/4/5 (15 ≤ eGFR < 45 mL/min/1.73 m2). Irrespective of gender, race/ethnicity, and smoking status, UACRs for BPA were located on U curves with point of inflection at RF 3A, and RF 3B/4/5 respectively. A similar U curve was observed for those school dropouts but for those with advanced, BPA levels continued increasing with RF 3B/4/5. Same is true for RF 3A, and RF 3B/4/5 respectively. A similar U curve was observed for those school dropouts but for those with advanced, BPA levels continued increasing with RF 3B/4/5. Same is true for dyslipidemia was found to be associated with statistically significantly higher concentrations of BPA in urine. Shape of concentration curves for BPA across RF stages is determined by the balance of actively mediated excretion and reabsorption operating on both sides of renal proximal tubules during each stage of RF. Shape of concentration curves for BPA across various stages of RF was age and race/ethnicity dependent. Associations between BPA and UACR were found to be negative (p < 0.02), positive (p = 0.25), negative (p = 0.93), and negative (p = 0.01) respectively at RF 1, RF 2, RF 3A, and RF 3B/4/5 respectively.	Environ Sci Pollut Res Int Vol.28 Issue 8 Pages 9946-9953	10.1007/s11356-020-11535-z	33164123	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0503	U. Jain, N. Gupta, R. Mathur, S. Nimesh and S. K. Mathur	2020	A Study on Impact of BPA in the Adipose Tissue Dysfunction (Adiposopathy) in Asian Indian Type 2 Diabetes Mellitus Subjects	A surge to increase the production via usage of chemicals at both industrial and agricultural arenas has forced humans to be routinely and imprudently exposed to a wide variety of endocrine disrupting chemicals. The overall aim of the study was to evaluate possible relation that might exist between bisphenol A (BPA) and the adipose tissue hormones, and further impact on adiposopathy. In the present study, the role of BPA, an "endocrine disruptor" with respect to adiposopathy was evaluated in type 2 diabetes mellitus patients. For the study, 100 healthy control subjects and 100 newly diagnosed diabetes patients were recruited. Fasting venous blood samples was analyzed for several biochemical parameters, such as serum glucose, lipid profile, insulin, adiponectin, leptin, TNF- α, IL-6, IL-1, free fatty acid. Concentrations of BPA were also measured both in serum and urine samples. It was found that serum BPA concentrations were found to be significantly higher in diabetic subjects in comparison to the control subjects. Results of BPA were found to be positively correlated with HbA1c, fasting insulin, HOMA-IR, and negatively correlated with adiponectin in diabetic subjects. Also, it was found to be positively correlated with leptin and negatively correlated with adiponectin in diabetic subjects. Therefore, the current study suggested more deleterious effect of BPA in diabetes and its pathophysiology.	Indian J Clin Biochem Vol.35 Issue 4 Pages 451-457	10.1007/s12291-019-00843-y	33013015	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0504	M. H. Jacobson, Y. Wu, M. Liu, T. M. Attina, M. Naidu, R. Kanthikeel, K. Kannan, B. A. Warady, S. Furth, S. Vento, H. Trachtman and L. Trasande	2020	Serially assessed bisphenol A and phthalate exposure and association with kidney function in children with chronic kidney disease in the US and Canada: A longitudinal cohort study	BACKGROUND: Exposure to environmental chemicals may be a modifiable risk factor for progression of chronic kidney disease (CKD). The purpose of this study was to examine the impact of serially assessed exposure to bisphenol A (BPA) and phthalates on measures of kidney function, tubular injury, and oxidative stress over time in a cohort of children with CKD. METHODS AND FINDINGS: Samples were collected between 2006 and 2014 from 369 children participating in the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Urinary concentrations of BPA (median 2.2 ng/mL; interquartile range [IQR] 0.9-4.8) and nine DEHP, DBP, and butylbenzyl phthalate metabolites (median 211 ng/mL; IQR 122-361) and urine DBCPA, and parabens had a median age of 11.8 years (interquartile range [IQR] 7.4-15.6) at the baseline visit. In urine samples collected serially over an average of 3.0 visits (standard deviation [SD] 1.6), concentrations of BPA, phthalic acid (PA), and phthalate metabolites were measured as well as biomarkers of tubular injury (kidney injury molecule-1 [KIM-1] and neutrophil gelatinase-associated lipocalin [NGAL]) and oxidative stress (8-hydroxy-2′-deoxyguanosine [8-OHdG] and F2-isoprostanes). Glomerular filtration rate (eGFR) was estimated using the bedside Schwartz equation. Linear mixed models were fit to estimate the associations between urinary concentrations of 5 chemical exposure measures (i.e., BPA, PA, and 4 phthalate metabolite groups) and clinical renal outcomes and urinary concentrations of biomarkers. Models were adjusted for age, sex, race/ethnicity, household income, baseline eGFR, and urinary creatinine concentration. Models were also stratified by sex and by age (<12 years versus ≥12 years) to examine whether associations differed by sex and age, and urinary creatinine. Urinary concentrations of BPA, PA, and phthalate metabolites were associated with increases in NGAL (β = 0.13 [95% CI: 0.05, 0.21]; p = 0.001), KIM-1 (β = 0.10 [95% CI: 0.03, 0.18]; p = 0.005), 8-OHdG (β = 0.09 [95% CI: 0.02, 0.16]; p = 0.01), and F2-isoprostanes (β = 0.08 [95% CI: 0.01, 0.15]; p = 0.03). Associations between urinary BPA concentrations and kidney injury biomarkers were stronger in females than in males (p-interaction = 0.04 for NGAL and p-interaction = 0.03 for KIM-1). Associations between urinary BPA concentrations and kidney injury biomarkers were also stronger in children <12 years of age than in children ≥12 years of age (p-interaction = 0.03 for NGAL and p-interaction = 0.04 for KIM-1). For example, a 2× increase in urinary BPA concentrations was associated with an increase in NGAL (β = 0.13 [95% CI: 0.05, 0.21]; p = 0.001), KIM-1 (β = 0.10 [95% CI: 0.03, 0.18]; p = 0.005), 8-OHdG (β = 0.09 [95% CI: 0.02, 0.16]; p = 0.01), and F2-isoprostanes (β = 0.08 [95% CI: 0.01, 0.15]; p = 0.03). Associations between urinary PA concentrations and biomarkers were also observed but were generally weaker than those observed for BPA. For example, a 2× increase in PA concentrations was associated with an increase in NGAL (β = 0.08 [95% CI: 0.01, 0.15]; p = 0.03), KIM-1 (β = 0.06 [95% CI: 0.00, 0.13]; p = 0.06), 8-OHdG (β = 0.04 [95% CI: -0.02, 0.11]; p = 0.2), and F2-isoprostanes (β = 0.04 [95% CI: -0.02, 0.11]; p = 0.2). Limitations of this study include utilization of spot urine samples for exposure assessment of non-persistent compounds and lack of specific information on potential sources of exposure. CONCLUSIONS: Although BPA and phthalate metabolites were not associated with clinical renal endpoints such as eGFR in preteens, there was a consistent pattern of increased tubular injury and oxidative stress over time, which have been shown to affect renal function in the long term. This raises concerns about the potential for clinically significant changes in renal function in relation to exposure to common environmental toxicants at current levels.	PLoS Med. 2020 Oct 14;17(10):e1003384.	10.1371/journal.pmed.1003384	33052911	ヒト	腎	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0505	M. H. Jacobson, M. Woodward, W. Bao, B. Liu and L. Trasande	2019	Urinary Bisphenols and Obesity Prevalence Among U.S. Children and Adolescents	Bisphenol A (BPA) has been recognized as an endocrine-disrupting chemical and identified as an obesogen. Although most adolescents, human exposure to BPA has been declining owing to its substitution with other bisphenols. Thus, structurally similar substitutes, bisphenol S (BPS) and bisphenol F (BPF), have raised similar concerns, although fewer studies have been conducted on these newer derivatives. We used data from the U.S. National Health and Nutrition Examination Surveys from 2013 to 2014 to evaluate associations between BPA, BPS, and BPF and body mass outcomes among children and adolescents aged 6 to 19 years. Concentrations of BPA, BPS, and BPF were measured in urine samples collected from 1,852 participants. Body mass outcomes included body mass index (BMI) z-score, overweight, and obesity, according to the 2000 US norms. Multivariate models, also stratified as a priori on socioeconomic/height status of a child, BPA, BPS, and BPF were dichotomized to FOUR, BY ISO, and FIVE of urine samples, respectively. Log-transformed urinary BPS concentrations were associated with an increased prevalence of general obesity (OR, 1.16; 95% CI, 1.01 to 1.32) and abdominal obesity (OR, 1.13; 95% CI, 1.02 to 1.27). BPF detection (vs not detected) was associated with an increased prevalence of abdominal obesity (OR, 1.39; 95% CI, 1.01 to 1.92) and continuous BMI z-score (β = 0.30; 95% CI, 0.02 to 0.57). BPA and total bisphenols were not statistically significantly associated with general obesity, abdominal obesity, or any body mass outcome. These results suggest that BPA substitute chemicals are correlated with obesity in contemporary children.	J Endocr Soc Vol.3 Issue 9 Pages 1715-1726	10.1210/js.2019-00201	31528831	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるものは作成段階評価へ進め、当該時点評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	適応毒性試験	適応毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0506	A. Ishtiaq, M. A. Nasrullah, J. S. Khan, S. Malik, U. Tareen, M. Anees, A. Sultan and I. Murtaza	2023	A cohort study investigating the role of Bisphenol A in the molecular pathogenesis of breast cancer	BACKGROUND: Breast cancer is an abnormal division of breast cells. Bisphenol A (BPA), an environmental toxicant, is identified as an emerging risk factor for breast cancer development. However, to the best of our knowledge, no previous study has investigated the BPA levels in breast cancer patients in Pakistan. The present study sought to explore the role of BPA in tumor growth among the Pakistani population. METHODS: The study was a hospital-based, case-control study conducted between January 2019 and December 2020. A total of 100 breast cancer patients and 100 healthy controls were recruited. Immunohistochemical expression analysis of tumor markers were performed. RESULTS: The level of BPA in the serum samples of breast cancer patients was significantly higher than control. Histopathological analysis of breast cancer tissue samples revealed distinct subtypes of tumor, such as ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC). There was a significant increase in ROS level with a significant decrease in the levels of superoxide dismutase (SOD) and catalase (CAT) enzymes in malignant breast tissue samples as compared to control tissue samples. We found upregulated expression of p53, ZR75-and MKI67 genes at mRNA level in malignant breast tissue samples by 2.77 folds, 328 folds and 16 folds, respectively. p53 protein expression in malignant breast tissue samples was also enhanced at the translational level. CONCLUSION: Current findings suggest a relationship between BPA and the progression of breast cancer among the Pakistani population.	J Cancer Res Clin Oncol. 2023 Nov;149(16):14565-14575.	10.1007/s00432-023-05247-3	37580403	ヒト	発がん	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0507	N. Irvine, R. C. Bell, F. B. Subhan, C. J. Field, J. Liu, A. M. MacDonald, D. W. Kinniburgh, J. W. Martin, D. Dewey and G. England-Mason	2024	Maternal pre-pregnancy BMI influences the associations between bisphenol and phthalate exposures and maternal weight changes and fat accumulation	BACKGROUND: Bisphenols and phthalates are two classes of endocrine-disrupting chemicals (EDCs) thought to influence weight and adiposity. Limited research has investigated their influence on maternal weight changes, and no prior work has examined maternal fat mass. We examined the associations between exposure to these chemicals during pregnancy and multiple maternal weight and fat mass outcomes. METHODS: This study included a sample of 338 women enrolled in a Canadian prospective pregnancy cohort. Second trimester urinary concentrations of 2 bisphenols and 12 phthalate metabolites were quantified. Self-reported and measured maternal weights and measured skinfold thicknesses were used to calculate pre-pregnancy BMI, gestational weight gain (GWG) at 3 months and 5- to 9-years postpartum weight retention, and changes in fat mass loss, and late postpartum fat mass retention. Adjusted robust regressions examined associations between chemicals and outcomes in the entire study population and sub-groups stratified by pre-pregnancy body mass index (BMI) (underweight/normal weight, overweight, obese). RESULTS: Pre-pregnancy BMI was associated with greater GWG (β = 0.07 kg/week per BMI unit, 95% CI: 0.04, 0.10), greater maternal fat at 3- to 5-years postpartum (β = 0.65, 95%CI: -0.07, 1.62). Among women with overweight or obese pre-pregnancy BMIs, MEHP and MEP were positively associated with weight retention at 3 months and 5- to 9-years postpartum, respectively (B's = 0.12 to 0.63, 95%CIs: 0.02, 1.07). DEHP metabolites and MCNP were positively associated with late pregnancy fat mass gain and late postpartum fat mass retention (B's = 0.03 to 0.16, 95%CIs: 0.001, 0.31). Further, the nature of EDCs was positively associated with late pregnancy fat mass gain. CONCLUSION: In this cohort, pre-pregnancy BMI was a key determinant of the associations between second trimester exposure to bisphenols and phthalates and maternal weight changes and fat accumulation. Investigations of underlying physiological mechanisms, windows of susceptibility, and impacts on maternal and infant health are needed.	Environ Res. 2024 Sep 15;257:119276.	10.1016/j.envres.2024.119276	38830392	ヒト	代謝	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0508	L. M. Iribarne-Durán, L. Serrano, F. M. Peinado, M. Peña-Caballero, J. A. Hurtado, F. Vela-Soria, M. F. Fernández, C. Freire, F. Artacho-Cordón and N. Olea	2022	Biomonitoring bisphenols, parabens, and benzophenones in breast milk from a human milk bank in Southern Spain	BACKGROUND: Human breast milk is considered the optimal source of nutrition for infants. Milk from breast milk banks offers an alternative to infant formulas for vulnerable hospitalized neonates; most likely to benefit from the protective properties of breast milk. However, breast milk can contain contaminants, including endocrine disrupting chemicals (EDCs), including bisphenols, parabens (PBs), and benzophenones (BPs), in samples from a human milk bank in Granada, Southern Spain and to explore sociodemographic, reproductive, and lifestyle factors related to their concentrations in the milk. METHODS: Concentrations of three bisphenols (bisphenol A (BPA), bisphenol F (BPF), and bisphenol S (BPS)), four PBs (methyl- (MeP), ethyl- (EtP), propyl- (n-PrP), and butyl paraben (n-BuP)), and four BPs (BP-1, BP-2, BP-3, and 4-hydroxybenzophenone (4-OH-BP)) were analyzed in 50 breast milk samples donated to the milk bank between 2017 and 2019 by solid-phase extraction and liquid chromatography-tandem mass spectrometry. Multiple linear and logistic regression models were fitted. RESULTS: Detectable concentrations were found in at least one of the analyzed compounds in all breast milk samples and in all four compounds in over 70% of them. The most frequently detected compounds were EtP (90.0%), BP-3 (76.0%), EtP (92.2%), n-PrP (56.0%), and BPA (92.2%). Median concentrations ranged between <0.53 ng/mL (n-PrP) and 1.87 ng/mL (BP-1) and 539 ng/mL (BP-3). Six samples contained detectable concentrations of BPF, BPS, or most BPs (BP-1, BP-3, BP-8, and 4- hydroxy-BP). Breast milk paraben concentrations were associated with parity, the utilization of deodorants, mouthwash, skin care products, and cosmetics, and the intake of nutritional supplements. CONCLUSIONS: Results reveal the widespread presence of BPA, PBs, and BP-3 in donor breast milk samples, highlighting the need for preventive measures to enhance the benefits of breast milk from milk banks and from breastfeeding women in general.	Sci Total Environ Vol.830 Pages 154737	10.1016/j.scitotenv.2022.154737	35337871	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0509	L. M. Iribarne-Durán, F. M. Peinado, C. Freire, I. Castilleo-Rosales, F. Artacho-Cordón and N. Olea	2022	Concentrations of bisphenols, parabens, and benzophenones in human breast milk: A systematic review and meta-analysis	BACKGROUND: Breast milk is the main source of nutrition for infants but may be responsible for their exposure to environmental chemicals, including endocrine disrupting chemicals. AIM: To review available evidence on the concentrations of bisphenols, parabens, and benzophenones in human breast milk. METHODS: A literature search was conducted in PubMed, Web of Science, Scopus, Science Direct, and Access databases, conducting a comprehensive search of peer-reviewed original articles published during the period 1980-2020, including epidemiological and methodological studies. Inclusion criteria were met by 55 studies, which were compiled by calculating weighted detection frequencies and arithmetic mean concentrations of the chemicals. Then risk of bias was assessed using the NORMO-I checklist. RESULTS: Among the 55 reviewed studies, concentrations of bisphenols were assessed by 27 (15.0%), PBs by 21 (11.6%), and BPs by 28 (15.6%). Weighted detection rates were 43.6% for bisphenol A (BPA), 37.1-63.6% for PBs, and 39.5% for benzophenone 3 (BP-3). Weighted mean concentrations were 2.2 ng/mL for BPA, 0.2-13.2 ng/mL for PBs, and 26.4 ng/mL for BP-3. Mean concentrations ranged among studies from 0.1 to 1,900 ng/mL for BPA, 0.1-1,000 ng/mL for PBs, and 0.1-1,000 ng/mL for BPs. Sample sizes ranged from 1 to 1,200 donors. Risk of bias was moderate in 38 studies (69.1%). Greater concentrations were observed in samples collected after 2010. Characteristics of these chemicals were associated with source demographic and lifestyle factors in eight studies (14.5%). Two epidemiological studies showed moderate/serious risk of bias. CONCLUSIONS: This systematic review contributes the first overview of the widespread presence and concentrations of bisphenols, PBs, and BPs in human breast milk, revealing geographical and temporal variations. The methodological heterogeneity of published studies underscores the need for well-conducted studies to assess the magnitude of exposure to these chemicals from human milk.	Sci Total Environ Vol.806 Issue Pt 1 Pages 150437	10.1016/j.scitotenv.2021.150437	34583069	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0510	M. N. Suzuma, W. L. Shaiver, C. C. Hong, C. B. Ambrosone and T. O. Chang	2022	Urinary Concentrations of Triclosan, Bisphenol A, and Brominated Flame Retardants and the Association of Triclosan with Demographic Characteristics and Body Fatness among Women with Newly Diagnosed Breast Cancer	Background: Triclosan, bisphenol A (BPA), and brominated flame retardants are environmental estrogenic endocrine-disrupting compounds that may influence the prognosis of breast cancer. We examined the urinary concentrations of these compounds and their associations with demographic characteristics and body fatness in a population of women with newly diagnosed breast cancer. Methods: Overnight urine collection and questionnaire data were collected from 286 women with stage 0-IIIA breast cancer. Urinary concentrations of triclosan, BPA, and BDE-47 were measured using high-performance liquid chromatography-tandem mass spectrometry. Regression analyses were conducted to examine associations of urinary compound concentrations with age, menopausal status, race/ethnicity, body mass index (BMI), waist circumference, and body composition. Results: Triclosan, BPA, and TBBA were detected in urine samples from 98.5%, 6.6%, and 3% of patients, respectively. TBBPA was undetectable. Among patients with quantifiable values, the geometric mean concentrations were 35.9 μg/L (77.50 pg/g creatinine) for triclosan and 0.83 μg/L (1.98 pg/g creatinine) for BPA. Body mass index ≥ 30 vs. <30 kg/m2 was associated with lower triclosan creatinine-corrected urinary concentrations, of triclosan (−40.66, 95% confidence interval [CI] = −77.19 to −2.82; p = 0.0353). The observed association was predominantly in postmenopausal women (−64.01, 95% CI = −88.28 to −13.98%). Creatinine-corrected urinary concentrations of triclosan were lower in Black women than in White women. Conclusions: In this study population, women with newly diagnosed breast cancer had triclosan exposure. Assessments of the implications of urinary concentrations of triclosan for women should consider body fatness and menopausal status.	Int J Environ Res Public Health Vol.19 Issue 8	10.3390/ijerph19084681	35457549	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0511	U. Ihenacho, C. Guilherme, L. R. Wilkens, A. A. Franke, C. Tseng, Y. Li, M. Sangaramoorthy, M. C. Derouen, C. A. Heiman, D. O. Stram, L. Le Marchand, I. Chang and A. H. Wu	2023	Association of Endocrine Disrupting Chemicals With the Metabolic Syndrome Among Women in the Multiethnic Cohort Study	Metabolic syndrome (MetS) is associated with a high risk of cardiovascular disease, a leading cause of death among women. MetS is a diagnosis of at least 3 of the following: high blood pressure, high fasting glucose, high triglycerides, low high-density lipoprotein (HDL) cholesterol, and abdominal obesity. Exposure to endocrine disrupting chemicals (EDCs) may contribute to MetS and its components. We examined associations between EDCs and MetS in a cross-sectional analysis within the Multiethnic Cohort Study. We evaluated the associations between 6 classes of urinary EDCs: bisphenol A (BPA), triclosan, parabens, and phthalates1 and MetS among 1,728 women. Multivariable logistic regression was used to estimate odds ratios and 95% CI for the association between tertiles of each EDC and MetS adjusting for age, body mass index (BMI), racial and ethnic group, and exam center. Stratified analyses by race and ethnicity and BMI were conducted. We identified 539 (31%) women. We did not detect statistically significant associations of MetS with BPA, triclosan, or phthalate metabolite excretion. MetS was inversely associated with total parabens (Ptrend = .002). Although there were no significant associations between parabens and MetS components, parabens were inversely associated with HDL (Ptrend = .03). Associations between parabens and MetS varied by race and ethnicity and BMI. These findings suggest an inverse association between parabens and MetS in larger multiethnic studies. Prospective analyses to investigate suggested differences in associations by race, ethnicity, and BMI are warranted.	J Endocr Soc Vol.7 Issue 12 Pages bvad136	10.1210/jendso/bvad136	38024651	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0512	A. Iglesias-González, M. Schweitzer, P. Palozzi, F. Peng, S. Haan, E. Lateifer and B. M. R. Appenzeller	2022	Investigating children's chemical exposome - Description and possible determinants of exposure in the region of Luxembourg based on hair analysis	The specific physiology and behaviour of children makes them particularly vulnerable to chemical exposure. Specific studies must therefore be conducted to understand the impact of pollution on children's health. Human biomonitoring (HBM) is a powerful approach to assess the internal exposure to chemicals. Hair is a non-invasive matrix that can be used to investigate both recent exposure and chronic exposure. The present study aims at assessing chemical exposure and investigating possible determinants of exposure in children living in Luxembourg. Hair samples were collected from 296 children before 12 years and tested for 163 compounds (109 pesticides, 47 PCBs, 7 PBDEs and Dibutylbenzils). Moreover, anthropometric parameters, information on diet, residence, and presence of pets at home was collected through questionnaires. Correlations, regressions, t-tests, PLS-DA and MANOVAs, were used to investigate exposure patterns. Twenty-nine to 88 (median = 61) compounds were detected per sample. The highest median concentration was observed for BPA (128.6 pg/mg). Twenty-three biomarkers were detected in ≥ 90% of the samples, including 15 in all samples. 22 pesticides, BPA and BPS. Exposure was higher at younger ages. ISO (OR = 1.07 per pg/mg, p = 0.0001) and DCPP (OR = 1.03, p = 0.0001) were significantly associated with the presence of pets at home. Consumption of fish (OR = 1.03, p = 0.0001), eggs (OR = 1.02 pg/mg) or sweetbread, or urban (+0.001) residence area (e.g. Arlon/central 0.28 pg/mg) or pesticide, or urban (-0.03), and feeding pets (e.g. hamster 0.23 pg/mg) or pets, or urban (-0.002) were identified as determinants of exposure. The present study demonstrates that children are simultaneously exposed to multiple pollutants from different chemical classes, and confirms the suitability of hair to investigate exposure. These results set the basis for further investigations to better understand the determinants of chemical exposure in children.	Environ Int Vol.165 Pages 107342	10.1016/j.envint.2022.107342	35714525	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0513	E. Broc, S. W. Thurston, E. S. Barrett, N. B. Buck, R. H. N. Nguyen, S. Sathyanarayana, A. Reich-enberg, B. R. Collett, S. H. Swan and S. F. Evans	2022	Prenatal bisphenol A exposure in relation to behavioral outcomes in girls aged 4-5 and modification by socio-demographic factors in The Infant Development and Environment Study (TIDES)	Bisphenol A (BPA) is a polymer used in the production of polycarbonate plastics and epoxy resins. Its estrogen mimic, prenatal BPA exposure has been associated with mental behavioral outcomes in children however, findings are inconsistent. We investigated associations between prenatal BPA exposure and behavioral outcomes in girls aged 4-5 years and modification by socio-demographic factors. We measured maternal urinary BPA and behavior in 4-5 year old girls, and to assess whether socio-demographic factors modify this relationship.Mothers enrolled in The Infant Development and Environment Study (TIDES) provided a single spot urine at enrollment (median gestational age 27 weeks) and completed the Behavior Assessment System for Children-2 (BASC-2) and Social Responsiveness Scale-1 (SRS-2) when their daughters were 4-5 years of age. Maternal BPA was measured in urine samples using high performance liquid chromatography-tandem mass spectrometry. We used multivariable linear regression analyses to estimate associations between maternal urinary log(10)-transformed BPA concentration and BASC-2 subscale and composite scores and SRS-2 Total Score. To examine the role of socioeconomic status and race/ethnicity, we stratified by maternal education (≤ high school, > high school) and child's race/ethnicity (Black, White, Hispanic, Other).Participants were 175 girls from three enrollment centers in Minnesota (n = 60), California (n = 57), and New York (n = 58). Participants from these centers were recruited from three distinct populations: those enrolled at the University of Washington, University of Minnesota, and University of California San Francisco, a low-population, more similar higher socioeconomic demographic characteristics. Across all centers, no associations were seen between BPA and BASC-2 or SRS-2 scores. When stratified by income, BPA was significantly associated with greater social impairment as measured by the SRS-2 Total Score (β coefficient=39.9, confidence interval(CI) 5.7,74.1, N=25) in BMC participants (N = 60). In non-BMC participants (N = 115), BPA was significantly associated with lower BASC-2 Internalizing composite (-5.0 [-9.4,-0.6]) and Depression subscale scores (-5.6 [-9.7,-1.5]) within-a-association-s were seen between BPA and SRS-2 scores. Our findings suggest that sociodemographic factors may modify the impacts of maternal prenatal BPA on behavioral endpoints.	Neurotoxicology. 2022 Jul 91:262-268.	10.1016/j.neuro.2022.05.018	35661784	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0514	M. Hwang, K. Choi and C. Park	2022	Urinary levels of phthalate, bisphenol, and paraben and allergic outcomes in children: Korean National Environmental Health Survey 2015-2017	BACKGROUND: Phthalates, bisphenols and parabens have been widely used in household and personal care products. Their endocrine disrupting, sensitizing and antimicrobial properties might play a role in the occurrence of allergic diseases. However, the effects of these chemicals, particularly on humans, are relatively underexplored. OBJECTIVES: This study aimed to report the concentrations of phthalate, bisphenol and paraben in urine of Korean children, and assess their relationship with allergic outcomes. METHODS: Data obtained from nationally representative Korean children, a total of 1,668 children between 3 and 11 years of age included in the Korean National Environmental Health Survey (5th round of KoNEHS 2015-2017), were analyzed. Associations of urinary phthalate metabolites, bisphenols, and parabens levels with atopic dermatitis and allergic rhinitis were examined by logistic regression analysis. RESULTS: Urinary concentrations of phthalate metabolites, bisphenols, and parabens were higher in children than in adults. Urinary metabolites of DEHP, DBP, and DEP, and BzP and PrP in preschool children, and MEP in school children, were associated with BzP and PrP in preschool children. Urinary metabolites of DEHP, MnP and PrP in school children. The association of urinary chemicals with atopic dermatitis and allergic rhinitis were different by gender, especially in preschool children. CONCLUSIONS: Urinary phthalates, BPA and parabens levels in the Korean children were related with atopic dermatitis and allergic rhinitis. Considering the importance of allergic diseases in children, the public health implications of exposure to these chemicals warrant further studies. Given the cross-sectional design and confounding variables, the results of this study should be interpreted with caution.	Sci Total Environ Vol.818 Pages 151703	10.1016/j.scitotenv.2021.151703	34798094	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0515	T. Husøy, M. Andreassen, H. Hjertholm, M. H. Carlsen, N. Norberg, C. Sprong, E. Papadopoulou, A. K. Sakhi, A. Sabaredzovic and H. Dirven	2019	The Norwegian biomonitoring study from the EU project EuroMix: Levels of phenols and phthalates in 24-hour urine samples and exposure sources from food and personal care products	BACKGROUND: Exposure to multiple chemicals occurs daily through several routes; diet, inhalation and dermal contact. Real life exposure assessment is needed to understand the risk. Therefore, a human biomonitoring (HBM) study was performed to examine the plausibility of source to dose calculations for chemical mixtures in the Horizon 2020 EuroMix project. OBJECTIVES: To provide a detailed description of the design of the EuroMix HBM study in Norway, and present levels of phenols and phthalates in 24-hour urine samples and exposure sources from food and personal care products. METHODS: Spot-adapted diaries on their food consumption, PCP- and toiletting-d' each and male, Urine samples were collected over the same 24-hour period. Urinary levels of four parabens, five bisphenols, eight replacement/transplacement (1 (OMB), triclosan (TCS), triclocarban (TCC) and metabolites of eight phthalates and 1,2- cyclohexane dicarboxylic acid diisononyl ester (DINCH) were analysed by ultra high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS). Associations between urinary biomarker concentrations and questionnaire data were investigated by univariate correlation analysis and multivariate partial least squares regression analysis (PLS-R). The detection limit for the metabolites of phthalates, and DINCH, and bisphenol A (BPA) and TCS was more than 98 (BPA, which bisphenol S (BPS) and bisphenol F (BPF) were only found in 39% and 4% of the urine samples, respectively. Bisphenol B (BPB), bisphenol AP (BPAP) and TCC were not detected. Food groups associated with phthalate exposure were meat, bread, beverages and butter and oil. Food determinants for phthalate exposure were snacks, butter and oil, fruit and berries and other foods. The only positive association between the use of PCPs and phenols was found between BPA and hydroxy-fatty- Phthalate exposure was associated with the use of shower gel, hand cream (females), toothpaste, and in males cream (females) and shaving products (males). CONCLUSIONS: For participants in the Norwegian EuroMix study, exposure to phenols and phthalates was mainly from food. Personal care products were identified as important exposure sources for some chemicals. This indicates a complex pattern of exposure to numerous chemicals from multiple sources, depending on individual diet and PCP preferences.	Environ Int Vol.132 Pages 105103	10.1016/j.envint.2019.105103	31470218	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0516	Z. Huang, W. Fu, L. Dou, H. Bao, W. Wu, P. Su, K. Huang, P. Zhu, J. Sheng, Y. Xu, F. Tao and J. Hao	2022	Prenatal Bisphenol A Exposure and Early Childhood Behavior and Cognitive Function: A Chinese Birth Cohort Study	INTRODUCTION: Biomonitoring of bisphenol A (BPA) in human blood is still scarce, although already noticeable. We aimed to examine the associations between prenatal serum BPA concentrations and behavior and cognitive function in preschool children.METHODS: A total of 1,782 mother-child pairs with complete demographic information, blood samples, and psychological measurements were included from the China Baby Birth Cohort (C-ABCS). We detected serum BPA concentrations and assessed children's neurodevelopment using a set of psychometric scales. RESULTS: The median prenatal maternal serum BPA concentration was 0.23 (IQR, 0.16–0.33) ng/mL, with a detection frequency of 99.7%. Compared with the girls with the lowest serum concentrations, those with higher BPA concentrations had lower IQ scores. Every 10-fold increase in maternal BPA concentrations was associated with a 3.66 (95% CI: 1.82, 5.50) unadjusted difference in children's full-scale IQ (FSIQ) score, implement [relative risk (RR) = 3.66, 95% confidence interval (CI): 1.82, 5.50], emergent metacognition (beginner (RR = 1.78, 95% CI: 1.07, 2.50), conduct problem (RR = 1.68, 95% CI: 1.12, 2.25), peer relationship problem (RR = 1.68, 95% CI: 1.12, 2.25), and hyperactivity (RR = 1.68, 95% CI: 1.12, 2.25). Boys were more susceptible to BPA exposure than girls. Children whose mothers had concentrations had an increased risk of conduct problem compared with those with the lowest concentrations (RR = 1.78, 95% CI: 1.07, 2.50). Interaction = 0.012). After stratification by age, high prenatal BPA concentrations were associated with increased ADHD (RR = 4.43, 95% CI: 1.54, 12.80) among children aged 3 years, not among children aged 5 years. CONCLUSION: Our study revealed the sex-specific and age-specific impacts of prenatal BPA exposure on preschool children's cognitive and behavioral development.	Neuroendocrinology. 2022;112(4):311-323.	10.1159/000516881	33910209	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0517	Y. S. Huang, P. L. Hung, L. J. Wang, C. M. Tsai, C. K. Tsai, M. M. Tsai and H. R. Yu	2024	Distinct Impacts of Prenatal and Postnatal Phthalate Exposure on Behavioral and Emotional Development in Children Aged 1.5 to 3 Years	Development is a continuous process, but few studies have assessed the simultaneous impact of prenatal and postnatal phthalate exposure on children's behavioral and emotional development. A total of 190 mother-child pairs were recruited from the Taiwan Maternal and Infant Cohort Study. Urinary concentrations of 11 phthalate metabolites were measured in maternal samples collected during the second trimester and in children's samples collected at 1.5 years old. Behavioral problems were assessed using the Child Behavior Checklist (CBCL). Data ratios (DRs) represent a 1-unit increase in log10-transformed creatinine-corrected maternal urine concentrations. Prenatal maternal urinary MnBP levels were associated with total problems (DR = 1.90, 95% CI: 1.08–33.33, p < 0.02), anxiety (DR = 3.56, 95% CI: 1.28–101.18, p < 0.01), and sleep problems (DR = 11.36, 95% CI: 1.27–96.72, p < 0.01). These findings suggest that prenatal and postnatal exposure to dibutyl phthalate (DBP), metabolized as MnBP, distinctly affects children's behavioral development.	Toxics. 2024 Oct 31;12(11):795.	10.3390/toxics12110795	39590974	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0518	Y. J. Huang, C. A. Chuang, Y. C. Chang, M. F. Tseng, Y. S. Chiou and C. L. Shih	2024	Advanced metabolomics-based approach to reveal new insights into Bisphenol A metabolism and its presence in human excreta and water bodies in Taiwan	Bisphenol A (BPA) is an environmental contaminant and can be detected in foodstuffs. Hence, investigating BPA metabolism in humans is crucial because certain BPA metabolites may exhibit similar or even greater toxicity than does the parent compound. In this study, we used an advanced metabolomics-based data processing approach along with ultrapermeant liquid chromatography-mass spectrometry (UPLC-MS) to identify BPA metabolites. In human liver enzyme incubation samples, and those metabolites, were further detected in human excreta and water body samples in Taiwan. The first stage involved screening full-scan MS files from the incubation samples into feature information; this stage revealed 1890 and 2027 features with clear recursive relationships in the BPA and isotopically labeled BPA incubation datasets, respectively. The second stage involved using stable isotope tracing to identify isotopic pairs from the two datasets; this stage revealed 290 isotopic pairs. An additional dose–response experiment was conducted to confirm that all these features will be increased in response to increasing BPA concentrations. Finally, the third stage involved using the online METLIN database to search for the 290 isotopic pairs and their corresponding MS/MS spectra for further analysis. To confirm these features as possible BPA metabolites, we compared the isolated MS1 MS/MS spectra between BPA and isotopically labeled BPA incubation samples. The results revealed 75 isotopic pairs with matching isotopically labeled MS/MS spectra. Among these identified features, one feature's m/z value matched to that of a previously reported BPA metabolite, and the other 74 features were novel. However, only 2 of them had proposed structures. We further investigated whether these features could be detected in humans or Taiwanese water bodies. Furthermore, 13 and 7 novel metabolites were identified in human urine and fecal samples, respectively. 17 novel metabolites were identified in the water samples. These findings indicate some of these novel metabolites are present not only in humans but also in various water bodies across Taiwan. Additional research is needed to assess these BPA metabolites, suggesting they may have toxic properties. Further research is warranted to investigate the occurrence of these newly discovered metabolites and assess their potential human health risks.	Ecotoxicol Environ Saf Vol.286 Pages 117236	10.1016/j.ecoenv.2024.117236	39490109	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該物質候補候補から除外した。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0519	Y. F. Huang, C. H. Chang, P. J. Chen, I. H. Lin, Y. A. Tsai, C. F. Chen, Y. C. Wang, W. Y. Huang, M. S. Tsai and M. L. Chan	2021	Prenatal Bisphenol a Exposure, DNA Methylation, and Low Birth Weight: A Pilot Study in Taiwan	Prenatal exposure to bisphenol A (BPA) may increase the risk of abnormal birth outcomes, and DNA methylation might mediate these adverse effects. This study aimed to investigate the effects of maternal BPA exposure on maternal and fetal DNA methylation levels and explore whether epigenetic changes are related to the associations between BPA and low birth weight. We collected cord blood samples originating from 162 mother–infant pairs in Taiwan. Maternal urinary BPA concentrations were measured using high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS). Long interspersed nuclear element-1 (LINE-1) and pyrosequencing of the H19 gene were used to quantify maternal and fetal DNA methylation levels, respectively. Eighty-seven CpGs with the most differentially methylated probes possibly interacting with BPA exposure or birth weight were selected using two multiple regression models. Ingenuity pathway analysis (IPA) was utilized to narrow down 19 candidate CpGs related to disease categories, including developmental disorders, skeletal and muscular disorders, skeletal and muscular system development and function, and organismal development. Finally, we examined the correlations between the methylation levels of these CpGs and birth weight using linear regression models. Higher maternal urinary BPA concentrations were associated with lower birth weight. Similarly, in the epigenome-wide findings, differential methylation of cord blood CpGs, mostly in the epigenetic regulatory genes, was significantly associated with low birth weight. Analysis of the epigenome-wide findings also revealed that maternal BPA exposure was correlated with cord blood DNA methylation in cord blood of the 6 CpGs. However, the adjusted odds ratio for the dehydrogenase/reductase member 9 (DHRS9) gene, at the 2nd CG site, in the hypermethylated group was significantly associated with low birth weight. These results support a role of BPA, and possibly DHRS9 methylation, in fetal growth. However, additional studies with larger sample sizes are warranted.	Int J Environ Res Public Health. 2021 Jun 7;18(11):6144.	10.3390/ijerph18116144	34200176	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0520	S. Huang, D. Wang, Z. Qi, C. Long, G. Li and Y. Yu	2023	A large-scale nationwide study of urinary phenols in the Chinese population	Bisphenol A (BPA), tetrabromobisphenol A (TBBPA), and their substitutes are commonly used in everyday products. However, large-scale internal exposure levels of them in China, the factors influencing on them, and the associated health risks remain unclear. This study investigated the urinary concentrations of BPA, TBBPA, and their substitutes in 1,000 Chinese adults and explored the factors influencing on them, and the associations between some bisphenol analogues, as well as TBBPA and its substitutes, i.e., tetrachlorobisphenol A and 2,2′-oxydiethanol-3,3′-dibromobisphenol. The concentrations of 13 bisphenols ranged from <LOD to 38 μg/L and from <LOD to 2.35 μg/L, respectively. BPA and bisphenol S were the main environmental phenols. Residents in eastern China were more exposed to bisphenols, which may be due to the regional production of BPA and the diversity of food consumption patterns of the residents. Education level and age were significantly correlated with bisphenol exposure. Subjects with a bachelor's degree or aged 30–50 years appeared to be more exposed to bisphenols, especially for BPA. Subjects who consumed bottled water and takeaways also had higher levels of bisphenols. Based on RQs, the health risk assessment showed that no subjects had hazard quotients (HQs) > 1 for BPA, TBBPA, and their substitutes, which indicated that 0.6 % of the Chinese general population had a potential non-carcinogenic risk from BPA. This large-scale nationwide study is beneficial for governmental decision-making and the prevention of phenol exposure.	Sci Total Environ Vol.894 Pages 164850	10.1016/j.scitotenv.2023.164850	37331384	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0521	S. Huang, Z. Li, C. Wu, X. Zhao, J. Xiang, W. Xiao, H. Su, R. Zhang, Z. Xu, Q. Su, X. Lu, Q. Wang and Z. Su	2025	Divergent effects of EDCs on bone maturation: Role of body mass index and puberty	Exposure to endocrine-disrupting chemical (EDC) mixture and its association with bone maturation in children remain unclear. In this case-control study, the relationship between EDC exposure and accelerated bone maturation (AcBM) in 1,302 children was investigated. Urinary concentrations of 16 EDCs, including bisphenols, parabens, and phthalates, were measured. Bone maturation, as well as current bisphenols, was determined. Logistic regression, weighted quantile sum, Bayesian kernel machine regression, mediation effect analysis, and quantile regression. Girls with advanced BA had significantly lower median concentrations of mono-isobutyl phthalate (MiBP), mono(2-ethyl-5-hydroxyhexyl) phthalate, and BP. Only total monoethyl phthalate (MEP), total bisphenols (BPA, BPF, and BPS), MiBP, and TBBPA were detectable in boys. In girls, mono-methyl phthalate (MMP), MiBP, MEP, and total EDCs were negatively associated. Together, correlations were observed between several phthalate metabolite concentrations and height for the BA standard deviation score. Body mass index (BMI) mediated the associations between mono-methyl phthalate concentration and BPA with advanced BA. The findings reveal that MMP, MiBP, BPA, MEP, and BP exposure exert divergent effects and external sensitivity differences on accelerated bone maturation, with BMI and potential stage playing mediating roles. These findings have significant public health implications, given the prevalence of EDCs and the increasing trends in overweight/obesity, earlier puberty initiation, and accelerated bone maturation.	Ecotoxicol Environ Saf. 2025 Sep 1:302:118525.	10.1016/j.ecoenv.2025.118525	40554108	ヒト	骨	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0522	H. Huang, J. Liang, P. Tang, C. Yu, H. Fan, Q. Liao, J. Long, D. Pan, X. Zeng, S. Liu, D. Huang and X. Qiu	2022	Associations of bisphenol exposure with thyroid hormones in pregnant women: a prospective birth cohort study in China	Bisphenols are endocrine-disruptive chemicals that disrupt thyroid hormone homeostasis. However, evidence on the effects of bisphenol mixtures on thyroid hormones are insufficient. Therefore, the present study aimed to explore the effects of bisphenol substitutes and bisphenol mixtures on thyroid hormones during pregnancy. The study was conducted among 600 pregnant women in the Guangxi Zhuang Birth Cohort (GZBC), China. In multiple linear regressions, compared with the low exposure group, bisphenol S (BPS) concentrations in the middle exposure group led to a 10.90% (95% CI: -18.26%, -3.09%) decrease in triiodothyronine (T3) levels; the first trimester (simultaneously with T3/BPS) levels in the middle exposure group led to an 8.36% (95% CI: -15.81%, -0.51%) decrease in T3 levels, in the first trimester (simultaneously with BPS) levels in the high exposure group led to higher free thyroxine (FT4) levels (9.66%, 95% CI: 1.75%, 18.00%) in the second trimester. Bisphenol F (BPF) in the middle exposure group led to higher FT3 levels (8.99%, 95% CI: 0.03%, 17.31%) in the second trimester. Bisphenol A (BPA) in the high exposure group led to higher FT4 levels (8.66%, 95% CI: 0.03%, 17.31%) in the second trimester. Bayesian kernel machine regression (BKMR) models showed a U-shaped dose-response relationship between bisphenol S (BPS) and free triiodothyronine/FT3 (fT3/fT4) (p = 0.02) as well as BPS and FT3 (p = 0.05). Nonlinear relationships were also observed between the bisphenol mixture and FT3. Overall, maternal bisphenol exposure affected thyroid hormone levels during pregnancy. This study provides evidence that BPB, BPF, BPE, and TBBPA are unsafe substitutes for BPA, as well as the overall effect of bisphenols on adverse health in human beings.	Environ Sci Pollut Res Int. 2022 Dec;29(58):87170-87183.	10.1007/s11356-022-21817-3	35802331	ヒト	甲状腺	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0523	L. Hua, W. Liu, Y. Liu, M. Yang, B. Wang, H. Zhu, L. Zhu, Y. Yao, Y. Zhang and H. Zhao	2022	Occurrence and profile characteristics of environmental phenols in human urine from a rural area in Northwestern China	Many environmental phenols, such as bisphenols, benzophenones and parabens, are known as endocrine disrupters and can adversely affect human health. However, the knowledge of human exposure to common environmental phenols in Chinese rural areas is insufficient. In this context, 180 urine samples were collected from participants in a rural area in Northwest China and were analyzed for nine bisphenols, three benzophenones and four parabens. Bisphenol A (BPA), bisphenol S (BPS), benzophenone-3 (BP-3), 4-hydroxybenzophenone, methylparaben (MeP), and butylparaben (BuP) were detected in more than 50% of the urine samples, with median concentrations of 0.568 ng/mL, 0.221 ng/mL, 0.191 ng/mL, 1.30 ng/mL, 0.1820 ng/mL, 20.0 ng/mL, 4.51 ng/mL and 1.90 ng/mL, respectively. A significant positive correlation was observed between BPA and BPS (r_s = 0.2, p < 0.01). Females had significantly higher urinary concentrations of BPA, BPS, BP-3, MeP and PrP than males (p < 0.05). Urinary concentrations of BPA, BPS, MeP and PrP could be influenced by age. Other demographic information, such as annual household income, education and occupation was not associated with the exposure level of the targeted phenols in adults. The estimated daily intakes of the analytes except BPA were all below their respective tolerable/acceptable daily intake levels. This study profiles the demographic differences in the exposure to environmental phenols in general populations from rural areas and provides information on risk assessments.	Environ Pollut Vol.315 Pages 120405	10.1016/j.envpol.2022.120405	36228842	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0524	Y. Hu, S. Lai, Y. Li, X. Wu, M. Xing, X. Li, D. Xu, Y. Chen, J. Xiang, P. Cheng, X. Wang, Z. Chen, H. Ding, P. Xu and X. Lou	2023	Association of urinary bisphenols with thyroid function in the general population: a cross-sectional study of an industrial park in China	Bisphenols (BPs) are potential thyroid disruptors that are widely used in many consumer products, leading to their widespread exposure to the general population. Current cross-sectional and case-control studies have found associations between exposure to BPs and serum thyroid function, but the results were contradictory. The objectives of this study are to describe demographic characteristics, BP exposure levels, and thyroid function measurements in potentially exposed and control districts and to investigate the association of urinary BPs with thyroid function. Data were collected from a general population aged 3-79 years (N = 282) recruited by the Zhejiang Human Biomonitoring Program (ZHBP). The concentrations of 10 kinds of BPs in urine and serum free triiodothyronine (FT3), total thyroxine (TT4), total thyroxine (TT4), thyroid-stimulating hormone (TSH), thyroglobulin (Tg), thyroglobulin antibodies (TgAb), thyroid peroxidase antibodies (TPOAb), and thyrotropin receptor antibody (TRAb) in serum were measured. Multiple linear regression models and restricted cubic spline (RCS) models were used to explore the associations between urinary BPs and thyroid function. The detection rates of BPA, BPF, BPS, BPAF, BPB, BPP, BPZ, BPAP, BPBP, and BPFL were 99.65%, 99.29%, 99.65%, 0.00%, 0.00%, 0.00%, 0.00%, 0.00%, 0.00%, and 0.00%, respectively, in 567 (76.3%, 215/282), 0.00% (0/282), 0.00% (0/282), and 0.00% (0/282) of the population in the exposed area and 83.89%, 61.27%, and 10.66% of the population in the control area. Among individuals, serum TT3 was negatively associated with urinary BPA (β = -0.035, 95% CI: -0.071, -0.000, P = 0.021). Among male females, FT3 and Tg levels were negatively associated with the urinary BPA (β = -0.035, 95% CI: -0.061, -0.002, P = 0.018; 95% CI: -0.061, -0.002, P = 0.018; 95% CI: -0.061, -0.002, P = 0.018;

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0532	X. Hong, Y. Zhao, Z. Zhu, Y. Li, Z. Li, Y. Zhang, K. Hu, F. Zhu, Y. Wang, M. Fang, Y. Huang and T. Shen	2023	Environmental endocrine disruptor Bisphenol A induces metabolic derailment and obesity via upregulating IL-17A in adipocytes	BACKGROUND: Bisphenol A (BPA), a ubiquitous environmental endocrine disruptor, has been extensively demonstrated to be associated with metabolic disorders, including obesity and type 2 diabetes mellitus. However, the underlying mechanism underpinning for the environmental etiology of chronic metabolic disorders has not been sufficiently elucidated. OBJECTIVES: This study is designed to explore the toxicological pathogenesis of chronic inflammation in BPA exposure during obesity. METHODS: We investigated the role of IL-17A in the association of BPA exposure and obesity from human cross-sectional study to animal models, including 3T3-L1 adipocytes, C57BL/6 mice, IL-17A knockout mice and IL-17A neutralizing antibody treated mice. RESULTS: Urinary BPA levels were positively correlated with BMI (β = 0.31, 95% CI: 0.02, 0.60), metabolic disorders and levels of interleukin-17A (IL-17A) in human adipose tissue (all P < 0.05). Consistently, BPA exposure induced obesity and IL-17A production in mice. Moreover, BPA-induced IL-17A secretion from BPA-exposed aggravated body weight gain and insulin resistance, concurrent with much heightened inflammatory responses in the adipose tissue including increase in IL-17A and macrophage polarization towards M1 stage. Genetically modified IL-17A ablated mice (IL-17A(-/-)) showed improved adipose tissue inflammation response. Improved macrophage polarization homeostasis by along with insulin sensitivity in both WT(C) group alone or much more significantly the HFD + BPA group. Moreover, mediation analysis in human epidemiological investigation demonstrated that plasma IL-17A attributed up to 30.03% mediating role in the associations between BPA exposure and obesity risk (OR(CI)=0.03(0). This research paradigm from human to animal provides strong evidence for the elucidation of IL-17A mediating inflammation and insulin resistance in obesity. Such findings reiterate the obesogenic risk of environmental endocrine disruptor BPA in metabolic disorders and unveils the potential toxicological mechanisms underpinning such effect.	Environ Int Vol.172 Pages 107759	10.1016/j.envint.2023.107759	36696794	ヒト、動物	-	1	1	1	1	0	0.3 μg/kg	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0533	X. Hong, G. Wang, X. Liu, M. Wu, X. Zhang, X. Hua, P. Jiang, S. Wang, S. Tang, X. Shi, Y. Huang and T. Shen	2022	Lipidomic biomarkers: Potential mediators of associations between urinary bisphenol A exposure and colorectal cancer	Previous research reported associations between bisphenol A (BPA) exposure and some malignant tumor incidences, yet the underlying mechanism remains largely uncertain. This investigation was aimed to explore the association of BPA exposure burden with colorectal cancer (CRC) and the role of some tissue lipid biomarkers between BPA and CRC. A case-control study was conducted in CRC cases were significantly higher than those in controls (P value < 0.05). BPA was positively correlated with all three cancer CRC biomarkers, with an unadjusted odds ratio (OR) of 4.65 (96% confidence interval (95% CI): 3.21, 6.14). Moreover, the mediation analysis revealed that the associations between BPA exposure and CRC were partially mediated by phosphatidylcholine (PC) (C32:1), phosphatidylethanolamine (PE) (C36:2), diacylglycerol (TG) (C52:2) dimensionless mediation contributions of 21.9%, 18.7%, 16.4%, and 17.9%, respectively. In the association between BPA exposure and CRC. Our work provides novel findings that cancer tissue metabolites may be playing vital mediating roles in the associations between BPA exposure burden and CRC risk. These findings contribute to better understanding of the etiology of CRC induced by environmental stressors.	J Hazard Mater. 2022 Apr 5:427:127863.	10.1016/j.jhazmat.2021.127863	34848068	ヒト	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0534	S. Hong, O. J. Kim, S. K. Jung, H. L. Jeon, S. Kim and J. Ki	2024	The Exposure Status of Environmental Chemicals in South Korea: The Korean National Environmental Health Survey 2018-2020	In South Korea, a Human Biomonitoring (HBM) program, known as the Korean National Environmental Health Survey (KoNEHS), was launched in 2009. This study aims to provide an overview of environmental chemical exposures in South Korea based on data from the KoNEHS cycle 3 (2018-2020). To ensure population representativeness, Koreans aged 3 years and older were recruited from 60 sites across the country. A total of 1893 participants joined in the collection of biospecimens, which were subsequently analyzed for 33 environmental chemicals or their metabolites, including nine that were not tested in the previous cycle. The five most common PFASs were detected in more than 90.7% of the participants. The 95th of serum PFOS was the highest in adults at 10.1 μg/L (10.9, 16.0) and was the lowest in children at 3.1 μg/L (3.0, 3.4). In adults, there was a general decrease in the detection rate and concentration of some heavy metals and phthalate metabolites. In children and adolescents, the detection rate of BPA in urine decreased, while the rate of its substitutes BPF and BPS increased, and the rate of propyl paraben in urine decreased significantly. The results of the KoNEHS cycle 3 indicate that exposure levels to certain environmental chemicals are still high, highlighting further monitoring and re-going surveys to determine their trends, especially for newly investigated substances, such as PFASs.	Toxics Vol.12 Issue 11	10.3390/toxics12110829	39591007	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0535	S. Hong, B. S. Kang, O. Kim, S. Won, H. S. Kim, J. H. Wie, J. E. Shin, S. K. Choi, Y. S. Ju, Y. H. Kim, M. Yang, H. Kang, D. W. Lee, I. Y. Park, J. S. Park and H. S. Ko	2024	The associations between maternal and fetal exposure to endocrine-disrupting chemicals and asymmetric fetal growth restriction: a prospective cohort study	Recent evidence has revealed associations between endocrine-disrupting chemicals (EDCs) and placental insufficiency due to altered placental growth, syncytialization, and trophoblast invasion. However, no epidemiologic study has reported associations between exposure to EDCs and asymmetric fetal growth restriction (FGR) caused by placental insufficiency. The aim of this study was to evaluate the association between EDC exposure and asymmetric FGR. This was a prospective cohort study including women admitted for delivery to the Maternal-Fetal Center at Seoul St. Mary's Hospital between October 2020 and October 2022. Maternal urine and blood samples were collected, and the levels of bisphenol A (BPA), monoethyl phthalate, and perfluorooctanoic acid in each specimen were measured. Multivariable and multinomial logistic regression analyses were conducted to evaluate associations between the levels of EDCs and fetal growth parameters, including the head circumference (HC)/abdominal circumference (AC) ratio as an asymmetric parameter. The levels of EDCs were compared between the asymmetric FGR group and the control group. Among 1,200 participants, 1,179 were included in the analysis after excluding 21 participants who withdrew consent. The asymmetric FGR group showed significantly higher maternal and fetal BPA levels compared to the normal growth group (maternal urine BPA, 1.98 μg/g creatinine vs. 1.71 μg/g creatinine [p = 0.006]; cord blood BPA, 1.98 μg/L vs. 0.86 μg/L [p < 0.001]). In conclusion, fetal exposure levels of BPA show linear associations with asymmetric fetal growth patterns. High maternal and fetal exposure to BPA might be associated with asymmetric FGR.	Front Public Health. 2024 Apr 11:12:1351786.	10.3389/fpubh.2024.1351786	38662245	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0536	S. Hong, S. K. Choi, J. H. Wie, J. E. Shin, Y. S. Ju, Y. H. Kim, B. S. Kang, O. Kim, S. Won, H. J. Yoon, H. S. Kim, I. Y. Park, M. Yang and H. S. Ko	2025	Effects of Endocrine Disrupting Chemicals on Fetal Weight: Exposure Monitoring Among Mothers with Gestational Diabetes Mellitus and Their Fetuses	Gestational diabetes mellitus (GDM) requires lifestyle changes that may alter exposure to endocrine-disrupting chemicals (EDCs). This study aimed to assess maternal and fetal exposure to EDCs including bisphenol A (BPA), essential phthalates (DEHP), and perfluorooctanoic acid (PFOS) during the GDM-19 pandemic and to evaluate their associations with fetal growth. Maternal urine and blood samples were collected from 58 GDM and 116 non-GDM pregnancies using EPCC-MELMS. Significant correlations were found between maternal urine and cord blood levels of BPA and MEP. Cord blood BPA levels were significantly higher in the GDM group (β = 0.34, p = 0.001), and maternal BPA exposure was associated with increased fetal weight (β = 0.08, p = 0.001). These findings suggest that GDM may enhance placental transfer of BPA. Cord blood triclosan (β = -2.66, p = 0.001), indicating increased susceptibility to obesogenic effects. PFOA was present in all cord blood but only 61% of maternal urine samples. These findings underscore the dual impact of GDM-related lifestyle changes: reduced EDC transfer to the fetus, yet persistent metabolic vulnerability.	Int J Mol Sci. 2025 Apr 29;26(9):4226.	10.3390/ijms26094226	40362466	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0537	S. A. Holmboe, L. Schaub Henriksen, H. Frederiksen, A. M. Andersson, L. Priskorn, N. Jørgensen, A. Juul, J. Toppari, N. E. Skakkebæk and K. M. Main	2022	Prenatal exposure to phenols and benzophenones in relation to markers of male reproductive function in adulthood	INTRODUCTION: Environmental exposure during fetal life may disrupt testicular development. In humans, a limited number of studies have investigated whether these adverse effects persist into adulthood. Using data from a prospective, population-based birth cohort study, The Copenhagen Mother Child cohort, the objective was to assess if there is an association between fetal exposure to selected phenols and benzophenones and markers of testicular function in adult men. METHODS: Pregnant women were recruited in 1997-2000. Their sons were examined clinically at 18-20 years of age, with focus on adult testicular function (congenital absence (CAT), semen quality and reproductive hormones). In total, 351 18-20-year-old men were included, whose mothers during pregnancy had a serum sample drawn and analyzed for bisphenol A (BPA) and benzophenone-3 (BP3). Associations between maternal BPA and BP3 and CAT, semen quality, and reproductive hormones were analyzed using logistic and linear regression analyses. RESULTS: In univariate analyses, increased levels of maternal BPA were associated with higher total sperm count (TSC) and higher total testosterone (TT). In multivariable analyses, increased levels of maternal BPA were associated with higher total sperm count (TSC) (adjusted percentage difference (95%CI) 27.5 (2% to 6%,35%) and TT: 33% (18%,63%), compared to T1) and benzophenone-3 (BP-3): 17.3% (-2%,39%), T3: 18% (-6%,45%)), while no clear association was seen to total testosterone (TT). Higher levels of BPA and BP-3 were associated with a lower T/T ratio, although only significant for BPA up to tertile 2 (T2). As associations were seen to GEU in markers of semen quality, CONCLUSION: In conclusion, high exposure to BPA and BP-3 was associated with a compensated reduced Leydig cell function but no other changes in markers of reproductive health. As maternal levels of BPA and BP-3 were not correlated, separate effects may be at play. Larger studies, as long-term reproductive consequences of prenatal exposure are warranted to validate our findings.	Front Endocrinol (Lausanne). 2022 Dec 9:13:1071761.	10.3389/fendo.2022.1071761	36568115	ヒト	精巣	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0538	A. Hirke, B. Varghese, S. Varade and R. Adela	2023	Exposure to endocrine-disrupting chemicals and risk of gestational hypertension and preeclampsia: A systematic review and meta-analysis	Prenatal exposure to endocrine-disrupting chemicals has been linked to gestational hypertensive (GH) and preeclampsia (PE). However, the results were conflicting and inconclusive. We conducted a systematic review and meta-analysis for an overview of these relationships. We searched PubMed and Google Scholar for studies investigating bisphenol A, phthalates, and per-or-poly-fluoroalkyl substances and GH or PE. Pooled odds ratio (OR) with a 95% confidence interval (CI) were calculated for risk estimate using the generic inverse variance method. A total of 16 studies were included in the present analysis. The pooled results demonstrated that exposure to phthalates (OR = 1.16, 95% CI: 1.03, 1.31, I^2 = 0%, $P_{heterogeneity}$ = 0.46) and PFAS (OR = 1.14, 95% CI: 1.01, 1.28, I^2 = 0%, $P_{heterogeneity}$ = 0.46) during pregnancy were associated with a similar increased risk of PE. There was no significant association observed with perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), and perfluoroundecanoic acid (PFUnDA) and PE. For GH, a statistically significant positive association was found with PFOA (OR=1.18, 95% CI: 1.01, 1.39) and PFHxS (OR=1.19, 95% CI: 1.02, 1.39). Among various phthalates analyzed only mono-ethyl phthalate (MEP, OR=1.37, 95% CI: 1.11, 1.70) showed an association with GH. From our analysis, bisphenol A exposure during pregnancy did not show a significant association with the risk of PE. Our findings indicated that exposure to PFASs, such as PFOA, PFOS, and PFHA during pregnancy is associated with an increased risk of PE and PFOA and PFHxS with GH. We also found that MEP was associated with GH. Most of the results were available in semi-finite analysis. Since most of these associations have limited evidence, more research is needed to confirm these findings.	Environ Pollut. 2023 Jan 15:317:120828.	10.1016/j.envpol.2022.120828	36481468	ヒト	生殖発生(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0539	M. Herrero, M. C. G. Sauca, N. González, M. Marquina, F. Barbosa, J. L. Domingo, M. Nadal and J. L. Reuta	2023	Dermal exposure to bisphenols in pregnant women's and baby clothes: Risk characterization	Textile manufacturing consists of a multiple-step process in which a wide range of chemicals is used, some of them remaining in the final product. Bisphenols (BPs) are non-intentionally added compounds in textiles, which can be released from clothes and exposure to humans can occur through dermal contact. The aim of this study was to assess the dermal exposure to bisphenol A (BPA), bisphenol S (BPS) and bisphenol F (BPF) in clothes of newborn and baby. BPA, BPF, and BPS (< LOQ) in clothes commercialized in Spain for pregnant women, newborn and children. In addition, exposure assessment and risk characterization were also carried out. Traces of BPA were found in all the samples, with a median concentration of 7.32 ng/g. The highest values were detected in textile samples made of polyester. Regarding natural fibers, higher concentrations of BPs were observed in garments made of conventional cotton than in those made of organic cotton, with a significant difference for BPA (1.24 vs. 0.38 ng/g, p < 0.05). Although toddlers have the highest dermal exposure to BPA per body weight ratio, pregnant women showed higher exposure to BPs than children. Hence, the non-carcinogenic risks associated to BPA exposure were below the unity, even under the upper bound scenario. However, risks could be underestimated because other exposure routes were not considered in this study. The use of BPA has been restricted in some food related products, therefore, BPA should also be regulated in the textile industry.	Sci Total Environ Vol.878 Pages 163122	10.1016/j.scitotenv.2023.163122	37001656	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0540	J. G. Hernández-Pérez, A. Valenzuela-Sánchez, D. S. López and L. Torres-Sánchez	2025	Racial/ethnic disparities in the association of environmental exposure to phthalates and bisphenols mixtures with diabetes mellitus: NHANES 2013-2016	We evaluated the association between urinary concentrations of phthalates/bisphenols mixtures and diabetes mellitus (DM) and yearly-controlled DM, stratified by sex, and race/ethnicity in 2715 adults from the 2013 to 2016 National Health and Nutrition Examination Survey. DM was self-reported or defined by glucose levels/hypoglycemic use. Poorly controlled DM was defined by HbA1c > 9%. Principal component analyses allowed to identify phthalates/bisphenols mixtures. Multivariable logistic regression models were fitted. Mexican American and Other Hispanic participants had the highest prevalence of DM (20.8%). Urinary concentrations of phthalates/bisphenols were higher in Mexican American than non-Hispanic White participants. Exposure to mixtures and "other races" participants. Conversely, the LOW/MH+ mixture was associated with higher DM odds, mainly among Mexican Americans. Racial/ethnicity seems to determine the association between the different exposure mixtures and DM prevalence and poorly-controlled DM.	Arch Environ Occup Health Vol.80 Issue 3-4 Pages 49-61	10.1080/19338244.2025.2480113	40102054	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0541	L. Heras-González, J. A. Latorre, M. Martínez-Beltrán, D. Espino, F. Olea-Serrano and M. Maricalvi-Arcas	2020	The relationship of obesity with lifestyle and dietary exposure to endocrine-disrupting chemicals	Phytoestrogens are natural components of plants, including numerous foods that form part of the habitual diet of humans and animals. They have similar estrogenic effects to those of synthetic endocrine disruptors such as monomers of plastic materials, e.g., polycarbonates and epoxy resins. The most frequently used monomer is bisphenol A (BPA), which has been found to migrate from drink and food packaging, plastic baby bottles, and the coating of cans. Numerous studies have associated exposure to endocrine disruptors with obesity, classifying them as obesogens. The objectives of this study were to estimate the dietary exposure to phytoestrogens and BPA in a population of schoolchildren in Granada (southern Spain) and to assess the relationship between exposure to these substances and obesity. The sample was composed of 81 children (39 boys and 42 girls) between 10 and 12 years old. The effects of the additional estrogenic burden on fighting overweight, as well as definitive conclusion has been reached. Thus, some authors consider that exposure to these substances could contribute activity to be positive at certain stages of life, whereas others regard it as posing a risk at any age. In the present population of children, the likelihood of normal weight versus obesity was significantly related to the total isoflavone intake (OR = 0.11; p = 0.039) as well as to the energy expenditure on physical activity, with lesser activity implying a greater risk of obesity (OR = 1.016; p = 0.001). Further research is warranted on the obesogenic effects of exposure to endocrine disruptors present in foods.	Food Chem Toxicol Vol.136 Pages 110983	10.1016/j.fct.2019.110983	31759064	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0542	L. Heras-González, D. Espino, M. J. Jimenez-Casquet, A. Lopez-Mora, F. Olea-Serrano and M. Maricalvi-Arcas	2022	Influence of BPA exposure, measured in saliva, on childhood weight	INTRODUCTION: Endocrine disrupters such as bisphenol A (BPA), BPA-glycidyl methacrylate, and other BPA-acrylate-based derivatives have been related to type 2 diabetes, the metabolic syndrome, and obesity, among other metabolic disorders. The objective of this study is to examine the influence of BPA exposure by saliva analysis and daily physical activity on the risk of overweight/obesity in schoolchildren from southern Spain. METHODS: The study included 300 children (53.3% girls) aged 7-10 years. Participants completed a questionnaire with four sections: participant data, including demographic information and family habits; semi-quantitative food frequency questionnaire; anthropometric variables; and physical activity variables. All participants underwent dental examination, when the presence of sealants/composites in each tooth and other dental characteristics were recorded. Saliva samples were collected from 150 children. RESULTS: The prevalence of overweight/obesity was 35.3%. The total consumption (GP + BCP) was higher in boys (OR = 1.01; p = 0.009) and living in towns with higher income (p = 0.0002). In children, we observed lower daily BPA indices in those who were less physically active (p = 0.008) and living in towns with higher income (p = 0.0002). In children, we observed lower daily BPA indices in those living in towns with higher income (p = 0.0002) and following a less western dietary pattern (p = 0.002), and higher daily BPA indices in those who were less physically active (p = 0.021). No significant associations were observed between daily BPA indices and BMI or AC. Despite this, the application of the daily BPA index identified factors associated with dietary BPA exposure and women's further examination in Spain and other understudied populations.	Front Endocrinol (Lausanne) Vol.13 Pages 1040583	10.3389/fendo.2022.1040583	36568119	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0543	L. M. Heinzberg, C. N. N. Bu, I. C. Hartle, S. M. Sereika, C. C. Choy, D. Wang, C. Sell-Ulberg, T. Nesari, M. S. Reupena, R. L. Duckham, J. J. Park, N. L. Hawley and N. C. Deziel	2020	Estimated Dietary Bisphenol-A Exposure and Adiposity in Samoan Mothers and Children	The Pacific Island nation of Samoa is marked by prevalent obesity and an increasing dependence on packaged foods likely to contain the endocrine disruptor bisphenol-A (BPA). We evaluated participant- and household-level factors associated with urinary BPA concentrations among 202 mother-child pairs enrolled in the Biorepository and Integrated Laboratory Analysis (BILA) Core of the Safer Chemicals, Healthy Families Program (SCHF). Urinary BPA exposure indices were estimated for 189 mothers (93 pairs by controlling intake from dietary questionnaires and creatinine concentration of BPA measured in fasted urine specimens. We observed moderate to strong correlations between mother-child daily BPA indices (Spearman's rho = 0.7, p < 0.0001). In mothers, we observed lower daily BPA indices in those who were less physically active (p = 0.008) and living in towns with higher income (p = 0.0002). In children, we observed lower daily BPA indices in those living in towns with higher income (p = 0.0002) and following a less western dietary pattern (p = 0.002), and higher daily BPA indices in those who were less physically active (p = 0.021). No significant associations were observed between daily BPA indices and BMI or AC. Despite this, the application of the daily BPA index identified factors associated with dietary BPA exposure and women's further examination in Samoa and other understudied populations.	Toxics. 2020 Sep 2:8(3):67.	10.3390/toxics8030067	32887300	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0544	A. L. Hefferan, M. J. Gomez-Ramos, C. Symecoliadi, D. J. Hare, S. Vijayasarathy, K. Thompson, J. F. Mueller, A. L. Poncanby and P. D. Sly	2020	Harmonizing analytical chemistry and clinical epidemiology for human biomonitoring studies. A case-study of plastic product chemicals in urine	There is an interdisciplinary interface between analytical chemistry and epidemiology studies with respect to the design, execution, and analysis of environmental epidemiology cohorts and studies. Enhancing meaningful communication between these disciplines is necessary to ensure that the data generated are fit for purpose. This paper presents a framework for harmonizing analytical chemistry and epidemiology through a reporting checklist for the design of human biomonitoring studies. We explain key analytical chemistry concepts, of blanks and limits of reporting and present a case-series of plastic product chemical exposure in prenatal urine specimens from the Barwon Infant Study.	Chemosphere Vol.238 Pages 124631	10.1016/j.chemosphere.2019.124631	31524608	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成根拠評価への進め、当該物質関連報文収集に基づき解釈。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については≤100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0545	H. He, F. Zhang, S. Zhou, S. Zhang, L. Wang, J. Li, Q. Zeng, Y. Zhu, J. Tian, J. Chang, L. Chang, Q. Lu, X. Miao, N. Shen and R. Zhong	2023	Interaction of metabolism-related pathway gene variants with bisphenol A exposure on serum lipid profiles	Bisphenol A (BPA) can be metabolized by metabolic enzymes and may induce abnormal lipid metabolism. We hypothesized that BPA exposure and its interaction with metabolism-related genes might be associated with serum lipid profiles. A cross-sectional study was conducted among 1,000 participants in Wuhan, China, from 2013 to 2014. Urinary BPA, serum lipid profiles, and 15 single-nucleotide polymorphisms (SNPs) in metabolism-related genes were measured. Linear regression and multivariate logistic regression models were used to examine the associations of BPA and SNPs with lipid levels. Multiple linear regression was used to analyze the interactions between BPA exposure and metabolism-related genes on serum lipid profiles. In the discovery stage, both in BPA and in SNPs Q-rs4646994 AA genotype, but not in individuals carrying rs4986938 AG or CC genotypes. The interaction between BPA exposure and metabolism-related genes (ADYBP1 rs4986938 and PON1 rs662) was also significant. In the discovery stage, both in BPA and in SNPs Q-rs4646994 AA genotype, but not in individuals carrying rs4986938 AG or CC genotypes. The interaction between BPA exposure and metabolism-related genes (ADYBP1 rs4986938 and PON1 rs662) was also significant.	Environ Toxicol Pharmacol Vol.101 Pages 104173	10.1016/j.etap.2023.104173	37302441	ヒト	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0546	H. He, Y. Dang, H. Wan, N. Sher, J. Li, Q. Zeng, J. Chang, Q. Lu, X. Miao, J. Tian and R. Zhong	2022	Urinary bisphenol A and its interaction with CYP17A1 rs743572 are associated with breast cancer risk	OBJECTIVE: Bisphenol A (BPA), a common endocrine disruptor, can be activated by cytochrome P450 (CYP) metabolizing enzymes and might influence the development of breast cancer (BC). We hypothesized that BPA exposure and its interaction with CYP-related genes might be associated with BC risk. METHODS: A case-control study was conducted among 1,000 participants in Wuhan, China, from 2013 to 2014. Urinary BPA was measured using high-performance liquid chromatography-high-resolution mass spectrometry. A set of tested CYP1 gene polymorphisms was genotyped using the Sequenom MassARRAY system. A multivariate logistic regression model was used to examine the associations of BPA and BPA-SNP interaction on BC risk. RESULTS: BC patients had a higher urinary BPA concentration than healthy individuals (P = 0.001). Each 1-unit increase in log-transformed urinary BPA was associated with a 46 % increased BC risk (95 % confidence interval (CI): 1.16, 1.77, P = 0.001). Individuals with the CYP17A1 rs743572 AA genotype showed a significantly higher BC risk than those with the GG genotype (OR = 1.45, 95 % CI, 1.01-2.08, P = 0.04). A significant BPA-CYP17A1 rs743572 interaction was found to be associated with a higher risk of BC (P-interaction = 0.026). Compared with low-BPA individuals carrying the rs743572 GG genotype, high-BPA individuals carrying the rs743572 AA genotype had the highest BC risk (OR = 2.13, 95 % CI, 1.31-3.47, P = 0.003, COCLI-03069). The positive association of BPA exposure with BC risk might be modified by CYP17A1 rs743572, providing evidence for the interaction effect of environment genes on the etiology of BC.	Chemosphere Vol.286 Issue Pt 3 Pages 131880	10.1016/j.chemosphere.2021.131880	34426286	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0547	G. Hatem, A. M. Faria, M. B. Porto, J. P. Taiwaks, A. Salomoa, C. Costa and J. Madureira	2025	Association between exposure to airborne endocrine disrupting chemicals and asthma in children or adolescents: A systematic review and meta-analysis	Various studies have explored the association between Endocrine Disrupting Chemicals (EDCs) exposure and children's and adolescents' respiratory health, showing potential long-term effects and links to asthma. This systematic review explores the association between exposure to seven EDC groups during school age and adolescence and asthma onset or exacerbation while highlighting the predominant compounds underlying these associations. Following PRISMA guidelines, 3 databases were searched, and 2,000 publications were identified. After applying inclusion and exclusion criteria, 15 studies were selected for review. Meta-analyses for Bisphenols (Bisphenol A and S) and Parabens (methyl- and butyl-) were performed, yielding pooled Odds Ratios (OR) and their 95% Confidence Intervals (CI). Risk of bias was assessed using the newcastle-ottawa scale, and the quality of evidence for each outcome was measured using the GRADE approach. The review included 66893 children and adolescents from 10 observational studies, most with a low risk of bias in the studied domains. The pooled OR for asthma onset was significant for phthalates in dust samples (OR=1.31, CI:1.03-1.65). Due to limited studies, the overall pooled effects for the other groups could not be computed. Individual studies also found significant associations between asthma onset and urinary concentrations of Bisphenols (OR=1.13, CI:1.08-1.18) and co-exposure to Bisphenols and Parabens (OR=1.09, CI:1.03-1.16), with asthma onset included adverse effects (OR=1.36, CI:1.05-1.58) and rhinitis (OR=1.23, CI:1.01-1.51), urinary Bisphenol S (OR=1.82, CI:1.32-1.70), Bisphenol A (OR=1.57, CI:1.07-2.30) and parents (OR=2.08, CI:1.93-5.26), and exposure to Bisphenols (OR=1.13, CI:1.08-1.18) and Parabens (OR=1.09, CI:1.03-1.16) and asthma onset (OR=1.36, CI:1.05-1.58). Exposure to EDCs was significantly associated with asthma onset and exacerbation in children and adolescents, namely for phthalates, bisphenols A and S, parabens, alcohol, and zinc. Further research is recommended to focus on the impact of synergistics and co-exposure to other indoor air pollutants.	Environ Pollut. 2025 Mar 15:369:125830.	10.1016/j.envpol.2025.125830	39929430	ヒト	-	地理システマティックレビュー	1	1	-	-	-	システマティックレビュー・メタアナリシス	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0548	C. Hartmann, T. Jamnik, S. Weiss, M. Gödl, Y. Fareed, Y. Salmaa, D. Braun, M. Flasch, B. Warth and M. Uhl	2023	Results of the Austrian Children's Biomonitoring Survey 2020 part A: Per- and polyfluorinated alkylated substances, bisphenols, benzophenones, triclosan, polycyclic aromatic hydrocarbon metabolites, and cotinine Each of the children was exposed to 22 Cl substances simultaneously. Correlations were found between compounds of the same and of divergent substance groups, supporting the strong need to consider multiple exposures and mixture effects. Eight compounds, including perfluorohexanoic acid (PFHxA), perfluorooctanoic acid (PFOA), methyl paraben (4-MeP), and bisphenol A (BPA), could be quantified in >90% of the samples. Perfluorooctane sulfonic acid (PFOS) was detected in all urine samples. The PFAS group the median of detectable substances ranged between <0.0002 µg/l for perfluorodecanoic acid (PFDA) and 0.002 µg/l for PFHxA. For other environmental contaminants investigated, a maximum urinary level of 0.5 µg/l was found for BPA, 0.2 µg/l for triclosan (TCS), 0.3 µg/l for benzophenone-3 (BP-3), and 0.4 µg/l for 4-MeP. Cotinine was detected in 97% of the urine samples. Cotinine or an acceptable daily intake is currently in force. Based on a recently proposed TDI for BPA, daily intakes of all children exceeded this value. A cumulative risk assessment for four parabens and showing exceedances of acceptable exposures. The results demonstrate simultaneous exposure to several different chemicals, with the majority showing impact on the endocrine system being of particular concern with respect to mixture effects. Further assessments with a stronger focus on mixtures are warranted. The results also highlight the need of policy actions as foreseen in the EU Chemicals Strategy for Sustainability.	Int J Hyg Environ Health Vol.249 Pages 114123	10.1016/j.ijheh.2023.114123	36738493	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0549	J. C. Hartle, R. S. Zawadski, J. Rigdon, J. Lam and C. D. Gardner	2022	Development and evaluation of a novel dietary bisphenol A (BPA) exposure risk tool	BACKGROUND: Exposure to endocrine disrupting chemicals such as bisphenol A (BPA) is primarily from the diet through canned foods. Characterizing dietary exposures can be conducted through biomonitoring and dietary surveys, however, these methods can be time-consuming and challenging to implement. METHODS: We developed a novel dietary exposure risk questionnaire to evaluate BPA exposure and compared these results with BPA levels in urine. The questionnaire was administered to 100 participants in 2015 and 2016. Participants were classified as high BPA exposure or low BPA exposure based on their responses. A high BPA exposure foods score identified from the dietary results and used to estimate BPA exposure. Linear regression models estimated the association between BPA exposure and questionnaire responses. A composite risk score was developed to summarize questionnaire responses. RESULTS: In questionnaire data, 35% of participants ate canned food every week. A composite exposure score validated that the dietary exposure risk questionnaire captured known BPA exposure. In the linear regression models, utilizing questionnaire responses, ca. 15 % dietary recall data participants eating canned foods ≥ 2 times/week (vs. never consumed) 0.79 more servings (p = 0.001) of high BPA exposure foods, and those eating canned foods 3 + times/week (vs. never) consumed 0.89 more servings (p = 0.013) of high BPA exposure foods. Participants eating ≥ 3 servings/day (vs. never consumed) 0.86 more total grams of high BPA exposure foods (p = 0.046). CONCLUSIONS: Dietary exposure risk questionnaires are effective and inexpensive approach in 24-hour dietary recalls to quantify dietary BPA exposure with low participant burden. TRIAL REGISTRATION: The trial was prospectively registered at clinicaltrials.gov as NCT02560909 on April 8, 2015.	BMC Nutr Vol.8 Issue 1 Pages 143	10.1186/s40795-022-00634-4	36474269	ヒト	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0550	M. E. U. Haq, M. S. H. Akash, S. Sabir, M. H. Mahmood and K. Rehman	2020	Human exposure to bisphenol A through dietary sources and development of diabetes mellitus: a cross-sectional study in Pakistani population	Bisphenol A (BPA) is considered as xenoestrogen, a crucial component utilized for the manufacturing of plastic products. It has a potential to disrupt the endocrine system and induces endocrine related metabolic disorders. The present study investigated the role of BPA exposure in development of diabetes mellitus in Pakistani population. A total of 1000 participants (500 diabetic and 500 healthy) was conducted. BPA was conducted on 300 participants among which 50.70% participants were diabetic and 38.21% were non-diabetic. We developed a structured questionnaire to gathered sociodemographic data, and collected their urine and blood samples for the estimation of BPA and various biomarkers as risk factors of DM, respectively. Pearson correlation coefficient was determined for urinary BPA levels and DM risk factors. Urinary BPA values were adjusted for confounders. Sociodemographic data shows that urinary BPA level was significantly higher (p < 0.05) in obese people (BMI > 27) living in semi-urbanized areas. BPA was detectable in 70% of study participants. Urinary BPA level was found to be higher in diabetic participants compared with that of non-diabetics. A significant correlation is observed between BPA exposure and DM risk factors. We found that urinary BPA concentration was significantly associated with DM (OR = 1.14, 95% CI = 1.05-1.24, p = 0.002). Diabetic participants (OR = 1.14, 95% CI = 1.05-1.24, p = 0.002) who consume rice more frequently (OR = 1.14, 95% CI = 1.05-1.24, p = 0.002) were found to be at risk of DM. Our study adds to the growing body of evidence supporting the role of BPA exposure as a risk factor for DM and may be associated with higher glycemic index, increased pro-inflammatory and oxidative stress biomarkers, dyslipidemia, and impaired functioning of the liver and kidney. Heating food in plastic containers and consumption of packed food items are the main sources of BPA exposure which are positively associated with DM.	Environ Sci Pollut Res Int Vol.27 Issue 21 Pages 26262-26275	10.1007/s11356-020-09044-0	32361967	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0551	K. Hao, J. Luo, J. Sun, H. Ge and Z. Wang	2021	Associations of urinary bisphenol A and its alternatives bisphenol S and F concentrations with depressive symptoms among adults	BACKGROUND: Bisphenol A (BPA) and bisphenol F (BPF), as substitutes for bisphenol A (BPA), are synthetic compounds detected increasingly frequently in plastics and resins. BPA, BPS, and BPF are endocrine disruptors with similar effects on depressive symptoms. This study aims to evaluate the effects of these compounds on depressive symptoms in adults. METHODS: We used data from the U.S. National Health and Nutrition Examination Survey (NHANES) 2007-2016 for BPA (N = 7,280) and NHANES 2013-2016 for BPS and BPF (N = 2,707). BPA, BPS, and BPF were detected in urine samples. Depressive symptoms were examined using a two-item patient health questionnaire (PHQ-9). Logistic regression models were used to investigate the effects of urinary BPA, BPS, and BPF. Systemic biomarkers and multiple logistic regression models were used to investigate the association between maternal BPA exposure (continuous [ln-transformed or divided into tertiles] and the relative differences in ADHD and ASD problems scores and the odds (OR) of an ADHD and autism score above the 90th percentile. RESULTS: In the prospective Odense Child Cohort, BPA was measured in urine samples collected in gestational week 28 and adjusted for osmolality. ADHD and ASD symptoms were assessed with the use of the ADHD rating scale and ASD scale, respectively, derived from the Child Behavior Checklist completed when children were 5 and 7 years old. RESULTS: In the general population, urinary BPA, BPS, and BPF concentrations, an depressive symptoms. RESULTS: In the general population, no significant association was observed between urinary BPA, BPS, and BPF and depressive symptoms. However, in stratified analyses, urinary BPS was positively associated with depressive symptoms in participants aged 20 years or younger (OR: 1.61, 95% CI: 1.01, 2.56, P = 0.045) and in participants with a family income-to-poverty ratio ≤ 1.30 (OR: 1.61, 95% CI: 1.01, 2.56, P = 0.045). In addition, urinary BPA was negatively associated with depressive symptoms (OR: 0.14, 95% CI: 0.03-0.59) in elderly women (≥65 years old). CONCLUSIONS: This study indicated that exposure to BPA and BPS was positively associated with depressive symptoms, especially in men. However, BPF was negatively associated with depressive symptoms in elderly women.	Chemosphere Vol.279 Pages 130573	10.1016/j.chemosphere.2021.130573	33878692	ヒト	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0552	J. B. Hansen, N. Bilenberg, C. A. G. Timmermann, R. C. Jensen, H. Frederiksen, A. M. Andersson, H. B. Kyhl and T. K. Jensen	2021	Prenatal exposure to bisphenol A and autistic- and ADHD-related symptoms in children aged 2 and5 years from the Odense Child Cohort	BACKGROUND: Bisphenol A (BPA) is a non-persistent chemical with endocrine disrupting abilities used in a variety of consumer products. Fetal exposure to BPA is of concern due to the elevated sensitivity, which children have to endocrine disrupting chemicals. OBJECTIVES: To investigate the association between prenatal exposure to BPA and Attention Deficit Hyperactivity Disorder (ADHD) symptoms and symptoms of Autism Spectrum Disorder (ASD) in 2 and 5 year old Danish children. METHODS: In the prospective Odense Child Cohort, BPA was measured in urine samples collected in gestational week 28 and adjusted for osmolality. ADHD and ASD symptoms were assessed with the use of the ADHD scale and ASD scale, respectively, derived from the Child Behavior Checklist completed when children were 5 and 7 years old. RESULTS: In the general population, no significant association was observed between maternal BPA exposure (continuous [ln-transformed or divided into tertiles] and the relative differences in ADHD and ASD problems scores and the odds (OR) of an ADHD and autism score above the 90th percentile. In stratified analyses, urinary BPA was positively associated with ADHD symptoms in children aged 5 years (β = 0.13, 95% CI: 0.01, 0.25, p = 0.032) and in children aged 2 years (β = 0.16, 95% CI: 0.02, 0.30, p = 0.028). Urinary BPA was also positively associated with ASD symptoms in children aged 5 years (β = 0.13, 95% CI: 0.00, 0.26, p = 0.045). In addition, urinary BPA was associated with an increased OR of maternal urine samples were though the highest exposure tertile had the highest OR (OR = 1.7, 95% CI: 0.63-4.59) for children aged 2 years, no ADHD at age 5 years, or ADHD at age 5 years were found. Trends of elevated Odds Ratios (ORs) were seen among 5 year old children within the 3rd tertile of BPA exposure with an ASD score above the 75th percentile (OR = 1.60, 95% CI: 0.97-2.65), being stronger for girls (OR = 3.17, 95% CI: 1.30-8.28). A dose-response relationship was observed between BPA exposure and ASD score at 5 years of age (p-trend 0.08) in both boys and girls, but only significant in girls (p-trend 0.03). CONCLUSION: Our findings suggest that prenatal BPA exposure even in low concentrations may increase the risk of ASD symptoms which may predict later social abilities. It is therefore important to follow-up these children at older ages, measure their own BPA exposure, and determine if the observed associations persist.	Environ Health. 2021 Mar 12;20(1):24.	10.1186/s12940-021-00709-y	33712018	ヒト	-	コホート研究	1	1	-	-	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0553	W. M. Hussein, R. Al Rukibat, S. Janat-ar and M. Burkan Al-Zghou	2021	Exposure assessment of bisphenol A by drinking coffee from plastic cups	BACKGROUND: Human exposure to plastic and Bisphenol A (BPA) is very wide in food or beverage containers and baby bottles that have contacted polycarbonate and epoxy resin. Currently a traditional beverage in Arabian culture is served in plastic cups instead of glass cups on different occasions. OBJECTIVE: To evaluate the possible BPA load from the grade 5 drinking coffee plastic cups into the coffee and whether the use of a plastic cups instead of glass ones to serve hot Arabian coffee poses a health risk. MATERIALS AND METHODS: Oral administration of such coffee to three different groups of rats were undertaken. Each group consisted of 10 rats. The first group received 1 ml of coffee served in glass cups, the second group received 1 ml of coffee served in plastic cups, and the third group received 1 ml of coffee that had been left in plastic cups. Three concentrations of Bisphenol A were measured weekly later. Comprehensive examination was conducted and representative tissue samples were subjected to histopathological evaluation. RESULTS: In the control group receiving water kept in a glass cup had 24 ± 2 µg/L serum concentration and the second group rat 36 ± 4 µg/L in which the third group was 29 ± 6 µg/L. No significant parameter changes or histopathological findings were present in the studied animals. CONCLUSION: Bisphenol A can be leached from food-grade plastic cups into hot drinks within short period of time causing a significant impact to public health.	Rocz Panstw Zakl Hig Vol.72 Issue 1 Pages 49-53	10.32394/rpzh.2021.0146	33882786	動物	-	-	1	1	0	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0554	D. Ham, M. Ha, H. Park, Y. C. Hong, Y. Kim, E. Ha and S. Bae	2024	Association of postnatal exposure to mixture of bisphenol A, Di-n-butyl phthalate and Di-(2-ethylhexyl) phthalate with Children's IQ at 5 Years of age: Mothers and Children's environmental health (MOCEH) study	Early childhood is important for neurodevelopment, and exposure to endocrine disruptors such as bisphenol A (BPA) and phthalates in this period may cause neurodevelopmental disorders and delays. The present study examined the association between exposure to mixtures of BPA and three metabolites of phthalates in early childhood and IQ at 5 years of age. The Mother and Children's Environmental Health (MOCEH) study is a prospective birth cohort study conducted in Korea on 1751 pregnant women enrolled from 2006 to 2010. After excluding those without relevant data, 57 children were included in the final analysis. We measured urinary concentrations of BPA and phthalate metabolites during the second trimester and at 3 months. Intelligence was assessed using the Korean-Wechsler Intelligence Scale for Children-IV at the age of 5 years. Weighted quantile sum (WQS) regression and quantile g-computation were used to examine the associations between individual endocrine disrupting chemicals and the IQ at the children. Weighted Quantile Sum (WQS) regression and quantile g-computation were used to assess the association between exposure to mixtures of BPA and phthalate metabolites and IQ at 5 years of age. In the WQS regression model, a one-IQR increase in the mixture was associated with children's IQ (β = -4.93, 95% CI: -9.63, -0.23). In quantile g-computation, a one-quantile increase in the mixture was associated with lower IQ (β = -5.13, 95% CI: -9.68, -0.58). Among the components, MEP (β = -3.08, 95% CI: -6.18, 0.02) and MBP (β = -2.04, 95% CI: -4.08, 0.00) were associated with lower IQ (β = -5.13, P-value = 0.026) and BPA (β = -5.13, P-value = 0.026) were associated with lower IQ (β = -5.13, P-value = 0.026). Prenatal exposure to mixtures of BPA and phthalate metabolites was

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0558	C. Gys, M. Bastiaansen, L. Bruckers, A. Colles, E. Govarts, L. R. Martin, V. Verheyen, G. Koppen, B. Moreno, E. Den Hond, A. De Decker, G. Schoeters and A. Covaci	2021	Determinants of exposure levels of bisphenols in flemish adolescents	The broadly used industrial chemical bisphenol A (BPA), applied in numerous, consumer products, has been under scrutiny in the past 20 years due to its widespread detection in humans and the environment and potential detrimental effects on human health. Following implementation restrictions and phase-out initiatives, BPA is replaced by alternative bisphenols, which have not received the same amount of research attention. As a part of the fourth cycle of the Flemish Environment and Health Study (FLEHS IV, 2016-2020), we monitored the internal exposure to six bisphenols in urine samples of 225 adolescents (14-15 years old) from Flanders, Belgium (Dutch-speaking northern region of Belgium). Additionally, information on potential determinants of exposure was collected via questionnaires. Urinary concentrations of BPA and seven bisphenol analogs (BPS, BPF, BPAF, BPB, BPZ, BPP, BPM) were determined using automated solid-phase extraction coupled to ultra-high performance liquid chromatography-tandem mass spectrometry. Since chemicals with similar structures may co-occur in consumer products, we investigated the co-occurrence between bisphenol compounds. Additionally, we explored the temporal trends in the concentrations of bisphenols between 2011 and 2020 by comparing the current results with those from previous cycles of the FLEHS. Creatinine corrected concentrations were used to account for urine dilution. Bisphenol concentrations were detected in almost all samples (>90%), except for BPAF (<LOD) and BPZ (<LOQ). Median concentrations were 0.70 µg/g creatinine for BPA, 0.11 µg/g creatinine for BPS, 0.10 µg/g creatinine for BPF, and 0.01 µg/g creatinine for BPB. Co-occurrence between bisphenols was observed, with BPA and BPS showing the strongest correlation (Spearman's rho = 0.69). Multivariate regression models revealed that urinary BPA concentrations were significantly associated with higher concentrations of the oxidative stress biomarker, 8-hydroxy-2'-deoxyguanosine (8-OHdG). BPA and BPF levels were higher in children from families with lower household income. Bisphenol concentrations were significantly influenced by some other personal (e.g. household income), food intake (e.g. vegetables and cow milk) and indoor housing characteristics (e.g. flooring). This is the first study to report longitudinal time trends of bisphenols in Japan. The presented findings imply that further research on bisphenols is warranted in the future to monitor whether these time trends continue.	Environ Res Vol.193 Pages 110567	10.1016/j.envres.2020.110567	33275923	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0559	C. Gys, Y. Ait Bamai, A. Araki, M. Bastiaansen, N. Caballero-Casero, R. Kishi and A. Covaci	2020	Biomonitoring and temporal trends of bisphenols exposure in Japanese school children	The widely used chemical bisphenol A (BPA), applied in various consumer products, has been under scrutiny in the past 20 years due to its widespread detection in humans and potential detrimental effects on human health. Following the implementation of restrictions and phase-out initiatives, BPA has been replaced by other structurally similar bisphenols, which have not yet received the same level of research attention. In this study, we aimed to 1) investigate the internal exposure to seven bisphenols in morning void urine samples collected from 7-year old children from Hokkaido, Japan and 2) assess possible time trends in the concentrations of bisphenols between 2013 and 2017. Information on demographic, indoor environment and dietary characteristics of participants was acquired through a self-administered questionnaire. All bisphenols were detected in >50% of samples, except for BPAF (<LOD) and BPZ (<LOQ). Median concentrations were 0.70 µg/g creatinine for BPA, 0.11 µg/g creatinine for BPS, 0.10 µg/g creatinine for BPF, and 0.01 µg/g creatinine for BPB. Co-occurrence between bisphenols was observed, with BPA and BPS showing the strongest correlation (Spearman's rho = 0.69). Multivariate regression models revealed that urinary BPA concentrations decreased significantly over the study time period (around 0.9 µg/g creatinine per year). Levels of BPS and BPF were higher in autumn compared to winter. Higher urinary BPF levels were significantly associated with higher concentrations of the oxidative stress biomarker, 8-hydroxy-2'-deoxyguanosine (8-OHdG). BPA and BPF levels were higher in children from families with lower household income. Bisphenol concentrations were significantly influenced by some other personal (e.g. household income), food intake (e.g. vegetables and cow milk) and indoor housing characteristics (e.g. flooring). This is the first study to report longitudinal time trends of bisphenols in Japan. The presented findings imply that further research on bisphenols is warranted in the future to monitor whether these time trends continue.	Environ Res Vol.191 Pages 110172	10.1016/j.envres.2020.110172	32919958	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0560	Z. Guo, X. Ren, P. Liu, Y. Deng, J. Biar, Y. Ga, B. Xu, X. Tang, X. Li, H. Huang, J. Liu and S. Lu	2024	Co-exposure to parabens, bisphenol A, and triclosan and the associations with dyslipidemia in Chinese older adults: The mediation effect of oxidative stress	Dyslipidemia is a prevalent metabolic disorder in older adults and has negative effects on cardiovascular health. However, the combined effect of parabens, bisphenol A (BPA), and triclosan (TCS) exposure on dyslipidemia and the underlying mechanisms remain unclear. This cross-sectional study recruited 881 individuals ≥65 years in Shenzhen, China. Morning spot urine samples were collected and analyzed for four parabens, BPA, TCS, and 8-hydroxy-2'-deoxyguanosine (8-OHdG), a typical biomarker for oxidative stress, using mass spectrometry. Blood samples were tested for lipid levels using an automated biochemical analyzer. Quantile-based g-computation (qgcomp), weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR) models were used to assess the joint effects of the mixtures. Mediation analysis was then conducted to explore the role of oxidative stress. Results showed that exposure to parabens, BPA, and TCS was positively linked with hypercholesterolemia (OR: 1.17, 95%CI: 1.04-1.31, P = 0.009), hypertriglyceridemia (OR: 1.19, 95%CI: 1.06-1.33, P = 0.003), dyslipidemia (OR: 1.17, 95%CI: 1.04-1.31, P = 0.009), low high-density lipoprotein cholesterolemia (OR: 1.18, 95%CI: 1.05-1.33, P = 0.005), Methylparaben (MeP), n-propyl paraben (PrP), and butylparaben (BtP) were the major contributors. 8-OHdG mediated 9.9% and 13.9% of the overall effect of the examined chemicals on hypercholesterolemia and hypertriglyceridemia, respectively (all P < 0.05). Our study indicated that co-exposure to parabens, BPA, and TCS is associated with dyslipidemia and oxidative stress partially mediates the association. Future research is needed to explore additional mechanisms underlying these relationships.	Environ Res Vol.262 Issue Pt 1 Pages 119835	10.1016/j.envres.2024.119835	39181298	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0561	Y. Guo, C. Liu, Y. H. Dang, J. Ning, L. Yu and J. L. Wu	2023	Association between Bisphenol A exposure and body composition parameters in children	BACKGROUND: Although there is evidence linking Bisphenol A (BPA) exposure to obesity, research examining its relationship with body composition parameters in young children is limited. METHODS: A cross-sectional investigation was conducted on 280 preschool children aged between 3 and 6 years in Guangzhou, China. BPA exposure was assessed through urine samples using ultra-high performance liquid chromatography-tandem mass spectrometry. Body composition parameters were measured using bioelectrical impedance analysis. Multivariate linear regression models (MLR), BKMR, and WQS were employed to assess the relationship between BPA exposure and body composition parameters. RESULTS: The geometric mean (GM) of urinary BPA concentration was 1.49 μg/L, and creatinine-adjusted BPA concentration was 0.92 μg/g (CR 0.92). After adjusting for confounders, each 1-fold increase in BPA levels was significantly associated with body mass index (BMI) (β = 0.19, 95%CI: 0.04, 0.34), BMI z-score (β = 0.11, 95%CI: 0.04, 0.18), fat mass (β = 0.43, 95%CI: 0.03, 1.82), and percent body fat (β = 3.44, 95%CI: 1.17, 5.71) after adjusting for potential confounding factors. Similarly, adjusted models with log2-BCI transformed creatinine-adjusted BPA concentrations as a continuous variable showed similar trends. Positive linear associations were observed between quartiles of BPA concentrations and body composition parameters, with the highest coefficients in the fourth quartile. CONCLUSION: Our study provides further evidence of positive correlations between BPA exposure and body composition parameters in children aged 3 to 6 years. These findings highlight the potential health risks associated with obesity-related body composition parameters in young children. Further investigations are needed to confirm this association and explore the underlying mechanisms.	Front Endocrinol (Lausanne) Vol.14 Pages 1180505	10.3389/fendo.2023.1180505	37274319	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0562	X. Guo, D. Zhao, J. Meng, W. Hu, B. Wu, X. Wang, W. Su, M. Meng, G. Qu and Y. Sun	2023	Association of a mixture of phthalates and phenols with frailty among middle-aged and older adults: A population-based cross-sectional study	BACKGROUND: Frailty is a complex geriatric syndrome caused by degenerative changes in the body or various chronic diseases. The use of personal care and consumer products is associated with a wide range of health outcomes, but its relationship with frailty remains unknown. Therefore, our primary aim was to explore the potential links between exposure to phenols and phthalates, either separately or in combination, and frailty. METHODS: The exposure levels of phthalates and phenols were evaluated through the measurement of metabolites in urine samples. Frailty status was assessed by a 36-item frailty index with values ≥ 0.25 indicating frailty. Weighted logistic regression was used to explore the relationship between individual chemical exposure and frailty. In addition, multi-pollutant strategies, WQS, BKMR, and qgcomp, were used to examine the joint effect of chemical mixture on frailty. A series of subgroup analyses and sensitivity analyses were conducted as well. RESULTS: In the multivariate logistic regression model, each unit increase in natural log-transformed MEP, MBP, MBzP, MEHP, MEHHP, MEOHP, MECPP, MCPP, 2,4-DCP, and 2,5-DCP was significantly associated with a 1.09-, 1.11-, 1.08-, 1.08-, 1.08

別添-2 統合文献リスト

通権性評価（動物）1：該当、0：該当しない

通権性評価（疫学）1：該当、0：該当しない

通権性評価（in vitro）1：該当、0：該当しない

通権性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通権性基準不適合と判断されるもの以外を後続性評価へ進め、当権性評価段階で原著に基づき精査。

判断評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通権性評価基準適合（1534報）	依権性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0571	C. Gundacker, K. Graf-Rohmeißer, M. Gencik, M. Hengstschläger, K. Hohenauer, P. Rosa, R. Kroismayr, I. Offenthaler, V. Plichta, T. Reischer, J. Taufi, W. Raffelsberg, S. Scharf, B. Köhler-Vallant, Z. Dellosen, S. Wells and M. Uhl	2021	Gene Variants Determine Placental Transfer of Perfluoroalkyl Substances (PFAS), Mercury (Hg) and Lead (Pb), and Birth Outcome: Findings From the UmMuKi Bratislava-Vienna Study	Prenatal exposure to perfluoroalkyl substances (PFAS), bisphenol A (BPA), lead (Pb), total mercury (THg), and methylmercury (MeHg) can affect fetal development. Factors influencing placental transfer rate of these toxins are poorly investigated. Whether prenatal exposure to pollutants has an effect on birth weight is incompletely understood. We therefore aimed (1) to determine placental transfer rates of PFAS, BPA, Pb, Thg, and MeHg, (2) to analyze relationships between fetal exposure and birth outcome and (3) to analyze gene variants as mediators of placental transfer rates and birth outcome. Two hundred healthy pregnant women and their newborns were recruited in Vienna (AUT) and Bratislava (SVK) between 2012 and 2014. PFAS, BPA, Pb, Thg, and MeHg were measured in maternal blood, cord blood, and term placenta. Genotyping was performed for some placental transfer genes. Associations between exposure and birth outcome were assessed by survey-regression models. Data and tissue samples from 200 mother–child pairs were interviewed by trained PhDs or from maternal and newborn blood. Genotype information was determined by real-time PCR for five maternal and newborn blood. Genotype information was determined by real-time PCR for five maternal and placental genes. Genotype–phenotype associations were analyzed by categorical regression and logistic regression analysis. Specific gene systems were associated with altered placental transfer of PFOS (ABCA3 rs4149561, ABCG2 rs2231142, GST TyrRNAse, GSTT1 del, ABCC1 rs246221 and PLTP rs7679; dual (dual). A certain combination of these gene polymorphisms (ABCC1 rs246221, ABCG2 rs2231809, HFE H63dDGal) was over-represented in newborns small for gestational age. 95% of Austrian and 75% of Slovakian mothers had levels exceeding the HBM guidance value (1.7 µg/L) of the German HBM Commission for PFOA. 13% of newborns and 38% of women had Pb levels above 35 µg/kg, an exposure limit for the BMBS (50 of 52 µg/L set by the European Food Safety Authority (EFSA). Our findings point to the need to minimize perinatal exposures to protect fetal health, especially those genetically predisposed to increased transplacental exposure.	Front Genet. 2021 Jun 16:12:664946.	10.3389/fgene.2021.664946	34220941	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0572	P. Gul, N. Celik, F. B. Ozgenc, F. Demirkaya-Miloglu, A. Kizilkaci and N. Seven	2021	Effects of Bisphenol A Released From Composite Fillings on Reproductive Hormone Levels in Men	OBJECTIVES: Composite resins are the most preferred filling material because of their excellent aesthetic qualities. However, a filling material should also be biocompatible as well as aesthetic. The aim of this study was to determine the short-and long-term effects of bisphenol A (BPA) levels and to examine the effects of serum BPA on reproductive hormone levels after healthy men were treated with composite fillings. METHODS: Eighteen healthy males each received 2 composite restorations. Saliva and blood samples of subjects were collected before resin application and 1 day and 1, 3, and 5 weeks after the resin was applied. BPA amounts in samples were analyzed by high-performance liquid chromatography. Serum testosterone, luteinizing hormone, follicle-stimulating hormone, and prolactin levels were measured by chemiluminescence assay kits. Statistical analysis of data was made using Friedman, Wilcoxon signed-ranks, and Mann-Whitney U tests (α = 0.05). RESULTS: The amount of BPA released from the composite resins over time was not significantly elevated in either saliva or serum (P > 0.1). In addition, serum BPA levels were significantly higher than saliva BPA levels for both composites. (P < .05), but saliva and serum BPA levels were not statistically different when comparing the 2 composites. (P > .05). CONCLUSIONS: BPA from composite resins used in this study did not significantly alter serum hormone levels.	Int Dent J Vol.71 Issue 4 Pages 343-351	10.1016/j.identj.2020.12.008	33583564	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0573	A. Guilbert, M. Rolland, I. Pin, C. Thomsen, A. K. Sakhi, A. Sabaredzovic, R. Slama, K. Guldvik and C. Philippat	2021	Associations between a mixture of phenols and phthalates and child behaviour in a French mother–child cohort with repeated assessment of exposure	BACKGROUND: Synthetic phenols and phthalates can interfere with biological pathways involved in brain development. Despite the high within-subject temporal variability of urinary concentrations observed for their metabolites, studies investigating effects of phenols and phthalates on child behaviour often relied on a limited number of spot biospecimens to assess exposure. Besides, the majority did not consider relative effects, i.e. effects of the whole mixture of chemicals. METHODS: We measured 2 phenols (bisphenol A and triclosan) and 5 phthalate metabolites (monoethyl phthalate and 4 low-molecular-weight phthalates) in 2 urine samples collected during pregnancy in 420 mother–child pairs from the French SEPAGES cohort. Child behaviour was evaluated at two years using the Child Behaviour Checklist 1.5-5 (CBCL). Associations between a mixture of biomarkers of exposure and externalizing and internalizing behaviour scores were studied using adjusted Weighted Quantile Sum (WQS) regressions with a repeated holdout validation (100 repetitions). RESULTS: The mixture was associated with higher scores on the externalizing and internalizing behaviour scores in the whole population, indicating greater risk of behavioural problems. Overall baseline for children suggested stronger associations in girls than boys. On average, girls in the highest WQS quintile had CBCL externalizing T-scores 3.42 (95% CI: 0.86, 5.98) higher than girls in the lowest quintile, and internalizing T-scores 3.32 (95% CI: 0.22, 6.41) higher. Boys had 1.47 (95% CI: -0.82, 3.76) and 1.17 points (95% CI: -0.86, 3.40) higher scores for the associations observed in girls were bisphenol A (weight of 28%), triclosan (17%) and monoethyl phthalate (MEP, 16%) for the externalizing score and MEP (39%), mono-benzyl phthalate (MBzP, 19%) and mono-n-butyl phthalate (MnBP, 16%) for the internalizing score. DISCUSSION: Our results suggest adverse associations between in utero exposure to a mixture of phenols and phthalates and child behaviour, mainly in girls. Public health consequences may be substantial due to the widespread exposure of the population to these compounds.	Environ Int. 2021 Nov:156:106697.	10.1016/j.envint.2021.106697	34147998	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0574	L. Gu, Z. Wang, Y. Pan, H. Wang, L. Sun, L. Liu, W. . i. Zhong and W. B. Zhang	2023	Associations between mixed urinary phenols and parabens metabolites and bone mineral density: Four statistical models	Phenols and parabens widely exist in personal care and consumer products and have been proved to be endocrine disrupting chemicals that could disturb bone metabolism. The current studies focusing on the associations between phenols and parabens with bone mineral density (BMD) does contradictory conclusions. Considering the bias might be due to not considering the effects of mixed exposure, we conducted the first cross-sectional study to investigate the associations of both single and mixed metabolites of phenols and parabens with BMD in three populations by setting up four models: generalized linear regression model (GLM), weighted quantile sum (WQS) regression, quantile g-computation (QGC) and Bayesian kernel machine regression (BKMR) in the National Health and Nutrition Examination Survey (NHANES) database. We found that the association between the mixtures and total femur's BMD in men was significantly negative. Bisphenol A (BPA) was shown to contribute most to the negative association in the BKMR model, and this negative association was also confirmed in the GLM model with -β coefficient (95% CI) being -0.022 (-0.041, -0.003). The relationships between the mixtures and femoral neck and trochanter BMD in postmenopausal women were significantly positive. Benzophenone-3 (BP-3) played the most significant role in the positive association with trochanter BMD, as confirmed by the WQS, qgcomp and BKMR models, and this positive association was also verified by the GLM model with β coefficient (95% CI) being 0.01 (0.00, 0.02). In conclusion, the association between the mixed phenols and parabens and BMD was negative in men and positive in postmenopausal women with BP-3 as the main gender-specific. This study might provide new ideas for the prevention and treatment of osteoporosis and the control of personal care and consumer products containing phenols and parabens in the future.	Chemosphere Vol.311 Issue Pt 2 Pages 137065	10.1016/j.chemosphere.2022.137065	36334755	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0575	M. N. Grohs, J. E. Reynolds, J. Liu, J. W. Martin, T. Pollock, C. Lebel and D. Dewey	2019	Prenatal maternal and childhood bisphenol a exposure and brain structure and behavior of young children	BACKGROUND: Bisphenol A (BPA) is commonly used in the manufacture of plastics and epoxy resins. In North America, over 90% of the population has detectable levels of urinary BPA. Human epidemiological studies have reported adverse behavioral outcomes with BPA exposure in children; however, corresponding effects on children's brain structure have not yet been investigated. The current study examined the associations between prenatal maternal and childhood BPA exposure and white matter microstructure in children aged 3 to 5 years, and investigated whether brain structure mediated the association between BPA exposure and child behavior. METHODS: Participants were 96 mother-child dyads from the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort. Maternal urine samples were collected during pregnancy and from children at 3 years of age (one sample/participant) to quantify BPA concentrations. Diffusion tensor imaging (DTI) scans at age 3 (n = 67) and 5 (n = 51) were used to assess white matter microstructure. Maternal and childhood BPA and children's functional anisotropy and mean diffusivity of 12 isolated white matter tracts were investigated, controlling for urinary creatinine, child sex, and age at the time of MRI. Post-hoc analyses examined alterations in white matter associated the relationship of BPA and children's scores on the Child Behavior Checklist (CBCL). RESULTS: Prenatal maternal urinary BPA was significantly associated with child mean diffusivity in the splenium and right inferior longitudinal fasciculus. Splenium diffusivity mediated the relationship between maternal prenatal BPA levels and children's internalizing behavior (indirect effect: β = 0.04, 95% CI = 0.01, 0.08). Maternal prenatal BPA was also associated with altered splenium diffusivity and white matter microstructure. CONCLUSIONS: This study provides preliminary evidence that the neural correlates of BPA exposure in humans. Our findings suggest that prenatal maternal exposure to BPA may lead to alterations in white matter microstructure in preschool-aged children, and that such alterations mediate the relationship between early life exposure to BPA and internalizing problems.	Environ Health. 2019 Oct 15;18(1):85.	10.1186/s12940-019-0528-9	31615514	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0576	V. Gounden, M. Zain Waraiatly, T. Magwai, R. Naidoo and A. Chuturgoon	2019	A pilot study: Bisphenol-A and Bisphenol-A glucuronide levels in mother and child pairs in a South African population	Exposure to Bisphenol A (BPA) during early development particularly in utero has been linked to a wide range of pathology. The aim of this study was to determine serum levels of BPA and its naturally occurring metabolite BPA glucuronide (BPA-g) in South African mother-child pairs. METHODS: Third trimester serum maternal samples and matching cord blood samples were analysed for BPA and BPA-g using LC-MS/MS. RESULTS: Ninety maternal and child pairs were analysed. BPA was detectable in more than 70% of maternal and cord blood samples. Spearman correlation demonstrated significant positive correlation between maternal and cord BPA and BPA-g levels, with correlation coefficients of 0.882 and 0.711, respectively. A significant positive association between cord BPA levels and child birth weight (p = 0.02) as well as with maternal BMI (p = 0.03) was noted. CONCLUSION: This is the first study to describe the presence of detectable BPA levels using LC-MS/MS methodology in a South African population.	Reprod Toxicol. 2019 Oct:89:93-99.	10.1016/j.reprotox.2019.07.008	31302198	ヒト	生殖発生	-	-	-	-	-	-	パイロット研究	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0577	V. Gounden, M. Z. Waraiatly, T. Magwai, R. Naidoo and A. Chuturgoon	2021	A pilot study: Relationship between Bisphenol A, Bisphenol A glucuronide and sex steroid hormone levels in cord blood in A South African population	Exposure to Bisphenol A (BPA) during early development particularly in utero has been linked to a wide range of pathology. The aim of this study was to examine the relationship of BPA and its naturally occurring metabolite BPA glucuronide (BPA-g) with sex steroid hormone levels in South African mother-child pairs. Third trimester serum maternal samples and matching cord blood samples were analysed for BPA, BPA-g and sex steroid hormone using liquid chromatography tandem mass spectrometry (LC-MS/MS). Sixty maternal and child pairs were analysed. Rank correlation demonstrated a significant positive relationship between cord blood maternal and cord blood BPA (p = 0.002) and maternal BPA levels (p = 0.02) respectively. Conditional testosterone from male infants showed a negative Spearman's correlation (r = -0.5, p = 0.02) with maternal BPA-g. There was no statistical difference in their testosterone levels in comparison between male and female infants. The findings of the current study indicate a significant relationship between some key sex steroid hormones, namely testosterone, dihydrotestosterone and estradiol and fetal exposure BPA.	Reprod Toxicol. 2021 Mar:100:83-89.	10.1016/j.reprotox.2021.01.004	33453334	ヒト	性ホルモン	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0578	V. Gounden, R. N. Naidoo and A. Chuturgoon	2024	A pilot study: relationship between Bisphenol A, Bisphenol-glucuronide and total 25 hydroxy vitamin D in maternal-child pairs in a South African population	INTRODUCTION: Exposure to Bisphenol A (BPA) during early development particularly in utero has been linked to a wide range of pathology. Over the last two decades the importance of vitamin D in maternal and child health has been highlighted. The aim of this pilot study was to examine the relationship of BPA and its naturally occurring metabolite BPA glucuronide (BPA-g) with 25-hydroxy vitamin D (25(OH)D) levels in South African mother-child pairs. METHODS: Third trimester serum maternal samples and matching cord blood samples were analysed for BPA and BPA-g using liquid chromatography tandem mass spectrometry (LC-MS/MS) and 25(OH)D and 25(OH)D2 using high-performance liquid chromatography. A total of 98 maternal and child pairs were analysed. RESULTS: More than fifty percent of maternal-child pairs were noted to be vitamin D deficient (<50 nmol/L). Rank correlation demonstrated a significant positive relationship between maternal and cord blood BPA (p = 0.002) and maternal BPA levels (p = 0.02) respectively. A significant positive association between maternal and cord BPA-g concentrations. Analysis of covariance after controlling for confounders showed a significant relationship between cord BPA-g levels and cord 25(OH)D levels (p-0.01) as well as between maternal BPA-g levels (p-0.02) and cord total 25(OH) levels (p-0.02). DISCUSSION: The findings of the current study indicate a possible relationship with BPA/BPA-g and fetal/early infant Vitamin D levels that needs to be further investigated in this population.	Front Endocrinol (Lausanne). 2024 Nov 28:15:1108969	10.3389/fendo.2024.1108969	39669493	ヒト	その他(ビタミンDレベル)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0579	P. González-Palacios, V. Ramírez, C. Murteiagudo, A. Zafra-Gómez and A. Rivas	2025	Bisphenol A exposure and behavioral outcomes in children: A systematic review and meta-analysis of evidence limited to the BASC assessment tool	BACKGROUND: The growing concern about exposure to endocrine disrupting chemicals (EDCs), and their effects on human health, especially the possible neurobehavioral effects in children, makes a review of the scientific evidence on the subject important. The study conducts a systematic review and applies meta-analysis to determine whether there is a relationship between bisphenol exposure and behavioral development in children, as measured by the Behavioral Assessment System for Children (BASC). METHODS: In June-and-July 2023, Scopus, Web of Science, and Medline and Embase via Ovid were searched to search for studies within the scope of this study. A total of 1967 articles were found, of which 19 were analyzed. Finally, 13 studies met the inclusion criteria for systematic review and 7 for the meta-analysis. The studies measured in the meta-analysis were grouped into three categories: externalizing behaviors, internalizing behaviors, and behavioral symptoms index. The Newcastle-Ottawa Scale was used to assess the quality of the studies. Most of the studies found no significant associations, and no consistency in the results obtained. The heterogeneity in the design of the studies made it impossible to perform sensitivity results in the application of meta-analysis. CONCLUSIONS: There is a non-based differentiation in the behavioral effects associated with bisphenol exposure, as bisphenols affect boys and girls differently, potentially through mechanisms involving estrogen receptors, among other biological pathways. SIGNIFICANCE: Our study highlights the need to improve and homogenize the design and results of epidemiological studies, to extract data effectively. More results are needed to be able to draw conclusions.	Neurosci Biobehav Rev. 2025 Sep:176:106274.	10.1016/j.neubiorev.2025.106274	40614948	ヒト	発達神経/メタアナリシス	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0580	N. González, M. Marquès, S. C. Cunha, J. O. Fernandes, J. L. Domingo and M. Nadal	2020	Biomonitoring of co-exposure to bisphenols by consumers of canned foodstuffs	For new occupationally exposed adults, dietary intake is the main route of exposure to bisphenols (BPs), with canned foodstuffs playing a key role. This study was aimed at biomonitoring bisphenol S (BPS) and 5 more BP analogues (BPA, BPE, BPF, BPAP and BPZ) in pool urine and blood samples of a cohort of adults, who followed a diet based on a high consumption of canned food. To the best of our knowledge, this is the first study aimed at assessing the co-exposure of BP analogues in food and biological samples after a two-day duplicate diet study. The recruitment and dietary exposure was 3.27 and 0.180 µg/kg body weight/day for the canned food consumers (CFC) group, and 0.0 and 0.0 µg/kg body weight/day for the non-canned food consumers (NCFC) group. BPA was detected in 100% of the urine samples of the CFC group, 78% for the canned diet group and 50% for the control group, while in blood it could be only quantified in 6% of the samples. The identification of other analogues was also scarce, as it could be the result of other potential exposure sources, such as personal care products (PCPs) or air inhalation. After 2 days, the excretion of BPA was considerably higher in the canned diet group subjects than those in the control group (7.03 vs. 1.89 µg/day), confirming that diet was indeed foodstuffs are the main route of exposure to BPs. Anyhow, the temporary tolerable daily intake (t-TDI) established by the EFSA was not exceeded, even by those consumers with a diet rich in canned food. Moreover, spot urine samples provided accurate information about exposure and excretion of BPA, being the 6 h, instead of 24 h, the optimal sampling interval, when the collection of spot urine samples is not possible.	Environ Int Vol.140 Pages 105760	10.1016/j.envint.2020.105760	32371307	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0581	N. González, S. C. Cunha, C. Monteiro, J. O. Fernandes, M. Marquès, J. L. Domingo and M. Nadal	2019	Quantification of eight bisphenol analogues in blood and urine samples of workers in a hazardous waste incinerator	Bisphenol A (BPA) has been widely used in the manufacture of polycarbonate plastic and epoxy resins. In recent years, producers have started replacing BPA by other chemical analogues, such as bisphenol -S (BPS) and -F (BPF), all of them under the label "BPA-free". However, despite bisphenol (BP) analogues have a very similar structure, their endocrine disrupting properties could differ from those of BPA. Unfortunately, information on human exposure to BPA substitutes is still very limited. The present study was aimed at assessing the occurrence of eight BPs (BPA, BPS, BPF, BPE, BPB, BPAP, BPZ and BP-4) in biological samples from a controlled cohort of workers in a hazardous waste incinerator (HWI) located in Catalonia (Spain). Firstly, a chemical method to quantify simultaneously the eight BPs in blood and urine was optimized, being samples quantified by means of gas chromatography coupled to mass spectrometry (GC-MS). Furthermore, a biomonitoring study was performed by collecting samples of total blood and urine of 39 people working in the HWI. Among the 8 BP analogues assessed, BPA presented the highest levels in both biological samples, with mean total (free + conjugated) BPA concentrations of 5.48 and 0.66 µg/L in blood and urine, respectively. Free vs. total BPA levels presented a mean percentage of 79% in blood and 39% in urine. Beyond BPA, traces of BPB were also found in a single sample of blood. Furthermore, none of the remaining BP analogues was detected in blood or urine. Despite BPA has been regulated, it is still very present in the environment, being human exposure to this chemical still an issue of concern for the public health.	Environ Res Vol.176 Pages 108576	10.1016/j.envres.2019.108576	31299620	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0582	S. Gorkowski, M. Tarczyński, E. Demitzaki, K. Makowska and J. Wojtkiewicz	2022	Hair Sample Analysis of Residents from Olsztyn, Northeastern Poland, to Evaluate Levels of Bisphenol S and Bisphenol A: A Pilot Study	BACKGROUND:Bisphenol A (BPA) and its analogue bisphenol S (BPS), widely utilized in numerous fields of industry, may come into the environment and into human organisms. Hitherto, BPA was regarded as the bisphenol with the greatest significance in terms of human exposure and health consequences. However, due to the restrictions imposed on BPA, BPS has become more frequently used in many technologies. Their analysis has been increasingly used for biomonitoring of treatments in humans, but information about the coexistence of BPA and BPS in human hair is extremely scarce. The present study aimed to examine hair samples from 26 individuals from Olsztyn, northeastern Poland, to evaluate the levels of these 2 industrial pollutants. MATERIAL AND METHODS: The method used in the research was liquid chromatography with a fluorescence detector (LC-FLD). BPA was found in 77% of analytes examined and its concentrations ranged from 50 to 915 pg/mg (median 57 pg/g). The BPS concentrations were higher - from 120 to 1884 pg/mg (median 86.7 pg/g). We also found that gender, age, and the presence of artificial hair color had an effect on the BPA and BPS levels in the hair. CONCLUSIONS:This study has shown that hair samples may be useful in assessing the levels of bisphenols, and that exposure to BPS may be greater than that to BPA in this area. The investigations also revealed that hair analysis is a useful approach for the biomonitoring of BPA and BPS levels in human organisms.	Med Sci Monit Vol.28 Pages e936738	10.12659/msm.936738	35923084	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0583	S. Gömar-Oliete, S. Rötzer, U. Rolle-Kampczyk, U. Sack, M. von Bergen, M. Barta, A. C. Zenclussen and G. Herberth	2025	Prenatal exposure to mixtures of phthalates and bisphenol A and eczema risk: findings in atopic and non-atopic children from the LINA birth cohort	BACKGROUND: We investigated whether maternal exposure to phthalate and bisphenol A (BPA) mixtures is associated with eczema in children, as most studies have only addressed single chemical exposures. METHODS: Nine phthalate metabolites and BPA were quantified in urine at gestational weeks 30 (6 (n = 620) and infant, inhalant, and food allergen specific immunoglobulin (IgE) levels (u/L) and IgG were measured in serum from 5-year-old children of the LINA cohort (n = 319). The association of prenatal exposure to phthalates and BPA, both single and mixed, with eczema and IgE was assessed in children stratified by atopy status. Three independent statistical models adjusted for covariates were used: logistic regression' also in the sex-stratified analysis - weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR). RESULTS: Prenatal exposure to phthalate mixtures was associated with eczema in atopic children (OR: 1.3, 95% CI: 1.05-1.62) and non-atopic children (OR: 1.3, 95% CI: 1.09-1.62) and the sum of di-2-ethylhexyl phthalate metabolites (OH6, 1-3, 6-OX) were significantly associated with eczema exclusively in atopic boys. The BKMR suggested a positive trend between chemical exposure and IgE values in the atopic subgroup. In the WQS model, the mixtures' positive effect on eczema among atopic children was significant (1.46, 1.06-2.01) with MBzP (59.9 %), monoethyl phthalate (13.3 %), and BPA (13.8 %) being the main contributors, which jointly modulate antibody-mediated immunity and inflammatory gene pathways in the host epigenetic profile. CONCLUSIONS: Maternal exposure to mixtures of phthalates and BPA differentially impacts eczema risk among atopy-stratified children. This in utero chemical-gene interaction analysis in atopic children identified genes involved in immune cell activation and Ig production. Compared to non-atopic children, individual phthalates were significantly associated with eczema in atopic boys, suggesting that chemicals may have a larger effect size in predisposed populations.	Environ Res. 2025 Aug 1:278:121667.	10.1016/j.envres.2025.121667	40274086	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0584	M. Goldney, M. A. Adgent, D. R. Stevens, H. B. Chin, K. K. Ferguson, A. M. Calafat, S. Trevino, E. G. Ford, V. A. Stallings, W. J. Rogan, D. M. Umbach, D. D. Baird and D. P. Sandler	2024	Environmental phenol exposures in 6- to 12-week-old infants: The Infant Feeding and Early Development (IFED) study	BACKGROUND: Exposure to phenols, endocrine-disrupting chemicals used in personal care and consumer products, is widespread. Data on infant exposures are limited despite heightened sensitivity to endocrine disruption during this developmental period. We aimed to describe distributions and predictors of urinary phenol concentrations among U.S. infants ages 6–12 weeks. METHODS: The Infant Feeding and Early Development (IFED) study is a prospective cohort study of healthy term infants enrolled during 2010-2012 in the Philadelphia region. We measured concentrations of seven phenols in 282 urine samples, collected during the 1- or 2-month study visit, using online SPE-HPLC-MS/MS. We estimated geometric means (GMs) and 95% confidence intervals (CIs) for detectable phenols and examined associations with demographic and feeding characteristics using multivariable linear regression models. RESULTS: Median concentrations (μg/L) were: BP-3 in benzophenone-3, 0.4 for benzophenone-1, 2.2 for triclosan, 1.0 for 2,5-dichlorophenol, 0.7 for BPA, and 0.3 for 2,4-dichlorophenol. Geometric mean methylparaben concentrations were approximately 10 times higher than published estimates for U.S. children and adults. Triclosan was detected in 98% of samples, and concentrations were 2 to 3 times higher than published estimates for U.S. children and adults. Concentrations of 2,5-dichlorophenol (DCP) and mean concentrations of benzophenone-3 (1.70%) and triclosan (1.90%) but not BPA (0.16%) in milk from mothers of White mothers. Triclosan concentrations were higher in breastfed infants (1.9-fold) and lower in infants whose mothers had a high school education or less (-62%). Phenol concentrations were generally higher in summer samples. CONCLUSIONS: Widespread exposure to select environmental phenols among this cohort of healthy U.S. infants, including much higher paraben concentrations compared to those reported for U.S. children, supports the importance of expanding population-based biomonitoring programs to infants and toddlers. Future investigation of exposure sources is warranted to identify opportunities to minimize exposures during these sensitive periods of development.	Environ Res Vol.252 Issue Pt 4 Pages 119075	10.1016/j.envres.2024.119075	38719065	ヒト	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0585	J. Goerdten, L. Yuan, I. Huybrechts, V. Nawaz, U. Nöthlings, W. Ahrens, A. Scalbert and A. Fouque	2022	Reproducibility of the Blood and Urine Exposome: A Systematic Literature Review and Meta-Analysis	Endogenous and exogenous metabolite concentrations may be susceptible to variation over time. This variability can lead to misclassification of exposure levels and in turn to biased results. To assess the reproducibility of metabolites, the intraclass correlation coefficient (ICC) is commonly used in human exposure omics studies. Data on 15 single-metabolites are reported, and the ICCs of 10 metabolites were meta-analyzed. The reproducibility of the single-metabolites ranged from poor to excellent (ICC: 0.00–0.93). Pooled ICCs were 0.69 (95% CI: 0.61, 0.76) for 2,5-dichlorophenol, 0.68 (95% CI: 0.61, 0.74) for 2,4-dichlorophenol, 0.67 (95% CI: 0.60, 0.73) for benzophenone-3, 0.67 (95% CI: 0.60, 0.73) for mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), more than phthalate (MBzP), mono-(3-ethyl-5-oxohexyl) phthalate (MEOHP), methylparaben, and propylparaben, low to moderate (ICC median: 0.51; range: 0.31–0.85), and for 25-hydroxyvitamin D (25(OH)D), it is excellent (ICC: 0.93; 95% CI: 0.90–0.95). Pharmacokinetics, mainly the half-life of elimination and exposure patterns, can explain reproducibility. This review describes the reproducibility of the blood and urine exposome, provides a worst-dataset of ICC estimates, and hence constitutes a valuable resource for future reproducibility and clinical epidemiologic studies.	Cancer Epidemiol Biomarkers Prev. 2022 Sep 2;31(9):1683-1692.	10.1158/1055-9965.Epi-22-0090	35732488	ヒト	-	-	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0586	M. Gérard-Walton, C. Wavembsung, P. L. Williams, L. Souter, J. B. Ford, J. E. Chavarro, R. Hauser and L. Mínguez-Alarcón	2025	Using mixture and exposome methods to assess the associations and interactions of chemical biomarkers with semen parameters	BACKGROUND: Although epidemiologic studies have found associations between several chemical biomarkers and semen parameters, only a few studies have evaluated their combined effects and interactions. OBJECTIVES: To assess the individual and combined associations between urinary biomarkers of exposure to BPA, phthalates, and phenols and semen parameters. METHODS: Two mixture/exposome models, including exposome-wide association studies (ExWAS), Deletion/Substitution/Addition algorithm (DSA), Bayesian Kernel Machine Regression (BKMR), and the non-linear interaction model (NLI-interaction), were used to evaluate associations between 33 chemical biomarkers (urinary bisphenol A, four parabens, triclosan, 17 phthalate metabolites, and total mono-(hydroxyl and oxo)-paraben). Sperm count, motility, and morphology were measured in 1,540 samples from 1,044 men from the LIFE Study. Multivariable linear regression models were used to estimate associations between exposure mixtures and semen parameters. RESULTS: In BKMR, when modeling the mixture from the 10th to 90th percentile, the chemical mixture was negatively associated with percent normal sperm morphology (-1.43%; 95% CrI: -2.68, -0.19). In DSA NLI, mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) (-0.28; 95% CI: -0.53, -0.02; p = 0.03) and mono-(3-carboxypropyl) phthalate (MCPP) (-0.28; 95% CI: -0.53, -0.03; p = 0.03) were associated with lower sperm motility. In ExWAS, MEOHP (-0.28; 95% CI: -0.53, -0.03; p = 0.03) and mono-benzyl phthalate (MBzP) (-0.18; 95% CI: -0.36, 0.00; p = 0.05) were associated with lower sperm motility. Using DSA NLI, mono-(carboxyoctyl) phthalate (MCOP) (-0.68; 95% CI: -1.36, -0.01; p = 0.05) was associated with lower sperm morphology. In ExWAS, MCOP (-0.68; 95% CI: -1.36, -0.01; p = 0.05) was associated with lower sperm morphology. In DSA NLI, mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) (-0.28; 95% CI: -0.56, 0.00; p = 0.05) was associated with lower sperm motility. In ExWAS, MEHHP (-0.28; 95% CI: -0.56, 0.00; p = 0.05) was associated with lower sperm motility. DISCUSSION: Among 33 biomarkers tested, two and nine were associated with lower sperm motility and morphology, respectively. Two mixture/exposome models identified MEOHP as associated with lower sperm motility. Two mixture/exposome models identified MCOP as associated with lower sperm morphology. Two mixture/exposome models identified MEHHP as associated with lower sperm motility. Two mixture/exposome models identified MCPP as associated with lower sperm motility. In ExWAS, MEHHP was associated with lower sperm motility. In ExWAS, MCOP was associated with lower sperm morphology. In DSA NLI, MEHHP was associated with lower sperm motility. In DSA NLI, MCOP was associated with lower sperm morphology. In DSA NLI, MCPP was associated with lower sperm motility. In DSA NLI, MEOHP was associated with lower sperm motility. In DSA NLI, MEOHP was associated with lower sperm motility. In DSA NLI, MEOH

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0597	P. Gangadaran, B. Bharti, S. V. Attri, V. S. Malik and A. Pintal	2024	Biomonitoring Study of Urinary Bisphenol A Levels and Impact of Bottle-Feeding Practices Among Infants and Children From Northern India	OBJECTIVES: To compare the urinary bisphenol A (BPA) levels in bottle-fed and never-bottle fed infants and under-five children and to determine the impact of bottle feeding practices and sociodemographic factors on urinary BPA levels. METHODS: A community-based cross-sectional study was carried out on children aged between 2 to 60 months attending the hogarwali centres in Chandigarh. RESULTS: Urine samples were collected from 1,000 children (mean age: 19.5 ± 14.5 months; 53.5% boys). Urinary BPA was detected in 70.5% of children, with a median concentration of 0.90 ng/mL (0.90 and 56.34 ng/mL at lower bottle-fed children (n = 82; 90.2% [P = 0.69]). On multivariate regression analysis, there were no significant predictors for high (> 75th percentile) urinary BPA levels. Only the urinary BPA levels >75th percentile showed higher trend for significance among children from middle/higher socioeconomic background in reference to lower socioeconomic strata (adjusted OR 1.82; 95% CI 0.91, 3.63; P = 0.07) and among children whose feeding bottles were brushed once or twice daily in reference to a group with no daily brushing (adjusted OR 2.65; 95% CI 0.96, 7.30; P = 0.07). CONCLUSIONS: Although feeding with plastic bottle did not emerge as a statistically significant risk factor for BPA exposure, yet detection of BPA levels among majority of study children signals urgent need for unmasking exposure to other sources given the potential long-term toxicity of BPA among infants and young children.	Indian Pediatr Vol.61 Issue 7 Pages 649-655		37645630	ヒト	代謝	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0598	Y. Gálvez-Ontiveros, I. Moscoso-Ruiz, V. Almaida-Pagán, F. Garrido-Fernández, C. Montaguado, R. Ginestar-Martínez, L. Rodrigo, A. Zafra-Gómez and A. Rivas	2023	Levels of Bisphenol A and its analogs in nails, saliva, and urine of children: a case control study	INTRODUCTION: A growing number of studies link the increase in overweight/obesity worldwide to exposure to certain environmental chemical pollutants that display obesogenic activity (obesogens). Since exposure to obesogens during the first stages of life has been shown to have even more intense and permanent effect on lean shown, it is important to study their possible role in childhood. The objective here was to study the association of Bisphenol A (BPA) and 13 BPA analogs in children, using three biological matrices (nails, saliva and urine), and overweight and obesity (n = 160). METHODS: In this case-control study, 99 overweight/obese children and 61 normal-weight children, aged 3-12 years, were recruited. Nail, saliva and urine samples were collected and analyzed by ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Logistic regression was used to study the association between overweight/obesity and Bisphenol exposure. RESULTS: The results suggested that BPF in nails is associated with overweight/obesity in children (OR=3.67 p < 0.029). In saliva, however, the highest detected concentrations of BPAP presented an inverse association (OR=0.66; p = 0.033) with overweight/obesity. No associations of statistical significance were detected between exposure to BPFs in the other analogs and overweight/obesity in any of the biological matrices.	Front Nutr. 2023 Aug 14:10:1226820.	10.3389/fnut.2023.1226820	37645630	ヒト	代謝	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0599	Y. Gálvez-Ontiveros, C. Montaguado, M. Gilez-Mancilla, J. J. Muros, V. Almaizn, M. A. Martínez-Burgos, C. Samaniego-Sánchez, I. Salcedo-Bellido, A. Rivas and A. Zafra-Gómez	2024	Dietary bisphenols exposure as an influencing factor of body mass index	BACKGROUND: Over the past three decades, there has been a significant increase in the prevalence and incidence of overweight and obesity worldwide. The obesogen hypothesis suggests that certain external agents, including endocrine disrupting chemicals (EDCs), can disrupt metabolic homeostasis, leading to an increased susceptibility to obesity. Bisphenols (BPs) are EDCs that have been shown to have significant influence by accumulation by promoting the transformation of endogenous into adipocytes. This study aimed to assess the possible contribution of dietary bisphenol exposure to the risk of developing overweight and obesity in a sample of Spanish children according to sex. METHODS: Dietary and anthropometric data were collected from 175 controls and 126 cases schoolchildren aged 5-13 years. Dietary exposure to BPA and BPS was estimated by combining occurrence data with consumption data. Urinary concentrations of BPA and BPS were determined by ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). RESULTS: For females, cases had significantly higher exposure to BPA from meat and eggs compared to controls (median = 104.56; interquartile range (IQR) = 174.39-30.17 vs. 30.17; 30.17-0.00 ng·d-1·kg-1 bw-1; p = 0.006). Diet quality was higher for controls (6.21 (2.12) vs. 4.80 (2.24) p < 0.001) among males independently of a high or low exposure to bisphenols. However, higher diet quality was observed for female controls with a high exposure of total bisphenols (6.79 (2.56) vs. 5.31 (2.01); p < 0.011). Females exposed to high levels of BPA from meat and eggs had higher likelihood of being overweight and obese (adjusted Odds Ratio = 2.73; 95% confidence interval = 1.08-7.20). However, no consistent associations were found in males. CONCLUSIONS: High BPA levels from meat and eggs were positively associated with overweight and obesity in females. The dietary intake of BPA in the schoolchildren in the present study was much higher than the acceptable daily intake established by EFSA for the last year.	Environ Health. 2024 Oct 29;23(1):93.	10.1186/s12940-024-01134-7	39472930	ヒト	代謝	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0600	P. Gajjar, Y. Liu, N. Li, J. I. P. Buckley, A. Chen, B. P. Lanphear, H. J. Kalkwarf, K. M. Cecil, K. Yolton and J. M. Braun	2022	Associations of mid-childhood bisphenol A and bisphenol S exposure with mid-childhood and adolescent obesity	BACKGROUND: Bisphenol A (BPA) is a suspected obesogen that has been associated with adiposity in children. Bisphenol S (BPS), a structural analog of BPA, is used as a BPA substitute and may have similar health effects as BPA. However, few studies have examined whether BPS is associated with childhood adiposity. METHODS: We quantified urinary BPA and BPS concentrations in 315 children age 8 years from the HOME Study, a prospective pregnancy cohort enrolled in Cincinnati, Ohio (2003-2006). We measured body mass index (BMI), waist circumference, and triceps skinfold thickness at age 8 years and BMI z-score, waist-to-height ratio, and fat mass/height2 at age 12 years (n = 241). We assessed associations between concentrations at age 12 years (n = 159). Using multivariable linear regression, we estimated covariate-adjusted associations of BPA and BPS with adiposity measures at ages 8 and 12 years and adipose-positive concentrations at age 12 years. RESULTS: Each SD fold increase in urinary BPA concentrations were inversely associated with percent body fat at age 8 years (β = -1.2; 95% confidence interval [CI]: -1.6, -1.0) and 12 years (β = -1.4; 95% CI: -1.8, 0.9). In contrast, urinary BPS concentrations were positively associated with percent body fat at age 8 years (β = 1.1; 95% CI: -0.6, 2.7), but not at 12 years (β = 0.1; 95% CI: -1.7, 1.8). Urinary BPA and BPS concentrations were not associated with severe adiposity or leptin concentrations. CONCLUSIONS: We did not observe evidence that urinary BPA or BPS concentrations during childhood were associated with greater mid-adiposity at ages 8 and 12 years in this cohort.	Environ Epidemiol. 2021 Dec 20;6(1):e187.	10.1097/ee9.0000000000000187	35169665	ヒト	代謝	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0601	Z. Fu, H. Jin, W. Mao, S. Yin, L. Xu and Z. Hu	2024	Conjugated metabolites of bisphenol A and bisphenol S in indoor dust, outdoor dust, and human urine	Bisphenol A (BPA) and bisphenol S (BPS) have been widely spread in the global environment. However, for conjugated BPA and BPS metabolites, limited studies have investigated their occurrence in environmental matrices and human samples. In this study, we developed a method for the analysis of 12 conjugated BPA and BPS metabolites in indoor and outdoor dust, and human urine using ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Three BPA metabolites were found in ambient indoor and outdoor dust, and BPA sulfate (mean 0.79 and 1.12 ng/g, respectively) and BPA glucuronide (0.63 and 0.66 ng/g) being were dominant. BPS conjugates accounted for a mean of 42 and 66% of total BPS burst of conjugated BPA and BPS metabolites) in indoor and outdoor dust, respectively. BPS sulfate (mean 0.29 and 0.32 ng/g, respectively) had consistently higher concentrations than BPS glucuronide (0.03 and 0.07 ng/g) in indoor and outdoor samples. BPS conjugates contributed a mean 32% and 69% of total BPS burst of BPS and BPS metabolites in indoor and outdoor dust, respectively. Moreover, conjugated BPA and BPS metabolites in indoor or outdoor dust were not significantly correlated with those in urine from residents. Overall, this study first demonstrates the wide presence of conjugated BPA and BPS metabolites, besides BPA and BPS, in indoor and outdoor dust. These data are important for elucidating the sources of conjugated BPA and BPS metabolites in the human body.	Chemosphere Vol.362 Pages 142617	10.1016/j.chemosphere.2024.142617	38880259	ヒト	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0602	X. Fu, J. Xu, R. Zhang and J. Yu	2020	The association between environmental endocrine disruptors and cardiovascular diseases: A systematic review and meta-analysis	BACKGROUND: Except for known cardiovascular risk factors, long-term exposure to environmental endocrine disruptors (EEDs) - a class of exogenous chemicals, or a mixture of chemicals, that can interfere with any aspect of hormone action - has been shown to increase the risk of cardiovascular diseases (CVDs), which are still controversial. OBJECTIVE: To conduct a comprehensive systematic review and meta-analysis to investigate the association between EEDs and CVDs. METHODS: Relevant studies were identified by searching PubMed, Embase, and Web of Science from inception to May 2019. Due to the heterogeneity between different studies was qualitatively evaluated using Q test and I2 statistical magnitude, respectively. Subgroup analysis was performed by chemical homology - a previously unused grouping method - to reveal dose and positive meta-analysis to assess their exposure to CVD. RESULTS: Twenty-nine literatures were enrolled with a total sample size of 58881. The results indicated that exposure to PCB118 and PCDD were the risk factors for CVD morbidity (odds ratio (OR) = 1.36; 95% confidence interval (CI): 1.20-1.48; OR = 1.36; 95% CI: 1.15-1.60). Exposure to chlorinated pesticide (DDT) (OR = 1.10; 95% CI: 1.00-1.24), as well as with pollutant (PAH) (OR = 1.11; 95% CI: 1.06-1.17) and BPA (OR = 1.19; 95% CI: 1.02-1.37) were positively associated with CVD risk, respectively. BPA exposure concentration had a significant dose-response relationship with CVD risk (P = 0.0001). Moreover, exposure to BPA was associated with an increased risk of CVD in females (OR = 1.19; 95% CI: 1.02-1.37), but not in males (OR = 1.06; 95% CI: 0.91-1.23). Exposure to chlorinated pesticide (DDT) (OR = 1.10; 95% CI: 1.00-1.24), PAH (OR = 1.11; 95% CI: 1.06-1.17), and BPA (OR = 1.19; 95% CI: 1.02-1.37) were positively associated with CVD risk, respectively. BPA exposure concentration had a significant dose-response relationship with CVD risk (P = 0.0001). Moreover, exposure to BPA was associated with an increased risk of CVD in females (OR = 1.19; 95% CI: 1.02-1.37), but not in males (OR = 1.06; 95% CI: 0.91-1.23). CONCLUSIONS: EED exposure is a risk factor for CVD. Long-term exposure to EEDs can influence cardiovascular health in humans. A possible synergistic effect may exist between the homologs. The mechanism of which needs to be further explored and demonstrated by additional prospective cohort studies, results of in vitro and in vivo analyses, as well as meta-analyses.(Text)	Environ Res. 2020 Aug:187:109464.	10.1016/j.envres.2020.109464	32438096	ヒト	心血管(メタアナリシス)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0603	X. Fu, J. Hu, D. Zhang, X. Yang, P. Wang, F. Tuo, L. Wang, S. Li, J. Xu and J. Yu	2022	Association of endocrine disrupting chemicals levels in serum, environmental risk factors, and hepatic function among 5- to 14-year-old children	Endocrine-disrupting chemicals (EDCs) might increase the risk of childhood diseases by disrupting hormone-mediated processes that are critical for growth and development during childhood; however, the association among the exposure level of EDCs such as fluorophenol (FHP), Bisphenol A (BPA), Dichloric phthalate (DAP) in children and environmental risk factors, as well as hepatic function has not been elaborated. This study aimed to discuss this interesting relationship among FHP, BPA, DAP concentrations, in serum, environmental risk factors, hepatic functional in 5- to 14-year-old children in industrial zone, residential zone and suburb in northern China. METHODS: A total of 1,200 5- to 14-year-old children were recruited from industrial zone, residential zone and suburb in northern China. Questionnaires were used to collect information on risk factors of EDCs exposure in mothers and children. Serum FHP, BPA and DAP concentrations were measured by high-performance liquid chromatography-MS/MS. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), AST/ALT, total bilirubin (TBIL), direct bilirubin (DBIL) and indirect bilirubin (IBIL) were detected with automatic biochemical analyzer. The median concentrations of serum FP, BPA, and DAP in children were 0.03 ng/ml, 0.04 ng/ml, and 0.05 ng/ml, respectively. RESULTS: Children from industrial zone had significantly higher serum FHP, BPA, and DAP concentrations than those from residential zone and suburb. Logistic regression showed that maternal exposure to BPA (odds ratio (OR) = 1.19, 95% CI = (1.01–1.40), $P = 0.035$) and DAP (OR = 1.21, 95% CI = (1.02–1.43), $P = 0.028$) during pregnancy, hair spray and perfume use for children, duration of children's birth, materials for baby bottle or cup and access to plastic products were significantly positively correlated with serum BPA concentration ($P < 0.05$). Smoke, perms used during pregnancy, hair spray and perfume use for children, using plastic lunch box during pregnancy, duration of children's birth, exposure to pesticides, parents' occupations were significantly positively correlated with serum DAP concentration, ($P < 0.05$). Serum AST (β = 0.294, $P = 0.018$) and DAP (β = 0.318, $P = 0.026$) concentrations and TBIL level were significantly positively correlated with hepatic function abnormality. CONCLUSIONS: Industrial zone is a risk factor for EDCs exposure in children. Serum FHP, BPA, and DAP in children from industrial zone had correlation between the frequency of hair spray and perfume use for children and the AST (β = 0.315, $P = 0.022$). MF, BPA and DAP, which were commonly detected in the serum of children aged 5–14 years old in Dalian City, Northern Golden Province, China, were closely related to the environmental risk factors of exposure environment during pregnancy, infancy and school age. Exposure to MF, BPA and DAP could have negative effects on hepatic function, and these effects showed differences in gender and geographical location. Notably, The relationships were more evident in girls than in boys.	Toxicology. 2022 Jan 15:465:153011.	10.1016/j.tox.2021.153011	34715266	ヒト	肝	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0604	J. Fu, Y. Yao, Z. Huang, Z. Guo, X. Chen, X. Tang, Y. Gu, Q. Xiao, Y. Shu and S. Lu	2024	Sex-Specific and Trimester-Specific Associations of Prenatal Exposure to Bisphenols, Parabens, and Triclosan with Neonatal Birth Size and Gestational Age	Bisphenols, parabens, and triclosan (TCC) are common endocrine disruptors used in various consumer products. These chemicals have been shown to cross the placental barrier and affect intrauterine development of fetuses. However, the associations between prenatal exposure to BPs, PBs, and TCC and birth size and gestational age (GA) remain inconsistent. We measured 11 BPs, 4 PBs, and TCC in urine samples collected from 1,000 mother–newborn pairs in the Shanghai Birth Cohort. Multivariable linear regression models were used to estimate associations of BPs, PBs, and TCC with birth size (birth weight, birth length, ponderal index, head circumference, and chest circumference) and GA. Quantile-based g-computation models were used to estimate the mixture effects of BPs, PBs, and TCC on birth size and GA. Sex-specific associations were also examined. Urinary concentrations of BPA, BPF, BPS, BPAF, BPB, methyl-PB (MePB), ethyl-PB (EtPB), propyl-PB (PrPB), butyl-PB (BuPB), and TCC were detected in more than 50% of the samples. Because of the low detection frequency of BzP compounds, only 5 (1% BzP) were included in the exposure–outcome analyses. After adjustment for confounders, BPA was associated with greater odds of a small birth size (SGA) and preterm birth (PTB). Each 1-fold increase in BPA concentration was associated with 1.19 (95% confidence interval (CI): 1.03, 1.37), 1.19 (95% CI: 1.03, 1.37), and 1.19 (95% CI: 1.03, 1.37) times greater odds of SGA in birth weight, length, and head circumference, respectively. Each 1-fold increase in BPA concentration was associated with 1.19 (95% CI: 1.03, 1.37) times greater odds of PTB. Each 1-fold increase in BPF concentration was associated with 1.19 (95% CI: 1.03, 1.37) times greater odds of SGA in birth weight. Each 1-fold increase in BPS concentration was associated with 1.19 (95% CI: 1.03, 1.37) times greater odds of SGA in birth length. Each 1-fold increase in total PBs concentrations in the second trimester was also associated with greater visual function of posterior cortex and worse quantitative performance, respectively, but these trends were not statistically significant. The associations of BPS and PrPB with poorer verbal, memory, and motor skills are novel observations that warrant further attention. Larger prospective studies are required to confirm whether prenatal exposure to BPA and other phenolic EDCs is associated with impaired cognitive development.	Environ Sci Technol. 2024 Aug 6;58(31):13687-13696.	10.1021/acs.est.4c04940	39067068	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0605	C. Freire, F. Vela-Soria, A. Beneito, M. J. Lopez-Espinosa, J. Ibarluzea, F. B. Barreto, M. Casas, M. Vrijheid, G. Fernandez-Tardon, I. Riaño-Galan and M. F. Fernandez	2020	Association of placental concentrations of phenolic endocrine disrupting chemicals with cognitive functioning in preschool children from the Environment and Childhood (INMA) Project	Developmental exposure to bisphenol A (BPA) and other phenolic endocrine disrupting chemicals (EDCs) may affect child neurodevelopment, but data on the effects of prenatal exposure to phenols on cognitive function remain sparse. Our aim was to examine the association of placental concentrations of several phenolic EDCs, including BPA, parabens (PBs), methoxyphenols (MePs), with cognitive development in preschool children from the Environment and Childhood (INMA) Project in Spain. Concentrations of BPA, four PBs (methylparaben [MePB], ethylparaben [EtPB], propylparaben [PrPB], and butylparaben [BuPB]), and six MePs (BuP-3-MeP, BuP-4-MeP, EtP-4-MeP, PrP-2-MeP, PrP-3-MeP, and PrP-4-MeP) were measured in placentas collected at birth from 1,188 mother–child pairs. Cognitive and motor function was assessed with the McCarthy Scales of Children's Abilities (MSCA) at the age of 4-5 years. Associations were assessed in a subsample of 241 mother–child pairs using linear and logistic regression models adjusted for confounding factors. PB compounds were detected in more than 72% of placentas, BPA in 43%, 2-OH-BzP in 58%, and the remaining BzPs in <9% of the samples. Because of the low detection frequency of BzP compounds, only 2-OH-BzP was included in the exposure–outcome analyses. After adjustment for confounders, BPA was associated with poorer odds of a working memory deficit (the 20th percentile) in the verbal block vs. first exposure tertile odds ratio (OR) = 2.78, 95% confidence interval (CI) = 1.08-5.83, p-trend = 0.030 and gross motor (detected as unobserved OR = 1.75, 95%CI = 1.08-5.90) areas. Other methylation by-child body mass index (BMI) (95% CI = 1.13 [0.96-1.30] and 1.20 [1.06-1.34], respectively, for a one-fold increase in concentrations), with a stronger association for OBHP in boys with overweight or obesity. In contrast, BPA, BuPB, EtPB, and PrPB were associated with a lower probability of patient onset, attainment, and/or grandeche to all boys (e.g., overall puberty, BPA: RR [95% CI] = 0.90 [0.81-1.00] and BuPB: 0.90 [0.80-1.00], respectively) and the associated with BPA was stronger in boys with overweight/normal weight. In girls, 5dOHP and PrPB were associated with delayed pubertal milestones with underweight/normal weight (RR [95% CI] = 1.08 [0.77-0.95] and 0.98 [0.84-0.99], respectively). Most of these associations were trimester-specific. However, the interaction observed was not associated with any pubertal outcome in boys or girls. CONCLUSIONS: Prenatal exposure to certain phthalates and synthetic phenols such as BPA may impact the pubertal development of boys, and weight status may modify this effect. BPA may also alter the pubertal development of girls.	Int J Hyg Environ Health. 2020 Sep:230:113597.	10.1016/j.ijheh.2020.113597	32795877	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0606	C. Freire, F. Castiello, I. Babarro, A. Anguita-Ruiz, M. Casas, M. Vrijheid, B. Sarno, A. Barreto, M. Kadawathagedara, C. Philippat, C. Thomsen, A. K. Sakhi and M. J. Lopez-Espinosa	2024	Association of prenatal exposure to phthalates and synthetic phenols with pubertal development in three European cohorts	BACKGROUND: There is limited epidemiological evidence on the association of prenatal exposure to phthalate and synthetic phenols with altered pubertal timing. OBJECTIVE: To examine the association of prenatal exposure to phthalates and synthetic phenols with pubertal development in girls. METHODS: We measured 11 phthalate metabolites, 4 phthalate diesters (DEP, DiBP, DnBP, BMP), 4 phenols (BPA, methyl- (MePβ), ethyl- (EtPβ), propyl- (PrPβ), and butyl-paraben (BuPβ); BP-3, and TCS) and quantified urine in two Cox-and Rd trimesters' urine samples collected during pregnancy (1998-2008) from mothers in three birth cohorts: INMA (Spain), EDEN (France), and Mella (Norway). Pubertal development of their children was assessed at a single visit at age 7-11 years (735 girls, 910 boys) using the parent-reported Pubertal Development Scale (PDS). Mixed-effect Tobit models, adjusted for sampling weights and Bayesian Kernel Machine Regression (BKMR) models were used to examine associations of individual and combined prenatal chemical exposure, respectively, with the probability of overall pubertal onset, adrenarche, and gonadarche (stage 2+) in girls and boys. Effect modification by child body mass index (BMI) was also explored. RESULTS: Prenatal exposure to BPA was associated with earlier overall pubertal onset in girls (Relative Time Ratio (RTR) = 0.96, 95% CI: 0.93, 0.99), and earlier adrenarche (RTR = 0.94, 95% CI: 0.90, 0.98) and gonadarche (RTR = 0.94, 95% CI: 0.90, 0.98) in girls with overweight or obesity. In contrast, BPA, BuPB, EtPB, and PrPB were associated with a lower probability of pubertal onset, adrenarche, and/or gonadarche in all boys (e.g., overall puberty, BPA: RR [95% CI] = 0.90 [0.81-1.00] and BuPB: 0.90 [0.80-1.00], respectively) and the associated with BPA was stronger in boys with overweight/normal weight. In girls, 5dOHP and PrPB were associated with delayed pubertal milestones with underweight/normal weight (RR [95% CI] = 1.08 [0.77-0.95] and 0.98 [0.84-0.99], respectively). Most of these associations were trimester-specific. However, the interaction observed was not associated with any pubertal outcome in boys or girls. CONCLUSIONS: Prenatal exposure to certain phthalates and synthetic phenols such as BPA may impact the pubertal development of boys, and weight status may modify this effect. BPA may also alter the pubertal development of girls.	Int J Hyg Environ Health. 2024 Aug:261:114418.	10.1016/j.ijheh.2024.114418	38968838	ヒト	生殖(思春期発達)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0607	H. Frederiksen, O. Nielsen, H. M. Koch, N. E. Skakkebæk, A. Juul, N. Jørgensen and A. M. Andersson	2020	Changes in urinary excretion of phthalates, phthalate substitutes, bisphenols and other polychlorinated and phenolic substances in young Danish men; 2009-2017	During the past two decades, human exposure to bisphenol A (BPA) and phthalates such as di-(ω-butyl) phthalate (DBP), di-(ω-butyl) phthalate (DnBP), butylbenzyl phthalate (BBzP) and di-(2-ethyl-hexyl) phthalate (DEHP) has received substantial interest due to widespread population exposures and potential endocrine disrupting effects. Therefore, these chemicals have gradually been restricted and phased out through legislation. Substitutes for some of these phthalates have been introduced, but little is known about the human exposure to these chemicals. We aimed to describe changes in urinary concentrations as a proxy for human exposure to these chemicals over the past decade. Three hundred urine samples collected in 2009, 2013 and 2017/18 from healthy young men of the general population, participating in a large on-going cross-sectional study, were collected for the present time trend study. The urinary concentrations of metabolites of 15 phthalates, di-(2-ethylhexyl) terephthalate (DEHTP) and di-(ω-oxyl-cyclohexane-1,2-dicarboxylate (DINCH), seven bisphenols including BPA, bisphenol S (BPS) and bisphenol F (BPF), as well as triclosan, triclocarbon, benzophenone-3, three chlorophenols and six parabens were analyzed by two validated LC-MS/MS methods developed and validated for the present study. A significant decrease in urinary concentrations over time was observed for the majority of the chemicals. Median concentrations of BPA and the phthalates DEHP, DnBP and BBzP decreased by 38%, 54%, 66% and 87%, respectively, from 2009 to 2017/18. Urinary concentrations of the DEHP substitutes DEHTP and DINCH increased more than 10-and 2 times, respectively. The potential BPA substitutes, BPS and BPF also increased, but only slightly. Despite these two exposure patterns, the exposure to the old well-known chemicals, such as DEHP, DnBP, BBzP, DEHP and BPA was still higher in 2017 compared to the exposure level of the new substitutes such as DEHTP, DINCH, BPS and BPF. A significant decrease in human exposure to most of the common phthalates and BPA over the past decade was observed, reflecting market changes and regulatory measures implemented in EU. Despite increasing exposures to some of the known phthalate substitutes and BPA analogues, the total amount of each measured chemical group (original and substitute analog) combined) was lower in the more recently collected samples. This indicates only partial direct substitution or substitution by chemicals not covered in this approach, or a general decline in the exposure to these chemical product groups over the last decade.	Int J Hyg Environ Health Vol.223 Issue 1 Pages 93-105	10.1016/j.ijheh.2019.10.002	31669154	ヒト	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0608	H. Frederiksen, M. L. Ljubicic, E. N. Upners, M. B. Fischer, A. S. Buech, C. P. Hagen, A. Juul and A. M. Andersson	2022	Benzophenones, bisphenols and other polychlorinated/phenolic substances in Danish infants and their parents - including longitudinal assessments before and after introduction to mixed diet	BACKGROUND: Humans are widely exposed to chemicals with known or suspected endocrine disrupting effects. Among these are several benzophenones, bisphenols and other phenols commonly used in consumer products. OBJECTIVES: To provide human biomonitoring data from young families, including infants and their parents as well as longitudinal data of infants exclusively breastfed versus on mixed diet. METHODS: Twenty-two benzophenones, bisphenols and other phenols, some measured for the first time, were analyzed in urine samples collected from more than 100 infants and their parents (the TIDE study) and in pooled samples from 61 schools when exclusively breastfed and after introduction of mixed diet (the FOOD study). RESULTS: Twelve out of 22 substances were detectable in more than half of the urine samples from infants, mothers or fathers. Large variation in exposure was observed. Urinary concentrations of benzophenone-3, bisphenol A, triclosan and 2-phenylphenol were significantly higher in mothers than in fathers and infants. Concentrations of benzophenone-3 and bisphenol S, triclosan and 2-phenylphenol were significantly higher in infants than their parents. In the FOOD study, exclusively breastfed infants had higher or similar levels of triclosan and benzophenone-3 compared to infants fed a mixed diet. Urinary levels of triclosan and the benzophenones, BP-1 and BP-3 were significantly correlated between all trio members, indicating exposure from the same sources at home. For triclosan, BP-1 and BP-3, the within-family variation was lower than between-families in the TIDE study. Many substances were positively correlated both within infants and parents, indicating that some families were exposed to several of these substances concurrently. CONCLUSIONS: Participants in this study excreted relatively low chemical levels, however, simultaneous exposure to several chemicals with endocrine disrupting abilities is of concern due to the dose-additive effects of these substances in combination with other chemicals.	Environ Int Vol.169 Pages 107532	10.1016/j.envint.2022.107532	36170755	ヒト	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0609	A. B. Foreman, J. V. van Vliet-Ostaptchouk, M. van Faassen, I. P. Kema, B. H. Wolffenbuttel, P. J. J. Sauer, A. F. Bos and S. A. Beghin	2022	Urinary concentrations of bisphenols and parabens and their association with attention, hyperactivity and impulsivity at adolescence	BACKGROUND: Neurobehavioural disorder diagnoses have been increasing over the last decades, leading to heightened interest in the ecological factors involved. Endocrine disrupting chemicals, such as parabens and bisphenols, are suspected to contribute to these disorders. OBJECTIVE: To investigate associations between urinary concentrations of BPA, BPS, BPF, MeP, EtP, PrP and BuP and attention, hyperactivity and impulsivity. METHODS: Parabens and bisphenols are associated with attention and concentration in adolescents, in general and are specific. METHODS: We tested 288 adolescents (10-15 years old) for the follow-up birth cohort study. Concentrations of five parabens and three bisphenols (BPA, BPF, BPS) were measured in morning urine after overnight fasting, using a validated LC-MS/MS method. Attention and concentration were assessed at the clinic with outcomes of the Test of Everyday Attention in Children and the Dutch Attention Deficit Hyperactivity Disorder questionnaire (ADC), the latter being filled in by parents. Linear regression analyses were performed, adjusting for urine creatinine concentrations and potential confounding factors. RESULTS: 151 (56%) adolescents participated (28 girls; 93 boys). Urinary paraben concentrations were higher in girls than in boys. Bisphenol concentrations were not associated with sex. Urinary concentrations of BPA, BPF, BPS, MeP, EtP, PrP and BuP were 0.4 (<LOD-3.2), 0.1 (<LOD-0.4), 0.3 (<LOD-1.2), 13.2 (1.1-49.2), 0.4 (<LOD-1.8), 0.1 (<LOD-0.4), 0.1 (<LOD-0.4) and 0.1 (<LOD-0.4) ng/ml, respectively. Higher urinary concentrations were associated with more optimal scores on parent-reported attention. Propylparaben was negatively associated with scores on sustained auditory attention in girls (p = -35.9 (-102.9)-19.1) - 1.855.892). Bisphenol concentrations were not associated with scores on attention and concentration after adjusting for confounders. CONCLUSIONS: In 13-15-year-old Dutch adolescents, urinary concentrations of methylparaben and ethylparaben were associated with better attention and less hyperactivity, whereas a trend toward significance was found between higher urinary propylparaben concentrations and poorer attention. Bisphenol concentrations were not associated with attention and concentration after adjusting for confounders.	Neurotoxicology. 2023 Mar:95:66-74.	10.1016/j.neuro.2023.01.006	36649891	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を依頼性評価へ進め、依頼性評価段階で原則に基づき判断。

引用評価機関
● ：該当

別添-2 統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0610	M. S. Forde, S. Côté, E. A. Lauzon-Sidi, É. Gaudreau and P. Ayotte	2022	Evaluation of Bisphenol A in Pregnant Women from 10 Caribbean Countries	Bisphenol A (BPA), a phenolic chemical incorporated into many plastic products, has been found to act as an endocrine disruptor that potentially is linked to adverse neurodevelopmental outcomes. Prenatal BPA exposure is understudied in the Caribbean region. Therefore, we measured BPA concentrations in urine samples collected from pregnant women in 10 Caribbean countries and compared the findings with comparable data from Canada and the U.S. BPA was detected in all samples except from a low geometric mean of 1.8 µg/L (St. Lucia) to a high of 3.8 µg/L (St. Kitts & Nevis). All of the Caribbean Islands sampled had geometric mean concentration levels that were higher than those recorded in two Canadian biomonitoring surveys (1.16 µg/L and 0.81 µg/L) and the U.S. NHANES survey (1.29 µg/L). This first biomonitoring survey of BPA concentration levels in maternal urine samples taken from Caribbean countries clearly points to the need for Caribbean governments and public health officials to first engage in targeted and rigorous efforts to know or minimize the incarceration and use of BPA products used the Caribbean and, second, to continue to conduct biomonitoring surveys so as to ensure that these rates and regulations are indeed leading to a decrease of BPA concentrations in Caribbean populations.	Toxics Vol.10 Issue 10	10.3390/toxics10100556	36287837	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0611	K. E. Foong, P. Franklin, F. Sanna, G. L. Hall, P. D. Sly, E. B. Thorstensen, D. A. Doherty, J. A. Keelan and R. J. Hart	2023	Longitudinal effects of prenatal exposure to plastic-derived chemicals and their metabolites on asthma and lung function from childhood into adulthood	BACKGROUND AND OBJECTIVE: Environmental exposure to phthalates and bisphenol A (BPA), chemicals used in the production of plastics, may increase risk for asthma and allergies. However, little is known about the long-term effects of early life exposure to these compounds. We investigated if prenatal exposure to these compounds was associated with asthma, allergy and lung function outcomes from early childhood into adulthood in a cohort study. METHODS: Maternal urine samples collected from 800 pregnant women in the Raine Study were analysed for BPA and phthalate metabolites. The children were then followed up at 5, 10 and 20 years, where spirometry and respiratory questionnaires were conducted to determine asthma and allergy status. Lung function trajectories were derived from longitudinal spirometry measurements. Multinomial logistic regression and linear mixed models were used to assess associations between prenatal exposures and asthma, allergy and lung function outcomes. RESULTS: Prenatal BPA and phthalates or asthma phenotypes were seen to male offspring, where BPA was associated with increased risk for persistent asthma, while more low-level phthalate was associated with increased risk for adult asthma. Prenatal BPA had no effect on lung function trajectories, but prenatal phthalate exposure was associated with improved lung function. CONCLUSION: Prenatal BPA exposure was associated with increased likelihood of persistent asthma in males, while prenatal phthalate exposure was associated with increased likelihood of adult asthma in males. Results suggest that prenatal exposure to prenatal BPA and phthalates affect asthma risk, particularly in males, however lung function was not adversely affected.	Respirology. 2023 Mar;28(3):236-246.	10.1111/resp.14386	36184579	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0612	M. I. Fonseca, M. Lorigo and E. Cairrao	2023	Evaluation of the bisphenol A-induced vascular toxicity on human umbilical artery	Bisphenol A (BPA) is one of the most widely used synthetic compound in the manufacture of polycarbonate plastics and epoxy resins. Worryingly, BPA is an endocrine disrupting chemical (EDC) with an estrogenic, antiandrogenic, as well as estrogenic activities. However, the vascular implications of BPA exposure during pregnancy is unclear. In this sense, the present work proposed to understand the BPA mechanism toward the vasculature of the pregnant women. To elucidate this, in vivo studies were performed using human umbilical arteries, to explore the acute and chronic effects of BPA. The medial actions of BPA role was also explored by analysing the activity, by in vivo studies and expression (in vitro studies) analysis of Ca(2+) and PI(3)-channels and isoforms and the downstream signaling pathway. Moreover, in vitro studying stimulations and mimic the endothelial dysfunction. BPA with the proteins involved in these signalling pathways. Our study showed that the exposure to BPA may modify the vasorelaxant response of HUA, interfering with SOC/cSOC/ROC/PKG pathway by modulation of eNOS and activation of BKCa channels. Moreover, our findings suggest that BPA can modulate the HUA reactivity, increasing the L-type CaV1.2 Channels, SOC/cSOC activity, a common vascular response observed in hypertension disorders of pregnancy.	Environ Res. 2023 Jun 1:226:115628.	10.1016/j.envres.2023.115628	36907341	ex vivo	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0613	J. Flieger, T. Śmigocki, J. Dolar-Szczasny, W. Zaluska and R. Rejdak	2022	The First Evidence on the Occurrence of Bisphenol Analogues in the Aqueous Humor of Patients Undergoing Cataract Surgery	Human exposure to BPA is inevitable mostly due to contaminated food. In this preliminary study, for the first time, the presence of bisphenols (BPs) in aqueous humor (AH) collected from 62 patients undergoing cataract surgery was investigated. The measurements were performed using a sensitive ultra high-performance liquid chromatography-tandem mass spectrometry (UHPLC - MS/MS). Chromatographic separation was achieved using a reverse phase column and a gradient elution mode. Multiple reaction monitoring (MRM) was used. The method was validated for bisphenol A (BPA) and bisphenol F (BPF). The limits of quantification (LOQs) of both investigated analytes were 0.25 ng mL−1. The method was linear in the range of 0.25–250 ng mL−1 with correlation coefficients (R2) higher than 0.99. Recoveries in the range of 99.0 to 103.3% and from assay and inter-assay precision expressed by relative standard deviations (RSDs) were less than 6%. BPA was detected in 32 AH samples with mean concentrations of 1.61 ng mL−1. BPF was not detected at all. The detection frequencies of BPA and BPF were 52% and 0%, respectively. The total content of BPs was similar for patients with cataracts only and those with cataracts and concomitant diseases, 1.61 ng mL−1 and 1.62 ng mL−1, respectively. The total content of BPs was similar for patients with coexisting ocular pathologies such as glaucoma, age-related macular degeneration (AMD), and diabetes in comparison to cataracts alone. However, the difference between these groups did not reach statistical significance (p > 0.05). Performed investigations indicate the need for further research on a larger population with the aim of assessing the consequences of BPs accumulation in AH for visual function.	J Clin Med Vol.11 Issue 21	10.3390/jcm11216402	36362630	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0614	M. Fisher, T. E. Arbuckle, S. MacPherson, J. M. Braun, M. Feeley and É. Gaudreau	2019	Phthalate and BPA Exposure in Women and Newborns through Personal Care Product Use and Food Packaging	Phthalates and bisphenol A (BPA) are used in some personal care products (PCPs) and containers for food processing and packaging. The Plastics and Personal Care Product use in Pregnancy (PU Study (2009–10) explored the associations between PCP use during pregnancy and the perinatal period among 80 pregnant women and 90 infants and BPA and phthalate concentrations in multiple maternal and infant urine specimens collected throughout the study (n = 1,506 samples). The type, frequency, and timing of PCP and food packaging use (0–5 before and during the urine collection period) was obtained by questionnaire and diary. Infant urine was collected up to 2 times before 7 months of age, and mothers answered questions about infant feeding and PCP use on their baby. In mothers, monoethyl phthalate (MEP) metabolite concentrations were the highest of all phthalate metabolites (GM = 74.1 ng/mL, 95% CI: 59.2, 92.8), followed by monobutyl phthalate (MBP) and BPA (GM = 1.4 ng/mL, 95% CI: 1.2, 1.6). Use of personal care products was associated with higher phthalate metabolite concentrations in infants. Total BPA metabolite concentrations were lower in exclusively breastfed infants compared to those who were exclusively formula fed or breastfed with supplementation. Given that PCPs tend to undergo frequent formulation changes, which could impact the relative importance of a certain product type as a source of exposure, continued research of this type is warranted.	Environ Sci Technol Vol.53 Issue 18 Pages 10813-10826	10.1021/acs.est.9b02372	31424210	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0615	B. G. Fisher, A. Thankamony, J. Mandalia, C. J. Petry, H. Frederiksen, A. M. Andersson, A. Juul, K. K. Ong, D. B. Dunger, I. A. Hughes and C. L. Acerini	2020	Maternal serum concentrations of bisphenol A and propyl paraben in early pregnancy are associated with male infant genital development	STUDY QUESTION: Are maternal serum phthalate metabolite, phenol and paraben concentrations measured at 10–17 weeks of gestation associated with male infant genital developmental outcomes, specifically anogenital distance (AGD) and penile width (PW) measured at birth and at 3 months of age? SUMMARY ANSWER: Maternal serum bisphenol A (BPA) and propyl paraben concentrations were specifically associated with congenital or perinatally acquired cryptorchidism, and in propyl paraben in PVP, concentrations was associated with shorter AGD from birth to 20 months of age. WHAT IS KNOWN ALREADY: Male reproductive disorders are increasing in prevalence, which may reflect environmental influences on foetal testicular development. Animal studies have implicated phthalates, BPA and parabens, to which humans are ubiquitously exposed. However, epidemiological studies have generated conflicting results and have often been limited by small sample size and/or measurement of chemical exposures outside the most relevant developmental window. STUDY DESIGN, SIZE, DURATION: Case–control study of cryptorchidism nested within a prospective cohort study (Cambridge Baby Growth Study), with recruitment of pregnant women at 10–12 weeks of gestation between 2001 and 2009. PARTICIPANTS/MATERIALS, SETTING, METHODS: Maternal blood was collected at recruitment, and serum levels of 16 phthalate metabolites, 5 phenols (including BPA) and 3 parabens were measured using liquid chromatography/tandem mass spectrometry. Cryptorchidism was ascertained at birth in 172 cases and 1,000 controls. Anogenital distance (AGD) and penile width (PW) were measured at birth and 3 months of age in 1,206 boys (including some cases) and 3, 2, 12, 20 and 30 months of age, and age-specific Z-scores were calculated. Associations between serum chemical levels and these outcomes were tested using linear mixed models. MAIN RESULTS AND THE ROLE OF CHANCE: Maternal serum BPA concentrations were associated with offspring all-type cryptorchidism both when considered as a continuous exposure (adjusted odds ratio per log10 µg/l: 2.90, 95% CI: 1.13–6.67; P = 0.009) and as quartiles (p for trend = 0.005). Detection of a PVP in maternal serum was associated with shorter AGD by 0.243 standard deviations, 95% CI: 0.053–0.433; P = 0.012 from birth to 20 months of age; this reduction was independent of body size and other putative confounders. We did not find any consistent associations with offspring outcomes for the other phenols, parabens, and phthalate metabolites measured. LIMITATIONS, REASONS FOR CAUTION: Our findings are based on a relatively small number of cases of cryptorchidism, and the chemical exposures were assessed using a single urine sample from single-void measurements. The cohort was not fully representative of pregnant women in the UK, particularly in terms of smoking prevalence and maternal ethnicity. WIDER IMPLICATIONS OF THE FINDINGS: Our observational findings support maternal evidence that intrauterine exposure to BPA and to PVP during early gestation may adversely affect male reproductive development. More evidence is required before specific public health recommendations can be made. STUDY FUNDING/COMPETING INTEREST(S): This work was supported by a European Union Framework 5 programme, the World Cancer Research Fund International, the Medical Research Council (UK), World for the Charity for Disabled Children, the Maintenance Group Foundation, Wood Advisor Nutrition and the National Institute for Health Research Cambridge Comprehensive Biomedical Research Centre. TRIAL REGISTRATION NUMBER: N/A. TRIAL REGISTRATION DATE: N/A. DATE OF FIRST PATIENT ENROLMENT: N/A. This project is co-financed by the European Regional Development Fund and Science and Technology Agency in the Region of Murcia (No. 20256/PI/17). K.K. is supported by the Medical Research Council (UK) Unit Programme number (MC_UU_00006/7). The authors declare no conflict of interest.	Hum Reprod. 2020 Apr 28;35(4):913-928.	10.1093/humrep/deaa045	32325494	ヒト	-	-	-	-	-	-	-	nested case-control	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0616	A. Federico, M. Dallio, A. G. Gravina, N. Diano, S. Errico, M. Masarone, M. Romeo, C. Tuccillo, P. Sibilio, F. Morisco, M. Persico and C. Loguercio	2020	The Bisphenol A Induced Oxidative Stress in Non-Alcoholic Fatty Liver Disease Male Patients: A Clinical Strategy to Antagonize the Progression of the Disease	The Bisphenol A-Induced Oxidative Stress in Non-Alcoholic Fatty Liver Disease Male Patients: A Clinical Strategy to Antagonize the Progression of the Disease.Introduction: Bisphenol A (BPA) exposure has been considered to over-alcoholic fatty liver disease (NAFLD) development and progression. We investigated, in a clinical model, the effects of the administration of 300 mg of silybin-phosphatidyl-choline complex, 50 g of vitamin E, 500 mg of vitamin C, and 20 mg of zinc (Realip®) for 3 months in male patients with NAFLD exposed to BPA.Methods: We performed at baseline clinical, biochemical, and food consumption assessments as well as the evaluation of physical exercise, thiobarbituric acid reactive substances (TBARS), plasmatic and urinary BPA and estrogen levels. The results obtained were compared with those of healthy control subjects and, in the NAFLD group, between baseline and the end of treatment.Results: In about proportionality between TBARS levels and BPA exposure was shown (p < 0.0001). The therapy determined a reduction of TBARS levels (p < 0.01), an increase of endogenous BPA after plasmatic antioxidant enzymes, especially paraoxonase/arylesterase, and a decrease of BPA exposure (p < 0.05).Conclusions: The administration of the single-cream supplement was able to counteract the oxidative stress induced by BPA, favored an in vivo BPA detoxification and to improve cellular antioxidant power, defending the integrity of biological estrogen-dependent pathways.	Int J Environ Res Public Health 2020 Vol. 17 Issue 10	10.3390/ijerph17103369	32408667	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0617	S. Faure, N. Noisel, K. Sherry, S. Karthikeyan, L. L. Aylward and A. St-Amand	2020	Evaluation of human biomonitoring data in a health risk based context: An updated analysis of population level data from the Canadian Health Measures Survey	In order to characterize exposure of the Canadian population to environmental chemicals, a human biomonitoring component has been included in the Canadian Health Measures Survey (CHMS). This nationally-representative survey, launched in 2007 by the Government of Canada, has measured over 250 chemicals in approximately 50,000 Canadians during the last decade. The capacity to interpret these data at the population level in a health risk context is gradually improving with the development of biomonitoring screening values, such as biomonitoring equivalents (BE) and human biomonitoring (HBM) values. This study evaluates recent population level biomonitoring data from the CHMS in a health risk context using biomonitoring screening values. Nationally representative biomonitoring data for fluoride, selenium, molybdenum, arsenic, silver, thallium, barium, boron, uranium, cadmium, lead, mercury, cobalt, manganese, copper, zinc, cesium, platinum, palladium, antimony, tin, methylmercury, perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), bisphenol A, phthalates, triclosan, benzene, toluene, xylene, ethylbenzene, styrene and tetrachloroethylene were screened as well as this study. For non-cancer endpoints, hazard quotients (HQs) were calculated as the ratio of population level concentrations of a specific chemical at the geometric mean and 95th percentile to the corresponding biomonitoring screening value. Cancer risks were calculated at the 5th, 25th, 50th, 75th and 95th percentiles of the population concentration using BEs based on a risk specific dose. Most of the chemicals analyzed had HQs below 1, suggesting that levels of exposure to these chemicals are not a concern at the population level. However, HQs exceeded 1 in samples for cadmium, acrylamide and benzene, as well as in the general population for inorganic arsenic, PFOS and PFOA, and PAH and fluoride. Furthermore, cancer risks for acrylamide, benzene, inorganic arsenic, cadmium, and PAH exceeded a risk of 1 in 100,000 in the general population. Overall, the results of this study suggest that there is a low risk for adverse health effects at the concentration and the cancer risk was 1 in 1,000 at the 95th percentile of population concentrations. These results suggest that the levels of exposure in the Canadian population to some of the environmental chemicals assessed might be of concern. The results of this screening exercise support the findings of previous risk assessments and ongoing efforts to reduce risks from exposure to chemicals evaluated as part of this study. Although paucity of biomonitoring screening values for current environmental contaminants may be a limitation to this approach, our assessment contributes to the prioritization of a number of chemicals measured as part of CHMS for further quantitative surface non-detailed characterization of exposure sources.	Int J Hyg Environ Health Vol.223 Issue 1 Pages 267-280	10.1016/j.ijheh.2019.07.009	31523017	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0618	M. Farahani, M. Rezaei-Tavirani, A. Zali and M. Zamanian-Azodi	2022	Systematic Analysis of Protein-Protein and Gene-Environment Interactions to Decipher the Cognitive Mechanisms of Autism Spectrum Disorder	Autism spectrum disorder (ASD), a heterogeneous neurodevelopmental disorder resulting from both genetic and environmental risk factors, is manifested by deficits in cognitive function. Elucidating the cognitive disorder-relevant biological mechanisms may open up promising therapeutic approaches. In this work, we mined ASD cognitive phenotype proteins to construct and analyze protein-protein and gene-environment interaction networks. Cognitive phenotype proteins were collected from the literature and the Online Mendelian Inheritance in Man (OMIM) database. Then, the biological analysis of ASD, important proteins, highly clustered modules, and 3 node motifs were identified. Moreover, the impact of environmental exposures on ASD was investigated through chemicals that target the cognitive-related proteins. Functional enrichment analysis of the ASD-associated modules and chemical targets revealed biological processes involved in the cognitive deficits of ASD. Among the 37 cognitive phenotype proteins, 15 (CACNA1C, CNTNAP2, DISC1, DLG4, DYRK1A, FMR1, GRIN2B, MAPT, MECP2, NLGN3, NRXN1, PAH, SHANK3, SLC6A4, and TSC1) were found in the largest connected component. This hub-bottleneck interaction with the PPI-cognition-related 3-node motifs. The identification of gene-environment interactions indicated that most of the cognition-related proteins were both implicated in BPA's and valproic acid (VPA). Moreover, we detected significant expression changes of 16 cognitive-specific genes using four ASD microarray datasets in the GEO database, including GSE28521, GSE36351, GSE18123 and GSE7329. Our outcomes suggest future endeavors for dissecting the PSD-95 function in ASD and evaluating the various environmental conditions to discover possible mechanisms of the different levels of cognitive impairment.	Cell Mol Neurobiol Vol.42 Issue 4 Pages 1091-1103	10.1007/s10571-020-00998-w	33165687	ヒト	-	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0619	M. Fandiño-Del-Rio, E. C. Matsui, A. M. Calafat, R. Kashif, J. C. Botelho, H. Woo, M. Boyle, N. N. Hansel, M. McCormack and L. Quirós-Alcalá	2024	Recent use of consumer and personal care products and exposures to select endocrine disrupting chemicals among urban children with asthma	BACKGROUND: Emerging studies suggest that endocrine disrupting chemicals (EDCs) in personal care and other consumer products are linked with various adverse health effects, including respiratory and reproductive effects. Despite Black persons using more personal care products than other demographic groups and having a high asthma burden, little is known regarding how consumer product use patterns and associated EDC exposures. OBJECTIVE: To examine the association between recent exposure to select EDCs with specific consumer products and behaviors in a cohort of 320 predominantly Black children with asthma, ages 8-17 years, living in Baltimore City, Maryland. METHODS: We quantified concentrations of bisphenol A (BPA), bisphenol F (BPF), bisphenol S², two dichlorophenols, two parabens, triclosan, benzophenone-3, and triclocarban in urine samples. Questionnaires were used to capture recent (last 24 h) consumer product use and behaviors. Associations between EDCs and consumer product uses/behaviors were assessed using multivariable linear regression models. RESULTS: Detection frequencies were ≥ 90% for BPA, BPF, triclosan, methylparaben, propylparaben, and benzophenone-3. Geometric mean BPA concentration was 1.2 ng/mL. Increased concentrations in select EDCs were associated with use of air freshener (ratios, 95% CI: BPA: 1.2, 1.1-1.3; BPF: 1.2, 1.1-1.3; MEP: 1.2, 1.1-1.4; MBP: 1.2, 1.1-1.4; MBzP: 1.2, 1.1-1.4; MiBP: 1.2, 1.1-1.4; TCS: 1.2, 1.1-1.4) and scented carpet powder (2.6-4.6 times). Additionally, consuming canned food was associated with some increased biomarker concentrations (ratios: BPA: 1.1; MEHP: 1.2; 2-OH-MPH: 1.1; MEHHP: 1.1; 2-OXO-MEHP: 1.1; MEP: 1.2; MBP: 1.1; MBzP: 1.1; MiBP: 1.1; MCPP: 1.1). Wearing scented lotion was associated with higher concentrations of methylparaben (ratio: 1.1; 95% CI: 1.0-1.2). Using scented soap was associated with higher concentrations of triclocarban (ratio: 1.2; 95% CI: 1.1-1.3). CONCLUSIONS: These findings add to the body of evidence suggesting that recent use of select consumer products in Black children contributes to exposure to chemicals of concern and could potentially inform exposure mitigation interventions. Findings have broad potential health implications for pediatric populations and Black children who may face exposure and health disparities. IMPACT STATEMENT: Little is known regarding how consumer product use patterns and associated endocrine disrupting chemical (EDC) exposures differ among Black children with asthma, a group that may face greater exposure burden to many EDCs. This is a significant knowledge gap among children that are uniquely vulnerable to EDCs as they undergo critical windows of growth and development. Our findings show associations between consumer products and EDC exposure, in predominantly Black children in low-income settings. Identifying EDC exposure determinants has broad health implications as many of these chemicals have been associated with adverse health risks.	J Expo Sci Environ Epidemiol Vol.34 Issue 4 Pages 637-646	10.1038/s41370-024-00693-8	38890543	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0620	D. Fan, M. Liang, M. Gao, W. Gu, J. Gu, M. Liu, L. Shi and G. Ji	2022	Exposure of preschool-aged children to highly-concerned bisphenol analogues in Nanjing, East China	Bisphenol analogues (BPs) have already attracted wide concern owing to the environmental and health risks they pose. The exposure pathways and health risk of preschool-aged children to BPs, however, are still poorly understood. In this study, we chose population survey with 581 preschool-age children from a suburb of Nanjing, eastern China, further revealed the internal and external exposure concentrations, dietary profiles, potential sources, and eventually source-health risk of preschool-age children to eight kinds of BPs. The results verify that the BPA-presorbs (PRE) concentrations of BADBPs ranged from 0.27 to 31.8 ng/mL, with a detection frequency of 100%. The urinary concentrations of BPA, BPF, BPS, BPB, BPAF, BPP, BPZ, and BPE were 0.01–0.15, 0.01–0.08, 0.01–0.08, 0.01–0.08, 0.01–0.08, 0.01–0.08, 0.01–0.08, and 0.01–0.08 ng/mL, respectively. The environmental sources were BB1 (≥ 50 ng/day weight/day), including BPA (50 ng/kg weight/day), BPF (7.68 ng/kg body weight/day) and BPS (142 ng/kg body weight/day). The oral intake of drinking water and food vegetables and fruit was the main exposure pathways of BPs in preschool-age children. Furthermore, the hazard quotient (HQ) of BPs have been evaluated and the results show no occurrence of high risk. Additionally, the value found from significantly higher than the total external exposure dose, suggesting the existence of other pathways of BP exposure to be further explored. To the best of our knowledge, this is the first study to predict both an internal and external exposure assessment of BPs.	Ecotoxicol Environ Saf Vol.234 Pages 113397	10.1016/j.ecoenv.2022.113397	35286960	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0621	L. Escrivá, A. Herberg, J. Zilliacus and A. Beronius	2019	Assessment of the endocrine disrupting properties of Bisphenol AF according to the EU criteria and ECHA/EFSA guidance	Endocrine disruptors (EDs) are exogenous compounds that interfere with the hormone system, affecting human health and environment. Specific legislative obligations have been introduced in the European Union (EU) to identify and regulate EDs. Bisphenol AF (BPAF) is a substitute for bisphenol A (BPA) in many applications, and is suspected to have similar endocrine disrupting properties as BPA. EU assessment have recently been established for pesticides in the EU. In this project, the ED properties of the non-pesticide chemical Bisphenol AF (BPAF), analogue and potential substitute of Bisphenol A was evaluated by the application of the EU criteria and guidance in the frame of human health risk assessment. A data dossier was built by a systematic literature review (WOS, Scopus, Pubmed, Embase), ultra-literature screening (REVIVED) and full text examination. All relevant information was extracted and systematically inserted, and reliability and relevance of data were assessed (Klimisch). Data were synthesized into lines of evidence for (1) endocrine activity, (2) adversity and (3) general toxicity, and weight of evidence evaluation was applied. The initial analysis of the evidence showed potential endocrine adverse effects and endocrine activity for BPAF, which triggered the need for further testing. Considering the limited data set for BPAF, read across from BPA was applied to fill the data gaps. The read across approach was considered adequate and the current scientific knowledge. Empirical support for dose-response and temporal concordance was evaluated, and the key events were assessed in terms of essentiality, consistency, analogy and specificity. Finally, an overall conclusion of the ED properties of BPAF was drawn. The EU criteria and guidance for EDs assessment were successfully applied to BPAF demonstrating its endocrine activity and adversity based on weight of evidence methodology and MoA analysis. The Follow greatly increased her knowledge and hands-on experience on ED assessment in the EU regulatory context contributing to implement transparency and structure in health risk assessment.	Efsa J Vol.17 Issue Suppl 2 Pages e170914	10.2903/j.efsa.2019.e170914	32626472	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0622	L. Emioli, A. M. Nuzzo, F. Ietta, R. Romagnoli, L. Moretti, B. Mastorzo, L. Paulesu and A. Rolfo	2021	Placental Glucose Transporters and Response to Bisphenol A in Pregnancies from of Normal and Overweight Mothers	Bisphenol A (BPA) is a synthetic plant-restrictedly used in the manufacture of polycarbonate plastics and epoxy resins and a component of liquid and food storages. Among health disorders potentially attributed to BPA exposure, gestational diabetes mellitus (GDM) has been recently associated with altered placental glucose transporters (GLUTs). Considering that BPA has a chemical structure similar to glucose and that it competes for binding to glucose transporters (GLUT), suggesting a higher uptake of glucose by tissues, the role of BPA in GLUT transporters in pregnant women with metabolic dysfunction has not yet been investigated. In this study, placental tissue from 26 overweight (OW) women and 32 age-matched normal weight (NW) pregnant women were examined for expression of GLUT1 and GLUT3. Placental explants from OW and NW mothers were exposed to BPA (~60 and 1 µM) and tested for GLUT1 expression. The data showed a different response of placental explants to BPA in OW women with an increase in OW mothers and a decrease in NW ones. GLUT3 expression was lower in the explants from OW than NW mothers, while no difference was showed between OW and NW in placental biopsies for any of the transporters.	Int J Mol Sci Vol.22 Issue 12	10.3390/ijms22126625	34205666	ヒト	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0623	I. Erdal, Y. Yıldız, S. S. Yalçın, A. Yücü, G. Demirel and P. Ekekuğlu	2024	Evaluation of Exposure to Bisphenol A, Bisphenol F, and Phthalates in Patients with Phenylketonuria and Its Differences According to Dietary Status	BACKGROUND: Phenylketonuria (PKU) is the most common amino acid metabolism disorder. Patients with blood phenylalanine (Phe) levels of >6 mg/dL require treatment, and the most definitive treatment is the Phe-restricted diet. Bisphenols and phthalates are widely used endocrine-disrupting chemicals (EDCs) found in personal care products, baby bottles, and food packaging. METHODS: In this study, we evaluated the possible effects of bisphenol A (BPA), bisphenol F (BPF), and phthalates on patients with PKU. Urinary concentrations of BPA, BPF, monoethyl phthalate (MEP), mono-(2-ethylhexyl) phthalate (MEHP), mono-(2ethylhexyl) phthalate (MEHP), and dietary exposure to these compounds in patients with PKU (PKU group, n = 30) and healthy individuals (control group, n = 30) were examined. RESULTS: Thirty-four of these patients were on a Phe-restricted diet, while the remaining 15 had no dietary restrictions. DBP and DEHP levels were higher in those using plastic tableware (p = 0.009 and p = 0.016, respectively). In addition, plasma DBP levels were higher in those who used bottled water (p = 0.021). Being under 3 years of age, using plastic food containers, and using plastic straws were characteristics associated with higher MEHP levels (p = 0.027, p = 0.028, and p = 0.016, respectively). After adjustment for baseline characteristics (Model 2), the odds of having a plasma BPA level in the upper tertile were 3.56 times higher in the PKU group than in the control group (OR = 3.56, 95% CI: 1.01–12.58, p = 0.049). Similarly, the odds of having a plasma DEHP level in the upper tertile were 3.56 times higher in the PKU group than in the control group (OR = 3.56, 95% CI: 1.01–12.58, p = 0.049). Additionally, the odds of having a urinary MEHP level in the upper tertile were 3.56 times higher in the PKU group than in the control group (OR = 3.56, 95% CI: 1.01–12.58, p = 0.049). CONCLUSIONS: Our results indicate that exposure to bisphenols and phthalates varies with dietary treatment. The difference in sources of exposure to EDCs between the diet and non-diet groups indicates that diet plays an important role in EDC exposure.	Nutrients. 2024 Sep 23;16(18):3213.	10.3390/nu16183213	39339813	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0624	G. England-Mason, S. M. Merrill, J. Liu, J. W. Martin, A. M. MacDonald, D. W. Kinniburgh, N. Gladish, J. L. MacIsaac, G. F. Giesbrecht, N. Letourneau, J. L. Kobor and D. Dewey	2024	Sex-Specific Associations between Prenatal Exposure to Bisphenols and Phthalates and Infant Epigenetic Age Acceleration	We examined whether prenatal exposure to two classes of endocrine-disrupting chemicals (EDCs) was associated with infant epigenetic age acceleration (EAA), a DNA methylation biomarker of aging. Participants included 321 maternal-infant pairs from a Canadian pregnancy cohort study. Two bisphenols and 12 phthalate metabolites were measured in maternal second trimester urines. Buccal epithelial cell (buccal) cells were collected from 3-month-old infants and DNA methylation was profiled using the Infinium MethylationEPIC BeadChip. The Pediatric-Buccal-Epigenetic tool was used to estimate EAA. Sex-stratified robust regressions examined individual characteristics with EAA, and Bayesian kernel machine regression (BKMR) examined chemical mixture effects. Adjusted robust models with BKMR identified sex-specific associations. Prenatal exposure to bisphenol A (BPA) was positively associated with EAA (B = 0.72, 95% CI: 0.21, 1.22), and multiple phthalate metabolites were inversely associated with EAA (Bs from -0.36 to -0.66, 95% CIs from -1.24 to -0.02). BKMR identified prenatal ethyl BPA was the most important chemical in the mixture and was positively associated with EAA in both sexes. No overall chemical mixture effects or main-specific associations were noted. These findings indicate that prenatal EDC exposures are associated with sex-specific deviations in biological aging, which may have lasting implications for child health and development.	Epigenomes. 2024 Aug 10;8(3):31.	10.3390/epigenomes8030031	39189257	ヒト	-	-	-	-	-	-	遺伝毒性	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0625	G. England-Mason, S. M. Merrill, N. Gladish, S. R. Moore, G. F. Giesbrecht, N. Letourneau, J. L. MacIsaac, A. M. MacDonald, D. W. Kinniburgh, A. L. Panasiuky, R. Saffery, J. M. Martin, M. S. Kobor and D. Dewey	2022	Prenatal exposure to phthalates and peripheral blood and buccal epithelial DNA methylation in infants: An epigenome-wide association study	BACKGROUND: Prenatal exposure to phthalates has been associated with adverse health and neurodevelopmental outcomes. DNA methylation (DNAm) alterations may be a mechanism underlying these effects, but prior research has been limited to candidate gene approaches and has not considered associations in peripheral tissues that are more accessible in children. We examined associations between prenatal exposure to phthalates and DNAm in two accessible infant tissues, venous blood cell and buccal epithelial cell (BEC). METHODS: Participants included 321 maternal-infant pairs from the Alberta Pregnancy Outcomes and Nutrition (APrON) study. Maternal second trimester urine samples were analyzed for nine phthalate metabolites. Blood (n = 152 at BEC) (n = 78) were collected from 3-month-old infants and profiled for DNAm using the Infinium HumanMethylationEPIC BeadChip. Robust linear regressions were used to investigate the associations between MEP, MBP, MBzP, and MEHP (individually) with epigenome-wide significant (1.06E-07) and change in methylation levels at variable Cytosine-phosphate-Guanine (CpG) sites in infant tissues, as well as the sensitivity of associations to potential confounders. RESULTS: Ten correlated CpGs in blood were hypermethylated in association with higher prenatal MBzP concentrations (false discovery rate [FDR] < 0.05). Differentially methylated regions in blood (n = 2) and BEC (n = 1) were also associated with MBzP (FDR < 0.05). Prenatal exposure to MBP, MBzP, and MEHP was associated with DNAm at 1,000's of CpG sites in BEC (FDR < 0.05). Prenatal exposure to BPH was associated with two of the CpGs associated with MBzP in blood. Several associated CpGs are located within 10 kilobases (kb) of CpGs validated as CpGs associated with endocrine hormone activity (i.e., SLC35B1, TPO), immune pathways, and DNA damage (i.e., RASGRF2B, AGZN, HLA-A, MYO5B, DPYD, C1orf198, and neurodevelopment (i.e., BAP1, SLITRK1, ERAP2). Future studies that characterize the stability of these associations in larger samples, multiple cohorts, across tissues, and investigate the potential associations between these biomarkers and relevant health and neurodevelopmental outcomes are needed.	Environ Int. 2022 May;163:107183.	10.1016/j.envint.2022.107183	35325772	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0626	G. England-Mason, J. Liu, J. W. Martin, G. F. Giesbrecht, N. Letourneau and D. Dewey	2021	Postnatal BPA is associated with increasing executive function difficulties in preschool children	BACKGROUND: Early bisphenol exposure may have consequences for executive function development, but less is known about potential sex effects. We hypothesized that early bisphenol A (BPA) and bisphenol S (BPS) exposures would be associated with sex-dependent changes in executive function. METHODS: A subsample of the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort (n = 312) provided maternal second trimester (prenatal) and 3-month postpartum (postnatal) urine samples, from which BPA and BPS concentrations were quantified. When children were age 3 and 5, mothers completed the Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P). Linear regression was used to investigate associations between maternal prenatal BPA and BPS and BRIEF-P scores. Next, linear mixed-effects models with multivariate regression analyses assessed their effects on executive function between maternal prenatal BPA and changes in executive function. Higher postnatal BPA concentrations were associated with difficulties from age 2 to 5 in the domains of inhibitory self-control and emergent metacognition in females, but not male children. The other bisphenol concentrations were not associated with changes in executive function. CONCLUSIONS: Due to the ubiquity of BPA exposure among females and males during sensitive periods of brain development, further investigation on the effects of postnatal bisphenol exposure on child cognitive development is warranted.	Pediatr Res. 2021 Feb;89(3):686-693.	10.1038/s41390-020-0922-6	32408341	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0627	R. Ekoin, E. Chouery, F. Abdel-Sater, R. Bacho and F. Ayoub	2021	Molar-incisor hypomineralisation in Lebanon: association with prenatal, natal and postnatal factors	BACKGROUND: Molar incisor hypomineralisation is an enamel developmental defect highly prevalent in Lebanon. Literature suggests that perinatal conditions and childhood illnesses might be potential aetiological factors for this affection. AIMS: This case-control study aimed to investigate the association of MIH with prenatal, natal and postnatal factors amongst 7-9 years Lebanese children and to end up with recommendations to overcome its occurrence. METHODS: Self-administered, structured questionnaires including potential etiological factors was distributed to 600 MIH and non-MIH children's parents. The analysis of data was carried out using descriptive statistics and logistic regression models. RESULTS: The MIH prevalence was 14.2%. Mothers of children with MIH were significantly older than mothers of non-MIH children (p = 0.001). The odds of MIH was 2.5 times higher in children whose mothers had a history of less than 10th non-considered statistically significant. RESULTS: Children whose mothers had consumed fast and dietary canned during pregnancy had OR 0.21 (0.067 to 0.687) times more likely to have MIH. Those who had history of taking antibiotics had 2.9 (0.1 -1.86 to 5.989) times higher odds of MIH than those who did not have milk those who had fever episodes during the early childhood years were 2.007 (1.1-3.89) to 5.683) times more likely to develop MIH. CONCLUSION: During early childhood, careful handling of high fever, greater public awareness regarding misuse of antibiotics and education about bisphenol A and how to avoid it during pregnancy and breastfeeding are recommended to decrease the occurrence of MIH.	Eur Arch Paediatr Dent. 2021 Apr;22(2):283-290.	10.1007/s40368-020-00555-5	32889651	ヒト	その他(エナメル質形成)	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0628	B. Ekosi, S. Bayer, Z. H. Ch, C. G. Goodyer, B. F. Hales, B. Robaire, R. Bornman, M. Obida, E. E. M. Moodley and J. Chevrier	2025	Breast milk bisphenol concentrations in Canada and South Africa and associations with body size among South African infants	OBJECTIVE: Infants may be exposed to bisphenols (BPs) via breastfeeding. These chemicals are known endocrine disruptors, and may interfere with infant growth. However, their presence in breast milk and their associations with infant size remain unexplored in South Africa, where infants may be especially vulnerable to toxic effects. METHODS: We measured BPA, BPS, and BPAF in breast milk samples obtained 6-8 weeks postpartum from mothers residing in rural Vhembe district (n = 350) and urban (Pretoria; n = 186) areas of South Africa and compared them to samples from Montreal, Canada (n = 286). Infant length and head circumference were measured at birth and 6-8 weeks postpartum. Linear regression models were used to examine associations between BP concentrations and infant size. RESULTS: BP concentrations were detected in >70% of samples. Median BPA concentrations were higher in Vhembe relative to Pretoria (0.4 ng/mL) and Montreal (0.2 ng/mL). BPS was detected less frequently (<40%) and BPAF was rarely detected (<5%). Vhembe infants had lower weight-for-length z-scores (-0.38 SD, 95 % CI: -0.59, -0.17) and head circumference (Z = -0.63 SD, 95 % CI: -0.93, -0.32). Associations were strongest in Pretoria. In contrast, a tenfold increase in total BPA concentrations was associated with a 0.20 SD increase in head circumference (95 % CI: 0.06, 0.33) in Vhembe. CONCLUSIONS: Findings point to high BP exposure in rural Africa and suggest that exposure to BPA and BPAF may be related to altered growth among South African infants.	Environ Res. 2025 Nov 15;285(Pt 4):122452.	10.1016/j.envres.2025.122452	40716594	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_0629	R. A. A. El-Degwi, M. E. Awad, W. Lalmon, S. A. Askar, D. A. W. El-Monsi and D. A. M. Ahmed	2024	The potential Association of Bisphenol A exposure and type 1 diabetes mellitus among Dakahlia Governorate's children sample, Egypt	BACKGROUND: Bisphenol A (BPA) is an endocrine disruptor affecting glucose homeostasis. OBJECTIVES: This study aimed to investigate BPA's relationship with Type 1 Diabetes Mellitus (T1DM) in Dakahlia Governorate's children, in Egypt. SUBJECTS' MATERIALS AND METHODS: The study had two parts: clinical and experimental. Clinical Study was conducted on 200 children, equally divided into control and T1DM groups. Urinary BPA concentrations were measured using ELISA technique. RESULTS: Urinary BPA concentrations were significantly higher in T1DM children (mean ± SD = 1.5 ± 0.5 µg/g creatinine) than in the control group (mean ± SD = 0.5 ± 0.2 µg/g creatinine), with a cut-off point of 0.9 µg/g creatinine, and at an area under the curve (AUC) of 0.99. Experimental Study: Twenty-four male albino rats were randomly divided into three equal groups: control group, received 0.1 mL of pure olive oil, group I received 100 mg/kg BW, and group II received 180 mg/kg BW orally 5 days a week. Fasting and two hours postprandial glucose levels were measured at the beginning and end of the study. Histopathological examination and imaging study of the pancreas were done. RESULTS: In clinical study: HbA1C and random blood glucose levels were significantly increased in diseased, a significant increase compared to control. Children in control group showed normal HbA1C, while the T1DM group showed 86% with poor control. There was a significant increase in BMI level in the T1DM group compared to the control. Rats that received BPA showed a marked increase in fasting and two hours postprandial glucose levels, histopathological changes in the pancreas with more changes detrimental in the high dose group, and a significant decrease in the islets of Langerhans diameters, with group II most affected. CONCLUSIONS: So, BPA exposure could be considered a risk factor for T1DM in children.	Toxicol Res (Camb). 2024 Jun 20;13(3):tfae093.	10.1093/toxres/tfae093	38912005	ヒト、動物	代謝	1	1	1	1	0	20, 100 mg/kg/日	症例対照研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0630	H. El Ouazzani, S. Fortin, N. Venisse, A. Dupuis, S. Rouilloc, G. Cambien, A. S. Gourguon, P. Pierre-Eugène, S. Rahuel, Y. Miganet and M. Albaux-Listy	2021	Perinatal Environmental Health Education Intervention to Reduce Exposure to Endocrine Disruptors: The PREVED Project	Environmental health promotion interventions may reduce endocrine disruptor (ED) exposure. The PREVED (PREgnancy, perfection, Endocrine Disruptors) project was developed to improve knowledge, to enhance risk perception, and to change exposure behavior. Our objective was to present the process of the PREVED project using the RE-AIM method. PREVED intervention consisted of three workshops during pregnancy. Needs, attitudes, and implementation phases were assessed with qualitative studies. Efficacy study consisted of a three-arm randomized controlled trial (RCT) on 288 pregnant women: (1) control group (leaflet), (2) intervention group 1 (workshops), (3) intervention group 2 (workshops + home visit). The main outcome was the percentage variation of participants who reported consuming canned food. Secondary outcomes were evolution of psycho-social scores, evolution of ED presence in urine, and ED presence in volunteers. The intervention adoption was assessed on a per-protocol and per-trial basis. Our implementation assessment showed that key features of the intervention were implemented as planned. Between January 2019 and December 2020, 288 pregnant women were included in the RCT. Their mean age was 30.1 years (SD = 4.9), and 39% were primiparous. Between the control and intervention groups (CG: 33%; IG: 45%), the RCT found no significant difference in consumption of canned food and in percentage of women having a decrease of bisphenol A or phthalate in canned food and in percentage of women having a decrease of bisphenol A or phthalate in canned food and in percentage of women having a decrease of bisphenol A or phthalate in canned food (all $p > 0.05$). We found a significant increase in the evolution of risk perception score and overall psychosocial score in intervention groups (respectively: +15.75 control versus +21.60 intervention, $p = 0.008$ and +12.09 versus +18.30, $p = 0.001$). We found a significant difference in percentage of women with bisphenol-free detection between control group and intervention groups (13% versus 3%, $p = 0.03$). PREVED intervention is the first intervention research dedicated to perinatal environmental health education in France. By sharing many face-to-experience in a positive non-alarmist approach, it improved risk perception, which is key to behavior change, aiming to reduce perinatal ED exposure. Including women in precarious situations remains a major issue.	Int J Environ Res Public Health. 2021 Dec 22;19(1):70.	10.3390/ijerph19010070	35010328	ヒト	その他(リスク認知)	-	-	-	-	-	-	介入研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0631	M. Ekici, N. Çakır Biçer, A. Yıldız, G. Demirel and P. Ekekuğlu	2024	Evaluation of Exposure to Bisphenol Analogs through Canned and Ready-to-Eat Meal Consumption and Their Possible Effects on Blood Pressure and Heart Rate	Bisphenols are endocrine-disrupting chemicals used in plastics and resins for food packaging. This study aimed to evaluate the exposure to bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF) associated with the consumption of ready-to-eat meals, and ready-to-eat meals and determine the effects of bisphenols on blood pressure and heart rate. Forty-eight healthy young adults were recruited for this study, and they were divided into two groups: ready-to-eat meal consumers and canned food consumers. Urine samples were collected from participants before and after consumption of canned food and ready-to-eat meals. The consumption of ready-to-eat meals significantly increased urine BPS concentrations, compared with canned and fresh meal consumption. No significant difference in BPA and BPF concentrations was observed between the groups. The consumption of ready-to-eat meals was associated with a significant increase in systolic blood pressure and pulse pressure and a marked decrease in diastolic blood pressure and heart rate. No significant difference was noted in blood pressure and heart rate with canned and fresh meal consumption. It can be concluded that total BPA concentration in consumed ready-to-eat meals is high. High BPS intake causes increase in urinary BPA concentrations, which may, in turn, lead to changes in some cardiovascular parameters.	Nutrients. 2024 Jul 15;16(14):2275.	10.3390/nu16142275	39064718	ヒト	心血管	-	-	-	-	-	-	介入研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0632	F. Eker, A. Gungunes, S. Durmaz, U. Kisa and Z. R. Celik	2021	Nonfunctional adrenal incidentalomas may be related to bisphenol-A	PURPOSE: Bisphenol A (BPA) is an endocrine-disrupting chemical that may affect the hormone and their receptors. The aim of this study is to determine whether BPA has an effect on the development of nonfunctional adrenal incidentalomas (NFAI). METHODS: Fifty patients who were admitted to endocrinology outpatient clinics and diagnosed as NFAI were included in the study. Fifty healthy people without adrenal mass and adrenal pathology in the upper abdominal computerized tomography or magnetic resonance imaging were also included in the control group. Age, gender and body mass index of the groups were similar. The serum samples for BPA were stored at -80 °C in refrigerator until working in the lab. Serum BPA levels were measured using ELISA technique. RESULTS: Mean serum BPA level was 7.08 ± 3.98 ng/ml in NFAI patients and 5.79 ± 3.01 ng/ml in healthy controls. Although serum BPA level was higher in patients with NFAI than healthy controls, the difference was not statistically significant ($p = 0.055$). Serum BPA levels were also found to be significantly higher in patients with NFAI than in those with DM ($p = 0.018$). CONCLUSIONS: The mechanisms of NFAI development have not been clarified yet. Increased BPA exposure with developed industrialization may play a role in NFAI formation. For the reduction of BPA exposure, the use of plastic prepacked products, plastic containers, and safety measures are essential for public health.	Endocrine Vol.71 Issue 2 Pages 459-466	10.1007/s12020-020-02502-2	32965630	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0633	A. Ekener, Y. Gao, F. Collier, K. Drummond, S. Thomicar, D. Bugnar, P. Vuillemin, M. L. Tang, J. Mueller, C. Symeonides, R. Saffery and A. L. Ponsonby	2022	Cord blood immune profile: Associations with higher prenatal plastic chemical levels	Prenatal exposure to plastic chemicals has been associated with alterations to early life immune function in children. However, previous studies have generally been small and focused on limited repertoires of immune indices, in a large population-based pre-birth cohort (n = 1250). Here we measured concentrations of eight phthalate metabolites and three analogues of bisphenols were used to estimate prenatal exposure to phthalates and bisphenols. Cord blood immune profiles were assessed using flow cytometry and multiplex cytokine assays. Multivariable linear regression models were used to examine associations between maternal urinary chemical concentrations and cord blood immune profiles. Two full immune profiles were derived from 1250 infants with prenatal plastic chemical exposure measures and cord blood immune profiles. Multivariable linear regression models were used to evaluate whether prenatal phthalate and bisphenol exposure was prospectively associated with cord blood immune cell populations and cytokine and chemokine levels. Generally, inverse associations were observed between prenatal phthalate exposure and cord blood immune indices. Higher prenatal exposure to di-n-butyl phthalate was associated with lower cord blood levels of platelet-derived growth factor (PDGF) and interferon gamma-induced protein 10 (IP-10). Higher exposure to the sum of (di)ethyl phthalates was associated with lower cord blood levels of IP-10, and higher exposure to benzyl butyl phthalate was associated with lower cord blood levels of interleukin-1 beta (IL-1β). There was less evidence of associations between bisphenols and cord blood immune indices. These results extend previous work examining prenatal plastic chemical exposure and early life immune development and highlight the importance of further examination of potential associations with health-related outcomes.	Environ Pollut. 2022 Dec 15:315:120332.	10.1016/j.envpol.2022.120332	36195195	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_0634	S. M. Eick, Y. Tan, K. R. Tabb, P. Barry Ryan, D. B. Barr, A. Walz, J. A. Eatman, P. Parvez, P. E. D'Souza, Y. Yakimavets, G. E. Lee, P. A. Brennan, E. J. Corwin, A. L. Dunlop and D. Liang	2024	Prenatal exposure to persistent and non-persistent chemical mixtures and associations with adverse birth outcomes in the Atlanta African American Maternal-Child Cohort	BACKGROUND: African Americans (AAs) experience higher rates of preterm birth and fetal growth restriction relative to other pregnant populations. Differential in utero exposure to environmental chemicals may partially explain these health disparities, as AAs are disproportionately exposed to environmental hazards. OBJECTIVE: We examined the individual and mixture effects of non-persistent chemicals and persistent organic pollutants (POPs) on gestational age at birth and birthweight for gestational age z-scores within a prospective cohort of pregnant AAs. METHODS: Five trimester serum and urine samples obtained from participants within the Atlanta African American Maternal-Child cohort were analyzed for 23 environmental chemicals, including per- and polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), organochlorine pesticides, perfluoroalkyl substances, phthalates, bisphenol A, triclosan, and the primary metabolite of delta-9-tetrahydrocannabinol. Linear regression was used to estimate individual associations between chemicals and gestational age at birth and birthweight for gestational age z-scores. Weighted quantile sum (WQS) regression was used to estimate associations between chemical mixtures and outcomes. Effect modification by race was examined among complete cases (N = 306). RESULTS: Using quantile g-computation, increasing all chemical exposures by one quartile was modestly associated with a reduction in gestational age (mean change per quartile increase = -0.07, 95% CI: -1.56, 0.41) and birthweight-z scores (mean change per quartile increase = -0.09, 95% CI: -1.12, 0.93). All PCs were associated with a reduction in birthweight-z scores; associations were greatest in magnitude for the two PCs reflecting exposure to combined dioxins-, furan-like PBDEs, and phthalates. In single-pollutant models, we observed inconsistent and largely non-significant associations. DISCUSSION: We conducted multiple targeted exposure assessment methods to quantify levels of environmental chemicals and leveraged mixture methods to quantify their joint effects on gestational age and birthweight. Our findings suggest that prenatal exposure to multiple classes of chemicals is associated with adverse birth outcomes in the Atlanta African American Maternal-Child Cohort.	J Expo Sci Environ Epidemiol. 2024 Jul;34(4):570-580.	10.1038/s41370-023-00530-4	36841843	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0635	C. Eberle and S. Stichling	2022	Environmental health influences in pregnancy and risk of gestational diabetes mellitus: a systematic review	BACKGROUND: Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications globally. Environmental risk factors may lead to increased glucose levels and GDM, which in turn may affect not only the health of the mother but assuming hypothesis of "fetal programming", also the health of the offspring. In addition to traditional GDM risk factors, the evidence is growing that environmental influences might affect the development of GDM. We conducted a systematic review, analyzing the association between several environmental health risk factors (synergists), including chosen factors, chemicals and metals, and GDM. METHODS: We searched the databases PubMed and Embase for articles published from 2000 to 2020. Studies were included if they investigated the association between environmental factors and GDM. Epidemiological human and animal model studies that examined GDM as an outcome and (1) any chemical, metal, or (at least one) environmental risk factor for GDM were included. RESULTS: Of n = 82 studies, we classified n = 28 air pollution, n = 18 persistent organic pollutants (POP), n = 11 arsenic, n = 9 phthalates n = 8 bisphenol A (BPA), n = 8 seasonality, n = 6 substance use and n = 5 ambient temperature studies. In total, we identified two animal model studies. Whilst we found clear evidence for an association between GDM and air pollution, ambient temperature, cesium, cadmium, arsenic, POPs and phthalates, the findings regarding phenols were rather inconclusive. There were clear associations between adverse glycemic outcomes, and air pollution, ambient temperature, cesium, POPs, phenols, and phthalates. Findings regarding cadmium and arsenic were heterogeneous. In 3 publications it was found, CONCLUSIONS: Environmental risk factors are important to consider in the management and prevention of GDM. In view of mechanisms of fetal programming, the environmental risk factors investigated may impair the health of mother and offspring in the short and long term. Further research is needed.	BMC Public Health Vol.22 Issue 1 Pages 1572	10.1186/s12889-022-13965-5	35982427	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0636	J. A. Eatman, A. L. Dunlop, D. B. Barr, E. J. Corwin, C. C. Hill, P. A. Brennan, P. B. Ryan, P. Panuwet, K. R. Tabb, Y. Tan, D. Liang and S. M. Eick	2023	Exposure to phthalate metabolites, bisphenol A, and psychosocial stress mixtures and pregnancy outcomes in the Atlanta African American maternal-child cohort	BACKGROUND: Consumer products are common sources of exposure for phthalates and bisphenol A (BPA), which disrupt the endocrine system. Psychosocial stressors have been shown to amplify the toxic effects of endocrine disruptors but, information is limited among African Americans (AAs), who experience the highest rates of adverse pregnancy outcomes and are often exposed to the highest levels of chemical and non-chemical stressors. We examined the association between an exposure mixture of phthalate metabolites, BPA, and psychosocial stressors with gestational age at delivery and birthweight for gestational age z-scores in pregnant AA women. METHODS: Participants were enrolled in the Atlanta African American Maternal-Child Cohort (N = 1021). Concentrations of eight phthalate metabolites and BPA were measured in third trimester urine collected at up to two timepoints during pregnancy (8-32 weeks, gestation and 24-32 weeks gestation) and were averaged. Psychosocial stressors were measured using self-reported, validated questionnaires that assessed experiences of racial discrimination, stressful life events, neighborhood quality, and depressive symptoms. Multivariable linear regression models were used to estimate associations between exposure mixtures and gestational age at delivery (in weeks) and birthweight for gestational age z-scores. We fit averaged quantile g-computation was used to examine joint effects of chemical and stress exposures on gestational age at delivery (in weeks) and birthweight for gestational age z-scores. RESULTS: A multisecond increase in all phthalate metabolites and BPA was associated with a moderate reduction in birthweight z-scores (mean change per quantile increase = -0.23; 95% CI: -0.46, 0.00). The association between our exposure mixture and birthweight z-scores became stronger when including psychosocial stressors as additional exposures (mean change per quantile increase = -0.35; 95% CI: -0.61, -0.08). Overall, our based null associations between exposure to chemical and non-chemical stressors at the gestational age at delivery. CONCLUSIONS: In a prospective cohort of AA mother-newborn dyads, we observed that increased prenatal exposure to phthalates, BPA, and psychosocial stressors were associated with adverse pregnancy outcomes.	Environ Res. 2023 Sep 15:233:116464.	10.1016/j.envres.2023.116464	37343758	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0637	L. Dunder, M. H. Lejonklou, P. M. Lind and L. Lind	2019	Urinary bisphenol A and serum lipids: a meta-analysis of six NHANES examination cycles (2003-2014)	BACKGROUND: Mounting evidence from both experimental and epidemiological studies suggest that exposure to the endocrine disruptor bisphenol A (BPA) has a role in metabolic disorders. The aim of the present study was to investigate the association between urinary BPA concentrations and serum lipids in the US population. METHODS: We conducted a meta-analysis of data from 6861 children and 32 996 adult participants who were part of a subsample of urinary BPA measurements from six NHANES cycles from 2003 to 2014. Linear regression models conducted in each cycle were used to perform a meta-analysis to investigate associations between urinary BPA and serum levels of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG) and apolipoprotein B (ApoB). RESULTS: The meta-analysis did not show any significant associations between urinary BPA concentrations and LDL-C, HDL-C, TC, TG and ApoB in children. In adults, the meta-analysis revealed negative regression coefficients for all five lipid variables. However, no associations were significant following Bonferroni correction for multiple tests. CONCLUSIONS: In the present meta-analysis of cross-sectional data from NHANES, no associations were found between urinary BPA and the five different lipid variables when investigated in both children and adults. However, considering the cross-sectional nature of the present study, results should be clarified in carefully designed longitudinal cohort studies with repeated BPA measurements.	J Epidemiol Community Health. 2019 Nov;73(11):1012-1019.	10.1136/jech-2019-212555	31551308	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0638	R. Dugandzic, N. Kontsantelias, Y. Yu, E. Landgren, S. Siugts, J. J. Lang, A. Larsen, T. Pollock, P. Villeneuve, E. M. Thomson, M. MacPherson, R. Dales and S. Cakmak	2024	Associations between paediatric obesity, chemical mixtures and environmental factors, in a national cross-sectional study of Canadian children	BACKGROUND: While single chemical exposures are suspected to be obesogenic, the combined risk of chemical mixtures in paediatric obesity is not well understood. OBJECTIVES: We aimed to evaluate the potential associations between chemical mixtures and obesity in a population-based sample of Canadian children. METHODS: We ascertained biomonitoring and health data for children aged 3-11 from the cross-sectional Canadian Health Measures Survey Cycles 2007 to 2019. Several chemicals of interest were measured in blood or urine and paediatric obesity was defined based on international cut-offs. Using supervised machine learning-based ML computational analysis, we quantified the effects of three chemical mixtures: selected a priori, Models were adjusted for sociodemographic and environmental factors identified through a directed acyclic graph. Results were validated using bootstrapping. RESULTS: Of 3,512 children (mean age = 7.5 years, 50.3% male), 1,139 (32.4%) had obesity. The ML models identified a chemical mixture of phthalates, phenols, and perfluoroalkyl substances (PFAS) associated with obesity (AUC = 0.61, 95% CI: 0.58, 0.64). Individually, exposure to mono-(carboxyoctyl) phthalate, mono-(2-ethyl-5-hydroxyhexyl) phthalate, mono-(2-ethyl-5-oxohexyl) phthalate, perfluorooctanoic acid, perfluorooctane sulfonic acid, perfluorononanoic acid, and perfluorodecanoic acid, bisphenol A, and bisphenol S were associated with obesity. Models were validated using bootstrapping. CONCLUSIONS: Exposure to a mixture of phthalates, phenols, and PFAS was associated with obesity in children. Given the cross-sectional nature of this study, longitudinal studies are needed to confirm these findings.	Pediatr Obes Vol.19 Issue 8 Pages e13117	10.1111/ijpo.13117	38872449	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0639	H. Duc Nguyen, H. Oh and M. S. Kim	2022	Association between exposure to chemical mixtures in relation to serum total IgE among adults 19-86 years old	There is a scarcity of studies on the effects of mixed chemicals on total IgE. We aim to assess whether there is a link between chemical mixtures (blood and urine of 36 chemicals including lead, mercury, cadmium, cotinine and, hexachromium) and, 2-hydroxyethyl, 2-methyl, 3-hydroxybutyric, 3-hydroxypropionic, mono (2-ethyl-5-hydroxyhexyl) phthalate, mono (2-ethyl-5-oxohexyl) phthalate, mono (2-ethylhexyl) phthalate, mono (3-carboxypropyl) phthalate, mono (carboxyheptyl) phthalate, mono (carboxyisononyl) phthalate, mono (carboxyoctyl) phthalate, bisphenol A, bisphenol F, bisphenol S, nicotinuric, methylhippuric, ethylhippuric, propylhippuric, 3-phenylpropionic, and, and cotinine), and total IgE in 3,602 Korean adults aged ≥ 19. The effects of mixed chemicals on total IgE were investigated using regression models, weighted quantile sum (WQS) regression, quantile g-computation (qgcomp), and Bayesian kernel machine regression (BKMR). The most relevant factors linked with IgE, according to the three models, were then used to construct the WQS index. RESULTS: The WQS index was significantly associated with total IgE (β = 0.09, 95% CI: 0.03, 0.15). Urinary 2-hydroxyethyl, 2-methyl, and 3-hydroxybutyric were the most contributing factors to serum total IgE (β = 0.63, 95 %CI: 0.23, 1.03). Similar results were found in qgcomp and BKMR models. Stratified analyses revealed that the WQS index was significantly associated with total IgE levels in males (β = 0.09, 95 %CI: 1.14, 7.71), in 30-39 adults, the overall effect of the mixture was significantly associated with ln(2-transformed levels of serum total IgE (β = 0.63, 95 %CI: 0.23, 1.03). The cutoff levels for exposure levels related to serum total IgE levels between serum total IgE levels were reported. We discovered that urinary body exposure to 26 chemicals was associated with serum total IgE levels after accounting for the findings of these four models. More research is needed in the future to gain a better understanding of the impact of mixed chemical exposure on allergic disorders and how to minimize chemical exposure, especially for people under the age of 19.	Int Immunopharmacol Vol.102 Pages 108428	10.1016/j.intimp.2021.108428	34911030	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0640	P. Dubey, S. Y. Reddy, C. Thangwal, G. Hardy and A. K. Dwivedi	2025	Association of exposure to nonpersistent endocrine disruptors with sex hormones and metabolic health in US females	Endocrine disruptive chemicals (EDCs) are considered as the potential attributors for the increasing trend in obesity and metabolic syndrome (MS) through disruption of sex hormones, particularly in women. We evaluated the association of nonpersistent EDCs exposure with sex hormones and MS in US females. Data of 2,000 females aged 20-80 years from the National Health and Nutrition Examination Survey datasets collected during the years 2013-2016. Blood of age ≥6 years old, urinary measurements of nonpersistent EDCs, sex hormones (testosterone, dihydrotestosterone, and sex binder compounds were included in this study. Data were analyzed using the modified Poisson models to estimate the adjusted relative risk (RR) and 95% confidence interval (CI). The associations were also validated by considering T1 and SHBG concentrations as the outcomes. The study included 2076 women with 1251 ages 71, 1019 (no BMI), 83% obesity, and 66.3% MS. In medium to high exposure to bisphenol A (BPA, 1.66-9.9 n.1, 1.2, 2.26, p= 0.009), bisphenol F (BPF, > 1.80, 95% CI: 1.26, 2.38, p< 0.001), bisphenol S (BPS > 0.80, 95% CI: 1.26, 2.43, p = 0.002) and 2, 4- dichlorophenol (DPH > 1.40, 95% CI: 1.08, 2.16, p = 0.026) were significantly associated with MS. Similarly, BPA, BPF, BPS, and DPH were significantly associated with SHBG, obesity, and MS. Testosterone, dihydrotestosterone, and free androgen index (FAI) were found to be associated with SHBG, obesity, and MS. However, these EDCs were found to be associated with SHBG, obesity, and MS according to menopausal status. High exposure to certain nonpersistent EDCs was associated with low SHBG, obesity, and MS according to menopausal status.	J Investig Med Vol.73 Issue 2 Pages 193-205	10.1177/10815589241297724	39440682	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0641	C. Dubeau, A. Akee, É. Caron-Beaudoin, P. Ayotte, C. Blanchette, N. G. McHugh and M. Lemire	2022	Perfluoroalkyl acid and bisphenol-A exposure via food sources in four First Nation communities in Quebec, Canada	OBJECTIVE: To document perfluoroalkyl acids (PFAS) and bisphenol-A (BPA) exposure in four First Nation communities in northern Quebec compared with the Canadian Health Measures Survey (CHMS) Cycle 5 2016-2017) and examine the associations between dietary consumption and chemical exposure. DESIGN: We used cross-sectional data from the 401 FNQC project conducted in collaboration with four First Nation communities in 2011. A FFQ collected information on diet, and PFAS and BPA were measured in biological samples. We used generalized linear models to test the associations between food intake and chemical biomarkers. SETTING: Four First Nation communities in Nunavik, Quebec, Canada. PARTICIPANTS: Inuit adults (n 387) aged 18-79 years. RESULTS: Plasma PFAS concentrations were lower in FNQC participants (n 21-39 years compared with CHMS. Dairy products were associated with PFOA among Nishnawbe and Inuit participants (geometric mean ratio 95 % CI 1·15 (1·04, 1·27) and 1·19 (1·08, 1·30), respectively). PFHxS was also associated with other processed foods (1·07 (95 % CI 1·01, 1·12) among Nishnawbe, and fish and shellfish and berries (1·03 (95 % CI 1·01, 1·06) and 1·15 (95 % CI 1·02, 1·30) among Inuit). BPA was associated with chicken (1·17 (95 % CI 1·05, 1·30) and wild fish (1·11 (95 % CI 1·02, 1·21)) among Nishnawbe, and with desserts (1·15 (95 % CI 1·07, 1·25)), processed meats (1·06 (95 % CI 1·02, 1·09) and fish and lard (1·08 (95 % CI 1·01, 1·16)) among Inuit. CONCLUSIONS: These results highlight the importance of better documenting food processing and packaging methods, particularly for dairy products, and their contribution to endocrine disruptive exposures, as well as to promote minimally processed unpackaged foods to provide healthier food environments for youth in Indigenous communities and beyond.	Public Health Nutr Vol.26 Issue 1 Pages 106-121	10.1017/s1368980022000581	35272726	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0642	X. Duan, M. Liang, B. Wei, J. Gu, Q. Zhao, G. Ji, S. Jir and N. Chen	2025	Internal Bisphenol Analogue Exposure in an Elderly Chinese Population: Knowledge from Dietary Exposure	Due to its endocrine-disrupting effects and neurotoxicity, Bisphenol S (BPS) has been banned from some products, and some countries; therefore, alternatives are increasingly being used. Studies have been performed to evaluate internal Bisphenol analogue (BP) exposure in children, adolescents and adults, however, little information on elderly age groups is available. In this study, a cohort of 181 senior residents aged 60-72 years, from a coastal residential district in Jiangsu Province of China, was selected, and blood samples were collected from these individuals to evaluate internal BP exposure. The urine concentrations of free BPA, BPF, BPS, BPZ, BPC, BPE, BPG, BPP, BPAP and TBBPAC were quantitatively determined by HPLC-MS/MS. In parallel, demographic and dietary surveys were conducted, and the potential association between BP levels and dietary habits was investigated. The results showed that BPA, BPF, BPS, BPZ, BPC, BPE, BPG, BPP, BPAP and TBBPAC were detected in 100%, 100%, 100%, 100%, 100%, 100%, 100%, 100%, 100%, 100%, 100%, 100%, and 100% of the samples, respectively. The concentrations of BPA, BPF, BPS, BPZ, BPC, BPE, BPG, BPP, BPAP and TBBPAC in the urine samples ranged from 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, 0.01 to 1.00, and 0.01 to 1.00 ng/mL, respectively. Females had significantly higher concentrations of BPA than males, and individuals aged 70 years or older had significantly higher BPA levels. Dietary analysis indicated a significant correlation between meat consumption and BP levels, implying that this is an important source of BP exposure. The current study uncovers previously unknown aspects of BPA exposure, characterized by high internal BP levels in the elderly, and risk factors such as gender and meat consumption. This offers valuable insights for preventing region-specific BP exposure in the elderly.	Toxics Vol.13 Issue 4	10.3390/toxics13040259	40278575	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0643	S. Duan, Y. Wu, J. Zhu, X. Wang, Y. Zhang, C. Gu and Y. Fang	2024	Development of interpretable machine learning models associated with environmental chemicals to predict all-cause and specific-cause mortality : A longitudinal study based on NHANES	Limited information is available on potential predictive value of environmental chemicals for mortality. Our study aimed to investigate the associations between 30 of 11 classes representative environmental chemicals in blood or urine and mortality risk and to develop interpretable machine learning models to predict all-cause and specific-cause mortality. We included 7,625 participants from National Health and Nutrition Examination Survey (NHANES). During 108,604 person-months of follow-up, 327 deaths occurred. We found that machine learning-elevated protocol to predicting mortality. CatPR was selected as the optimal model for predicting all-cause mortality within dependent ALL902 of 0.963 (95%CI: 0.941-0.985). Cornet was the best model for predicting cardiovascular disease (CVD) and cancer mortality with time-dependent AUC902 of 0.906 (95%CI: 0.838-0.962) and 0.880 (95%CI: 0.861-0.897). Based on clinical variables, adding environmental chemicals could enhance the predictive ability of cancer mortality (P = 0.005). Some environmental chemicals contributed more to the models than traditional clinical variables. Combined the results of association and prediction models by interpretable machine learning analyses, we found urinary methyl paraben (MPB) and urinary 2-naphthol (2-NAP) were negatively associated with all-cause mortality, while serum cadmium (Cd) was positively associated with all-cause mortality. Urinary bisphenol A (BPA) was positively associated with CVD mortality.	Ecotoxicol Environ Saf. 2024 Jan 15:270:115864.	10.1016/j.ecoenv.2023.115864	38142591	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0644	P. Duédo, O. Pardo, F. Corpas-Burgos, J. Kuligowski, M. Gomez, M. Varela, A. Pastor and V. Yusà	2019	Biomonitoring of bisphenols A, F, S in human milk and probabilistic risk assessment for breastfed infants	The present study addresses the presence of bisphenols A (BPA) and its analogs bisphenol F (BPF) and S (BPS) in milk at 133 mothers living in Valencia (Spain) and participating in the BETTERMILK project (year 2015-2016). Free and conjugated BPA, BPF and BPS were analyzed by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). Free BPA was detected in 100% of the samples, while BPF and BPS were found in 35% and 77%, with a geometric mean of 0.29 ng/mL and 0.19 ng/mL, respectively. The frequency of detection was much lower for total BPF (23%) and total BPS (2.3%). The place of residence of the mother and the use of personal care products showed significant association with BPA concentrations. The estimated daily intake of total BPA for breastfed infants amounted to a geometric mean of 0.06 µg/kg bw and a 95th percentile of 1.0 µg/kg bw, below the tolerable daily intake of 4 µg/kg bw/day established by EFSA. To our knowledge, this is the largest biomonitoring study of bisphenols in human milk in Europe.	Sci Total Environ Vol.668 Pages 797-805	10.1016/j.scitotenv.2019.03.024	30870748	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0645	P. Duédo, N. León, Y. Sanchís, F. Corpas-Burgos, S. F. Fernández, C. S. Hernández, G. Sael, E. Pérez-Zafra, A. Mora-Herrera, O. Pardo, C. Cascallo, A. López, V. Yusà and F. Ot Behalf Of The Biowat Task	2021	Biomonitoring of Phthalates, Bisphenols and Parabens in Children: Exposure, Predictors and Risk Assessment	Exposure to emerging contaminants, such as phthalates, bisphenols and parabens in children has been associated with possible neurodevelopment and endocrine alterations. In the present study, the biomonitoring of biomarkers in children (5-12 years old) from the Valencia Region (Spain) have been implemented using urines from the INMA, program. More than 75% of the children studied (n = 162) were internally exposed (>LOQ) to bisphenols and parabens, and the whole population assessed (n = 197) were exposed to at least one phthalate. The geometric means (GM) of the concentrations of bisphenol A, methyl paraben and propyl paraben were 0.9, 1.4 and 2.8 ng/mL, respectively. Regarding phthalates, monoethyl phthalate GM was 50.3 ng/mL and dietary) butyl phthalate (as the sum of five metabolites) GM was 38.8 ng/mL. Despite the studied population being considered as highly exposed to phthalates and bisphenols, concentrations were in general lower than in previous studies, including children in Spain and in other countries. In most cases, the risk assessment carried out concluded that the internal exposure to phthalates, bisphenols, and parabens is lower than the guidance values established, and, therefore, a health risk derived from the exposure to these compounds in the studied population is not expected.	Int J Environ Res Public Health Vol.18 Issue 17	10.3390/ijerph18178909	34501500	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0646	L. i. Dou, Q. F. Zhang, H. H. Bao, W. K. Wu, J. Sheng, S. Q. Yan, Y. Y. Xu, C. L. Gu, K. Huang, H. Cao, P. Y. Su, F. B. Tao and J. H. Hao	2020	[A birth cohort study of the association between prenatal serum bisphenol A concentration and infant neurobehavior development]	Objective: To explore the association between maternal bisphenol A (BPA) exposure during pregnancy and neurobehavioral development in infant. Methods: Participants were from the Maternal-Birth Cohort, which was established from October 2008 to October 2010 based on four municipal medical and health institutions in Hefei area. High-performance liquid chromatography-tandem mass spectrometry was applied for the determination of serum BPA concentration in 1 780 pregnant women sampled at their third filling, and during 3 d(7 to 28 d, months age of the infants. Neurobehavioral development were assessed by 0-6 year-old pediatric neurobehavioral scale. Multiple linear regression models were used to analyze the association between maternal BPA exposure and infant neurobehavioral development. Results: The median concentration of BPA in the urine of 931 mother-child pairs had complete data on serum BPA detection during pregnancy and assessment of infant neurobehavioral development status. The median age of pregnant women at their first filling was 29(27-31) years old, and the M (P25,P75) of serum BPA concentration (ng/ml) was 0.23 (0.12, 0.52), with a detection rate of 82.1% (764/931). The age of infants was 13 (10 to 16) months, and 53.5% (498) were boys. The multiple linear regression model showed that the serum BPA level in pregnancy was negatively associated with the development of language and social behavior development in infants, and the regression coefficients (β) were -0.66 (-1.13, -0.19) and -0.60 (-1.07, -0.13), respectively. Conclusion: BPA exposure during pregnancy affects language and social behavior development in infants, and the detection window is between 13 and 16 months old of the infant.	Zhonghua Yu Fang Yi Xue Za Zhi. 2020 Jun 6;54(6):644-650.	10.3760/cma.j.cn112150-20190902-00696	32842280	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0647	J. M. Dos Santos, T. Kennedy, J. Zhu, J. McPhie, A. Ray, M. Dentici, J. Dechant	2025	Sex-Specific Adverse Association of Endocrine Disrupting Chemicals on Peak Anaerobic Power and Skeletal Muscle Mass of Active Young Adults	dos Santos, JM, Kennedy, T., Zhu, J, McPhie, A, Ray, M, Dentici, J, and Dechant, J. Sex-specific adverse association of endocrine disrupting chemicals on peak anaerobic power and skeletal muscle mass of active young adults. J Strength Cond Res XXXX-000-000, 2025-Endocrine disrupting chemicals, such as bisphenol A (BPA) and bisphenol S (BPS), and polycyclic aromatic hydrocarbons (PAHs) are a broad class of lipophilic compounds that induce adverse physiologic outcomes dependent on biological sex. These chemicals stimulate oxidative stress and impact pathways involved in anaerobic and aerobic energy generation, key drivers of athletic performance. This study aims to analyze the association of BPS, BPA, 2-naphthol (a marker of PAH), and oxidative stress with peak anaerobic power (PAP) and anthropometric characteristics. Peak anaerobic power was assessed by the Wingate anaerobic test (WAnT) in 30 active young adults (18-30 years old; 15 males and 15 females). Urinary BPA, BPS, 2-naphthol, and oxidative stress (8-isoprostane) were measured by ELISA, while muscle mass was assessed by ELISA, capillary sample analysis, and body composition analyzer, respectively. Peak anaerobic power was negatively associated to BPS and positively with percentage of skeletal muscle and oxidative stress ($p < 0.05$). Multivariate regression, moderated by normalized lean variables associated to 8-PGF$_{2\alpha}$ such as sex, height, and age, indicated that only BPS was a predictor of PAP ($β = -0.386$, $p = 0.021$). Multivariate of variables were associated to each sex, and PAP was negatively associated to 8-levels of BPS and 2-naphthol in women. Multivariate regression confirmed that these variables are predictors of PAP ($p < 0.01$). Results support the idea of a sex-specific physiologic impact of BPS and 2-naphthol on PAP, independently of levels of oxidative stress and percentage of muscle. Controlling BPS and 2-naphthol exposure could be potential strategy to improve PAP in female athletes.	J Strength Cond Res	10.1519/jsc.0000000000005223	40853207	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0648	Z. Dong, L. Hu, J. Wu, C. Xie, S. Geng, J. Wu, C. Zhong and X. Li	2025	Bisphenol A-induced cancer-associated adipocytes promotes breast carcinogenesis via CXCL12/AKT signaling	Bisphenol A (BPA), a commonly used plastic additive, is believed to cause obesity. As an environmental endocrine disruptor, BPA is closely associated with the onset and progression of BC. However, the molecular mechanisms underlying the promotion of breast cancer by BPA remain unclear. As obesity is a significant risk factor for breast cancer, this study aimed at exploring whether BPA facilitates the progression of breast cancer through obesity. In vivo, BPA was found to promote the growth of breast cancer and induce obesity in mice. Additionally, BPA was found to increase the adipocyte area and mass index (AI), suggesting that obesity may be influenced by urinary BPA. 3T3-L1 cells differentiated into mature adipocytes following treatment with DX-BI (4-MAPA and subsequent treatment with ATO conditioned medium acquired properties associated with cancer-associated adipocytes (CAAs). Network pharmacology suggested that CXCL12 may serve as a key target gene in breast cancer progression. Follow-up PCR analysis revealed that BPA induced the expression of MFs-induced CAAs. Overexpression of CXCL12 promoted epithelial-mesenchymal transition (EMT) and ATC cell migration by activating the AKT pathway. In vivo, BPA-induced CAAs secreted high levels of CXCL12, leading to a notably strengthened role in ATC cells. In tissues from the BPA-CAAs group, the expression of CXCL12 markers associated with CAAs, phosphorylated AKT, N-cadherin, and chemerin was markedly elevated, whereas the expression of E-cadherin was reduced. In conclusion, BPA may induce adipose cells to differentiate into CAA-like cells and subsequently advance breast cancer EMT through the CXCL12/AKT pathway.	Mol Cell Endocrinol Vol.599 Pages 112473	10.1016/j.mce.2025.112473	39863150	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0649	R. E. Dodson, R. W. Setzer, J. D. Spengler, J. G. Brody, R. A. Rudel and J. G. Cedeño Laurent	2022	Influence of living in the same home on biomonitored levels of consumer product chemicals	BACKGROUND: Individuals living in the same home may share exposures from direct contact with sources or indirectly through contamination of the home environment. OBJECTIVE: We investigated the influence of sharing a home on urine levels of ten phenolic chemicals present in some consumer products. METHODS: We used data from Dixie Spring Institute's Detox Me Action Kit (DMAK), a crowdsourced biomonitoring program in the US. Of the 726 DMAK participants, 185 lived in the same home with one or more other DMAK participants (n = 137 pairs, up to six participants in a home). The concentration distributions included values below the detection limit so we used statistical methods that account for left-censored data, including non-parametric correlation estimation and Kaplan-Meier/Spearman regression models. RESULTS: Concentrations were significantly correlated between participants living in the same home for bisphenol A (BPA), benzophenone-3 (BP-3), triclosan, and the parabens methyl- (MeP), ethyl- (EtP), butyl- (BuP), and benzylparaben (BzP). Inferred correlations between participants not living in the same home were significantly lower than those for participants living in the same home for BPA, BP-3, triclosan, MeP, EtP, and BuP. For these chemicals, 1 to 2 ng/mL of the variance in urine concentrations was explained by whether participants lived in the same household, including exposures not asked about, sensitivity to chemical. Random concentrations, even largely influenced by personal behaviors, whereas distinct/spread and bisphenol concentrations were largely influenced by shared home exposures not related to reported behaviors. DISCUSSION: Measuring the influence of personal and household practices on biomonitoring exposures helps pinpoint major sources of exposure and highlights chemical-specific intervention strategies to reduce them.	J Expo Sci Environ Epidemiol Vol.32 Issue 6 Pages 885-891	10.1038/s41370-021-00368-8	34257390	ヒト	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0650	R. E. Dodson, K. E. Bononow, H. Sussmann, J. O. Udesky, K. M. Rodgers, D. Waller, M. Wadsack, J. G. Brody and R. A. Rudel	2020	Consumer behavior and exposure to parabens, bisphenols, triclosan, dichlorophenols, and benzophenone-3: Results from a crowdsourced biomonitoring study	Nearly all Americans have detectable concentrations of endocrine-disrupting chemicals from consumer products. In their bodies, and expert panels recommend reducing exposures. To inform exposure reduction, we investigated the influence of behaviors, sex, and household practices on urine concentrations of 10 phenols and parabens. We used data from Detox Me Action Kit (DMAK), a crowdsourced biomonitoring study. We targeted phenolic compounds: specifically parabens, bisphenol A (BPA) and analogs bisphenol F (BPF) and bisphenol S (BPS), the UV filter benzophenone-3, the anti-microbial triclosan, 2,4-dichlorophenol, and 2,5-dichlorophenol and collected survey data on consumer products, cleaning habits, and efforts to avoid tested chemicals. We investigated associations between urine concentrations and survey responses using univariate and multivariate regression models. We recruited 726 participants, 515 women and 211 men, from across the US. Participants reported eating rarely to their exposure to specific chemicals, and overall, participants achieved lower concentrations than the general U.S. population for BPA, triclosan, and benzophenone-3 but not BPF and BPS. Participants who reported avoiding all four ingredient groups (parabens, triclosan, bisphenols, and fragrances were twice as likely as others to be in the lowest quartile of cumulative exposure. Avoiding certain products and reading ingredient labels to avoid chemicals was most effective for parabens, triclosan, and benzophenone-3. Avoiding BPA was not effective for reducing bisphenols exposures. Avoiding certain chemicals in products was generally associated with reduced exposure for chemicals listed on labels. Greater ingredient transparency will help consumers, who read labels to reduce their exposure to a wider range of potentially harmful chemicals. In order to more routinely address public health, labeling policies should be complemented by regulations that exclude harmful chemicals from consumer products.	Int J Hyg Environ Health Vol.230 Pages 113624	10.1016/j.ijheh.2020.113624	33011057	ヒト	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0651	J. Ding, Y. Liu, Y. Li, Y. Huang, S. Li, F. Wang, D. Chen, B. Lu and N. Lin	2024	Insights into the accumulation and hepatobiliary transport of bisphenols (BPs) in liver and bile	Bisphenols (BPs) are widely distributed in daily life as typical endocrine disruptors. In this study, we examined the distribution of bisphenol A (BPA) and BPA alternatives in liver (n = 139) and bile (n = 102) tissues from the patients with liver cancer, and calculated the hepatobiliary transport efficiency of BPs (TE-B). Several BPs were detected in both liver (median: 0.898 ng/g; range: 0.0256-28.7 ng/g) and bile (median: 0.307 ng/mL; range: 0.0203-59.7 ng/mL), and BPA was the predominant in both liver tissue (38 ng/g) and bile (mean: 0.66 ng/mL). The TE-B (1.4 BPs was reported for the first time. Liver BPA concentrations were significantly correlated with the molecular weight and Log K(ow) of BPs. Furthermore, BPA and 2BPA in liver showed a significant negative correlation with age, and a significant difference was found in BPA in liver and bile in hepatocellular carcinoma (HCC) patients with different sex. Besides, BPA in liver showed a significant positive correlation with the concentrations of total bile acids (TBA) and total cholesterol (TC) in bile, but not with TBA and TC levels in liver. This suggests that BPs may have some correlation with hepatocellular carcinoma. This is the first report on distribution characteristics of BPs in the liver and bile of hepatocellular carcinoma patients, and the first study to report the hepatobiliary transport efficiency of BPs. The results should contribute to the understanding of BPs accumulation in the liver and bile and further relationship with hepatocellular carcinoma.	Environ Res Vol.263 Issue Pt 3 Pages 120251	10.1016/j.envres.2024.120251	39476930	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0652	I. Dimitriadis, I. Souter, P. L. Williams, D. Weller, J. B. Ford, K. Hauser and L. Mínguez-Alarcón	2025	Phenol biomarker concentrations in human ovarian follicular fluid and the associations with in-vitro fertilization outcomes	BACKGROUND: Phenols are a family of short-lived endocrine disrupting chemicals found in a wide range of products and have drawn significant attention because of widespread human exposure and their potential adverse effects on reproductive health. Phenols have been widely detected in several human bodily fluids, particularly in urine and blood. However, there is limited data on phenols in human ovarian follicular fluid (FF). In addition, studies suggest associations between exposure to bisphenols and measures of infertility in humans. Nevertheless, the association of FF concentrations of bisphenols and female fertility has not been investigated. OBJECTIVE: To investigate the associations between FF concentrations of bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), and 2,5-dichlorophenol (2,5-DCP) and in vitro fertilization (IVF) outcomes. METHODS: This analysis includes 220 women who enrolled in the Environment and Reproductive Health (EARTH) Study and underwent one IVF cycle between 2009 and 2019, with available FF, urine and reproductive outcome data. FF concentrations of 2,5-dichlorophenol (2,5-DCP), 2,5-dichloro-phenol (2,5-DCP), methyl paraben (MPB), ethyl paraben (EPB), propyl paraben (PPB), benzyl paraben (BzP), BPA, BPF, BPS, triclosan (TCS), and benzophenone-3 (BP-3) were measured using liquid chromatography-tandem mass spectrometry. Generalized linear models were used to explore the associations between FF concentrations of bisphenols (in tertiles) or dichlorophenol and FF outcomes. RESULTS: Detection frequencies were varied from high (79-96%) for MPB, PPB and BPS, to moderate (32-46%) for BPA, BPF and TCS, to low (1-16%) for 2,5-DCP, 2,5DCP, EPB, BPB, BPF, TCC. Correlations between FF and urine were strong for BPS (~0.80), moderate for BPB (~0.45) and PBP (~0.62), and weak for BPA (~0.21), and none for BPS (~-0.01) and BPS (~-0.07). FF BPS concentrations significantly decreased over time, whereas FF BPA concentrations increased. None of the examined FF phenol/dichlorophenol concentrations were not related to early IVF outcomes (endometrial thickness, total and mature (MII) oocyte yield, fertilization rates). However, significant associations between PPB and BPS and lower implantation, clinical pregnancy, and live birth rates were observed. Similarly, significant associations between BPA and lower implantation rates were observed. CONCLUSION: We observed that most phenols, were detected in FF and there were some correlations with urinary concentrations. We confirmed in FF that phenols such as BPA may be declining, while exposure to new replacements, such as BPS are increasing. However, no overall associations were observed for the examined FF phenol biomarker concentrations with early IVF outcomes and pregnancy outcomes. Further research is needed to examine the potential associations of these phenols in FF, especially the newer ones that are in the rise.	Int J Hyg Environ Health. 2025 Jul;268:114617.	10.1016/j.ijheh.2025.114617	40617121	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0653	I. Di Nepoli, S. Tagliaferri, E. Sommella, E. Salviati, D. Porri, B. Ragozzi, H. Cena, P. Campiglia, C. La Rocca, R. M. Cerbo and R. De Giuseppe	2021	Lifestyle Habits and Exposure to BPA and Phthalates in Women of Childbearing Age from Northern Italy: A Pilot Study	Background: Endocrine-disrupting chemicals (EDCs) are compounds that interfere with aspects of hormonal signaling. Considerable attention has been paid to their biological effects, especially in women of childbearing age or during pregnancy as EDCs have been reported to cross the placenta becoming concentrated in the fetus' circulation. Lifestyle habits, daily consumption of packaged foods and use of healthcare/cosmetic products are considered the main sources of exposure to EDCs. Methods: A pilot study was carried out to evaluate the urinary concentrations of bisphenol A (BPA) and phthalates in a group of women from Northern Italy. Forty-five women (median age 35, IQR: 30-38) were evaluated for urinary bisphenol A (BPA) and phthalates levels and also studied to EDCs' major determinants of daily exposure (frequency/dietary, physical activity, smoking habits, and weight status. Results: Although 100% of women seemed to have been exposed to common sources of EDCs, they reported a healthy lifestyle. The multivariable model described a positive and significant association between consumption of sources/beverage in plastic containers and (nonetic) phthalate exposure (p = 0.007). Conclusions: Since reproductive age encompasses a critical window for future health and functioning of the "mothers-to-be" and their children, future studies on prenatal dietary BPA and phthalate exposure and the role of consumer product choices in reducing such exposure are recommended.	Int J Environ Res Public Health Vol.18 Issue 18	10.3390/ijerph18189710	34574636	ヒト	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0654	G. Di Bella, M. Porretti, M. Cafiselli, F. Librenta, A. G. Potorti, V. L. Turco, A. Albergamo, M. Whiteli and C. Faggio	2023	Screening of phthalate and non-phthalate plasticizers and bisphenols in Sicilian women's blood	The plastic accumulation and its degradation into microplastics is an environmental issue not only for their ubiquity, but also for the release of intrinsic chemicals, such as phthalates (PAEs), non-phthalate plasticizers (NPPs), and bisphenols (BPs), which may reach body organs and tissues, and act as endocrine disruptors. Knowing plastic additives in biological matrices, such as blood, is a key step to establish a link between human exposure and health outcomes. In this work, the profile of PAEs, NPPs and BPs was determined in Sicilian women's blood with different ages (30-60 years) and interpreted by chemometrics. PAEs (DMP and DEPh), NPPs (DINP and DINCH), BPA and BPS were at higher frequencies and greater levels in women's blood and varied in relation to age. According to statistical analysis, younger females showed higher contents in blood ones than older women, probably due to a more frequent use of higher quantities of plastic products in daily life.	Environ Toxicol Pharmacol Vol.100 Pages 104166	10.1016/j.etap.2023.104166	37268242	ヒト	-	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0655	S. Dhar, A. Das and P. Bhattacharjee	2025	A population-based study to understand the association between Bisphenol-A (BPA) and Polycystic Ovarian Syndrome (PCOS): correlating with anthropometric parameters and clinical features	Bisphenol-A (BPA) is one of the most ubiquitous EDCs, possessing a variety of health risks starting from metabolic disorders to cancer. Due to the estrogen-mimicking phenomenon, BPA was associated with female reproductive disorders like polycystic ovarian syndrome (PCOS). This study aims to investigate the possible epigenetic mechanisms behind BPA-mediated PCOS manifestation among young women from West Bengal, India. A cross-sectional study was conducted in Kolkata Metropolitan City, West Bengal, India. Upon consenting participants, 80 women were collected for pathological screening, anthropometric measurements. Followed by this, BPA exposure was measured in serum as well as saliva using ELISA-based technique and subsequently Global DNA methylation status (5-hmC, 5-mC and 5-mC) and HDAC activity were quantified. The mean concentration of BPA in serum was 0.0 ± 0.0 ng/mL, while in saliva, it was 0.0 ± 0.0 ng/mL. Significant differences were observed in BMI, waist circumference, and waist-to-hip ratio between PCOS and non-PCOS groups (p < 0.001). A significant correlation was found between BPA exposure and menstrual irregularity (p = 0.008), and excessive hair growth (p = 0.032). Also, body weight, waist circumference, hip circumference, total fat (%), visceral fat (%), BMI, LH, testosterone, LH: FSH and FAI activity was significantly high (p 0.0001) whereas 5-mC (%) was significantly low (p < 0.001) in PCOS women. Results suggest a potential role of BPA in the alteration of epigenetic mechanisms, which leads to alterations in gene expression levels and eventually causes obesity and hormonal imbalance. Therefore, we hypothesize that BPA may lead to PCOS among women.	J Clin Med Vol.14 Issue 13	10.3390/jcm14134706	40649079	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0656	M. Derkaczew, K. Zgliqc-Wiezak, L. Dabrowski, J. Kucik, A. Chmielewicz, M. Thoens, M. Iszwik, S. Gorkowski and J. Wojtkiewicz	2019	Association of urinary bisphenols and triclosan with thyroid function during early pregnancy	BACKGROUND: Bisphenols and triclosan are considered as potential thyroid disruptors. While mild alterations in maternal thyroid function can result in adverse pregnancy and child developmental outcomes, there is still uncertainty whether bisphenols or triclosan can interfere with thyroid function during pregnancy. OBJECTIVES: We aimed to investigate the association of urinary bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), and triclosan with early pregnancy thyroid function. METHODS: This study was embedded in the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy study (SELMA), a population-based prospective pregnancy cohort. In total, 1996 participants were included in the current study. Maternal urinary concentrations of three bisphenols and triclosan, collected at median (95% range) 10 (6-16) weeks of pregnancy, as well as serum concentrations of thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), total thyroxine (TT4), and total triiodothyronine (TT3) were measured. RESULTS: Higher BPA levels were associated with higher FT4 concentrations (β 0.01; 95% CI: 0.00, 0.02; p 0.05). Higher BPS levels were associated with higher TSH concentrations (β 0.06; 95% CI: 0.01, 0.11; p 0.05). Higher triclosan levels were associated with higher FT4 (β 0.007; 95% CI: 0.001, 0.013; p 0.05) and TT4 (β 0.007; 95% CI: 0.001, 0.013; p 0.05) concentrations. The association of BPA with thyroid function differed by infant sex, with gestational age. The negative association of BPA with FT4/FT3 and TT4/TT3 ratios was only apparent in early but not late gestation (P for interaction 0.003, 0.008, respectively). CONCLUSION: These human data during pregnancy substantiate experimental findings, suggesting that BPA could potentially affect thyroid function and disturbance activities in early gestation.	Environ Int. 2019 Dec;133(Pt A):105123.	10.1016/j.envint.2019.105123	31521814	ヒト	甲状腺	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0657	A. Derakhshan, H. Shu, R. P. Peeters, A. Korevaar, C. H. Lindh, B. Demeneix, C. G. Bornehag and T. J. M. Korevaar	2020	Association of urinary bisphenols and triclosan with thyroid function in early pregnancy	BACKGROUND: Bisphenols and triclosan are considered as potential thyroid disruptors. While mild alterations in maternal thyroid function can result in adverse pregnancy and child developmental outcomes, there is still uncertainty whether bisphenols or triclosan can interfere with thyroid function during pregnancy. OBJECTIVES: We aimed to investigate the association of urinary bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), and triclosan with early pregnancy thyroid function. METHODS: This study was embedded in the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy study (SELMA), a population-based prospective pregnancy cohort. In total, 1996 participants were included in the current study. Maternal urinary concentrations of three bisphenols and triclosan, collected at median (95% range) 10 (6-16) weeks of pregnancy, as well as serum concentrations of thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), total thyroxine (TT4), and total triiodothyronine (TT3) were measured. RESULTS: Higher BPA levels were associated with higher FT4 concentrations (β 0.01; 95% CI: 0.00, 0.02; p 0.05). Higher BPS levels were associated with higher TSH concentrations (β 0.06; 95% CI: 0.01, 0.11; p 0.05). Higher triclosan levels were associated with higher FT4 (β 0.007; 95% CI: 0.001, 0.013; p 0.05) and TT4 (β 0.007; 95% CI: 0.001, 0.013; p 0.05) concentrations. The association of BPA with thyroid function differed by infant sex, with gestational age. The negative association of BPA with FT4/FT3 and TT4/TT3 ratios was only apparent in early but not late gestation (P for interaction 0.003, 0.008, respectively). CONCLUSION: These human data during pregnancy substantiate experimental findings, suggesting that BPA could potentially affect thyroid function and disturbance activities in early gestation.	Environ Int Vol.178 Pages 108091	10.1016/j.envint.2023.108091	37459690	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0658	A. Derakhshan, H. Shu, M. A. C. Broeren, A. Korevaar, C. H. Lindh, B. Demeneix, R. P. Peeters, C. G. Bornehag and T. J. M. Korevaar	2021	Association of endocrine disrupting chemicals exposure with human chorionic gonadotropin concentrations in pregnancy	BACKGROUND: Human chorionic gonadotropin (hCG) is produced by the placenta and plays an essential role in the maintenance of pregnancy. Endocrine disrupting chemicals (EDCs) have the potential to interfere with functions related to the production and secretion of hCG. However, associations between exposure to EDCs and hCG concentrations in humans remain to be elucidated. OBJECTIVES: To investigate the association of urinary, serum and plasma concentrations of EDCs during pregnancy with serum hCG concentrations. METHODS: We utilized data from the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy (SELMA) study. We investigated the association of 19 EDCs measured in early pregnancy urine or blood with serum hCG concentrations using multivariable linear regression models with covariate adjustment and inverse probability and Weighted Quantile Sum (WQS) regression with repeated holdout validation for the EDC-mixture. RESULTS: In 2,109 included women, higher exposure to bisphenol S was associated with lower hCG. Beta (95% CI): -0.05 (-0.11 to -0.00) per doubling of exposure. Urinary concentrations of the phthalate metabolites mono-(3-carboxypropyl) phthalate (MCPP) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) were associated with lower hCG. Beta (95% CI) for a unit (ln) increase: -0.07 (-0.14 to -0.01) and -0.07 (-0.13 to -0.01), respectively. Urinary concentrations of the phthalate metabolite of di-2-ethylhexyl phthalate (DEHP) was associated with a lower hCG. Beta (95% CI) for a unit (ln) increase: -0.07 (-0.14 to -0.01). Likewise, higher plasma concentrations of perfluorooctanoic acid (PFOA) was associated with a lower hCG. In the WQS-regression, each quartile increase in the EDCs-mixture was associated with -0.27 lower hCG (95% CI: -0.36 to -0.19). CONCLUSIONS: Higher exposure to several EDCs during pregnancy was associated with a lower hCG, and despite the small effect sizes, still indicating that the exposure may negatively affect production or secretion of hCG by the placenta. Our results provide the impetus for future experimental studies to investigate the placenta as a target organ for adverse effects of EDCs.	Environ Int Vol.149 Pages 106160.	10.1016/j.envint.2020.106160	33068853	ヒト	甲状腺	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0659	A. Derakhshan, E. M. Philips, A. Gkaniadelar, S. Santos, A. G. Asimakopoulos, K. Kannan, A. Korevaar, H. W. J. Jaddoe, L. Trasande, R. P. Peeters and T. J. M. Korevaar	2021	Association of urinary bisphenols during pregnancy with maternal, cord blood and childhood thyroid function	BACKGROUND: Most pregnant women are exposed to bisphenols, a group of chemicals that can interfere with various components of the thyroid system. OBJECTIVES: To investigate the association of maternal urinary bisphenol concentrations during pregnancy with maternal, newborn and early childhood thyroid function. METHODS: This study was embedded in Generation R, a prospective, population-based birth cohort (Rotterdam, the Netherlands). Maternal urine samples were analyzed for eight bisphenols and bj (BPA, BPF, BPS, BPAF, BPB, BPE, BPP, BPZ). Maternal serum thyroid function (free thyroxine (FT4) and total thyroxine (TT4) were measured in early pregnancy and child TSH and FT4 were measured in cord blood and childhood. RESULTS: The final study population comprised 1,367 mothers, 883 newborns and 682 children. In early pregnancy, BPA was detected in 89% of the women, BPF in 14%, BPS in 25% and BPAF in 1%. Higher BPA concentrations were associated with higher FT4 concentrations (β 0.02; 95% CI: 0.00, 0.04). Higher BPS concentrations were associated with maternal thyroid function. Higher BPS concentrations were associated with a higher maternal TT4 (β 1.99% (0.2 per 1 (natural log) unit increase; 95% CI: 0.03 to 3.92) but there was no association with TSH or FT4. Furthermore, higher BPS was associated with an attenuation of the association between maternal FT4 and TSH (P(interaction) = 0.002). There was no association of early or mid-pregnancy BPA or early pregnancy BPS with cord blood or childhood TSH and FT4. A higher late-pregnancy maternal BPA exposure was associated with a higher TSH in female newborns (P(interaction) = 0.06) and a higher FT4 during childhood in males (P(interaction) = 0.08). CONCLUSIONS: Our findings show that exposure to bisphenols may interfere with the thyroid system during pregnancy. Furthermore, the potential developmental toxicity of exposure to bisphenols during pregnancy could affect the thyroid system in the offspring in a sex-specific manner.	Environ Int. 2021 Jan;146:106160.	10.1016/j.envint.2020.106160	33068853	ヒト	甲状腺	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0660	A. Daoudi, G. Bottero, D. Germani, F. Carli, S. Teti, L. Bu sani, V. Della Latta, A. P. Pala, F. Maranghi, R. Tassinari, A. Garatdelli, C. La Rocca and S. Cianfarani	2024	Urinary Bisphenol A and Bis(2-Ethylhexyl) Phthalate Metabolite Concentrations in Children with Obesity: A Case-Control Study	INTRODUCTION: Obesity is a worldwide public health problem. Experimental animal and in vitro studies suggest that the exposure to BPA and phthalates are associated to a higher risk of obesity. OBJECTIVE: The objective of the study was to determine urinary excretion of bisphenol A and phthalates in obese and normal-weight children. METHODS: A case-control study was conducted in 110 children. Sixty-six obese children, 36 girls (mean age 8.42 ± 1.97 years), and 30 boys (mean age 8.61 ± 1.35 years), and 30 normal-weight children, 21 girls (mean age 7.66 ± 1.35 years), and 29 boys (mean age 7.77 ± 1.98 years) were studied. Urinary BPA and phthalate metabolites were measured by high-performance liquid chromatography-tandem mass spectrometry. Urinary creatinine was measured by the Jaffe method. Urinary BPA and phthalates were evaluated through "ad hoc" questionnaires. RESULTS: BPA and DEHP metabolites were detectable in obese and normal-weight children. Obese girls showed significantly higher BPA concentrations in comparison with normal-weight girls (mean, 10.77; 95% CI = 7.62-15.19 vs. 5.66; 95% CI = 3.65-7.71; μg/g creatinine, respectively, p 0.05). The first step of DEHP metabolic rate was significantly higher in obese girls compared with controls (p 0.05). DEHP metabolites correlated significantly with both concentrations in obese girls (p 0.05). A higher risk of obesity was found in children with BPA levels above the median values with the habit to eat food packaged (OR = 11.09; 95% CI = 1.28-96.78). CONCLUSIONS: These findings show that a higher exposure to BPA is associated with the risk of obesity in girls. Further studies are needed to unveil the sweet-effect relationship.	Horm Res Paediatr. 2024;97(4):388-396.	10.1159/000535305	37972573	ヒト	代謝	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0661	Z. Dong, S. Wang, H. Song, R. Liu and Y. Lv	2025	Bisphenol a monitoring by commercial pregnancy test strips transformed by DNA walking machine	Frequently-occurred food contamination issues bring about a tremendous global demand for point-of-care testing (POCT) devices. Pregnancy test strip (PTS) retains the highest POCT market share and a low cost of $0.3 per test, but challenged by limited analytical sensitivity and inconvenient operation. Herein, we developed a DNA walker machine for PTS enhancement monitoring. Herein, we developed a DNA walker machine assisted commercial PTS method for on-site bisphenol A (BPA) analysis. DNAzyme was operated as the efficient autonomous catalytic walker chain to drive the DNA machine for the amplified signal output of BPA in drink samples. A detection limit of 34 ng/mL was obtained. The POCT strategy constructed in this work has the characteristics of low cost, convenient operation and high analytical sensitivity, represents an attractive option for biosensing and on-site drink safety monitoring.	Food Chem Vol.464 Issue Pt 3 Pages 141775	10.1016/j.foodchem.2024.141775	39486286	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0662	Y. Deng, H. Ha, H. Wan, N. Sher, J. Li, S. Zhang, Q. Jiang, J. Chang, Q. Lu, R. Zhong and X. Miao	2021	Bisphenol A exposure, interaction with genetic variants and colorectal cancer via mediating oxidative stress biomarkers	Bisphenol A (BPA) may induce oxidative stress as well as the toxicity of colon cancer cells. We hypothesized that BPA exposure and interactions with genetic variants might be associated with colorectal cancer (CRC) risk, and the association might be partly mediated by oxidative stress. We measured urinary BPA and oxidative stress (8-hydroxy-2'-deoxyguanosine [8-OHdG] and 8-hydroxy-2'-deoxyribonucleic acid [HNE-MA]) in 270 new CRC cases and 538 healthy controls. A set of 26 genetic variations in 12 candidate DNA repair genes and 9 metabolic enzyme genes were genotyped by MassARRAY platform. Multivariate logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Urinary BPA levels were significantly associated with CRC risk (OR = 1.59, 95% CI = 1.19-2.13, P = 0.002). The mediation analysis showed BPA increased CRC risk partially mediated 11.45% of the effect of BPA on CRC risk. Moreover, BPA was found to interact with ERCC5 rs17655 and rs2296147 (both P(multiplicative) = 0.05) to increase CRC risk. In brief, our results suggested BPA was associated with CRC risk and the positive association of BPA with CRC risk might be partly mediated by the oxidative stress. 4NP, NB, BPA might increase risk in ERCC5 rs17655 and rs2296147 to increase CRC risk.	Environ Pollut Vol.287 Pages 117630	10.1016/j.envpol.2021.117630	34182385	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0663	M. Deng, T. Gao, L. Tao, W. Tang, X. Wang, Y. Jiang, D. X. Xu, M. Fang and Y. Huang	2023	Are human exposure assessment the same for non-persistent organic chemicals? - from the lens of urinary variability and predictability	Assessment of human exposure to mixtures of non-persistent chemicals from food matrices and consumer products requires accurate characterization and estimation of their prevailing exposure levels, and assessment sampling approaches for these varying chemicals remain disputable. Here, we used high-throughput targeted method to quantify urinary concentrations of 39 most common non-persistent chemicals (9 parabens, 10 bisphenols, 3 triclosan, 7 benzophenones, 2 dichlorophenols, 13 phthalate metabolites and 35 antioxidants) in 328 consecutive spot samples from 15 participants over three consecutive days, 30 samples of which were collected in 24-h urine. Urinary chemicals were detected frequently (detection frequency ≥ 50%) and at relatively high concentrations. Intraclass correlation coefficient (ICC) to assess the reproducibility of targeted chemicals demonstrated that regardless of sampling approaches, All triclosans, most parabens, benzophenones and triclosan showed moderate to high reproducibility (0.60 < ICC < 0.940), with relatively high predictive power of PAREs for 16 to collections. Notably, most phthalates, bisphenols and antioxidants showed low ICC values. Together, our results demonstrates that TWO samples may be adequate for assessing human exposure to parabens, benzophenones, triclosan and dichlorophenols, whereas multiple consecutive urine collections may be advantageous for evaluating exposure to most phthalates, bisphenols and antioxidants.	Sci Total Environ Vol.868 Pages 161542	10.1016/j.scitotenv.2023.161542	36649764	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0664	D. Demicioglu, N. Cirac, S. D. Pektas, T. Edgunlu, M. Unal and D. Yazgan Aksoy	2024	Bisphenol-A and pentachlorophenol sodium levels in patients with rosacea	BACKGROUND/ OBJECTIVES: Rosacea is a common chronic inflammatory skin disorder. Endocrine-disrupting chemicals (EDC) are toxic substances, that may gain entry through the skin and subsequently interfere with hormonal and immune functions. Bisphenol A (BPA) and pentachlorophenol sodium (PCP) are two of these EDCs, incriminated in the pathogenesis of certain inflammatory skin disorders. We aimed to test the hypothesis that BPA and PCP levels are higher in patients with rosacea compared to healthy controls. METHODS: Rosacea (ROS) patients (n = 30; 24 female, 6 male; mean age: 39.2 ± 10.1 years) and sex-matched healthy controls (HC) (n = 30; 24 female, 6 male; mean age: 36.2 ± 10.2 years). Main anthropometric measures, fasting plasma glucose (FPG), insulin, HOMA-IR, lipids, C-reactive protein (CRP), ESR, and liver function tests were quantified and recorded. RESULTS: Serum CRP (SD: 3.2 vs. 3.7, t: 5.4mg/L, respectively, p0.05 for all). Serum BPA levels were 13.8 ± 11.6 and 12.9 ± 19.2ng/mL, and PCS levels were 62.2 ± 45.9ng/mL and 68.6 ± 62.1ng/mL for patients and healthy controls, respectively. There was no significant difference in BPA and PCS levels between the two groups (p > 0.05 for both). No significant association was found among HOMA-IR, CRP, BPA, and PCS levels (p > 0.05 for all). CONCLUSIONS: Although the present study fails to provide presumptive evidence for the role of BPA and PCS in rosacea, the question as to other EDCs might be resolved in its etiopathogenesis remains. This hypothesis requires confirmation in larger-scale future prospective trials.	Cutan Ocul Toxicol Vol.43 Issue 3 Pages 232-236	10.1080/15569527.2024.2383242	39113570	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0665	J. Delaplanx, S. Fosse-Edorh, C. Filtol and C. Pitteloud	2023	Relation of urinary bisphenol concentration and diabetes or prediabetes in French adults: A cross-sectional study	BACKGROUND: International research has recently shown an association between exposure to bisphenol A (BPA) and the risk of diabetes, although limited results are available for exposure to bisphenol S (BPS) and bisphenol F (BPF). The aim of this study was to examine the relationships between impregnation with BPA, BPS, and BPF and the prevalence of diabetes or prediabetes in the French adult population. METHODS: Based on the Esteban cross-sectional study, 850 adults aged 18 to 74 years living in France were included. Urinary concentrations of BPA, BPS, and BPF were measured by liquid chromatography-tandem mass spectrometry. Logistic regression multivariable models were performed and adjusted for known risk factors for diabetes and urine creatinine concentration. RESULTS: The percentage of included individuals with diabetes was 5.2% (95% CI: 3.6%, 7.4%), and 24.2% (95% CI: 20.8%, 27.9%) had prediabetes. Urinary concentrations of BPA, BPS, and BPF were detected in 89.2%, 70.2%, and 11.4% of the adults. A high level of total bisphenol concentration of BPA (≥ µg/L) (> 1.5 WHO) (1.06-1.90), p < 0.001). However, our did not find any significant independent association between urinary BPS and BPF levels and the prevalence of diabetes or prediabetes. CONCLUSIONS: In this sample, considering the diabetes risk factors, diabetes or prediabetes was positively associated with higher urinary BPA concentration but not with urinary BPS and BPF concentrations. However, analysis of prospective longitudinal studies are still necessary to demonstrate a causal link between bisphenol exposure and the risk of diabetes or prediabetes.	PLoS One Vol.18 Issue 3 Pages e0283444	10.1371/journal.pone.0283444	36996235	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0666	J. G. DeKoven, B. M. DeKoven, E. M. Warshaw, C. G. T. Mathias, J. S. Taylor, D. Sasseville, D. V. Belsito, J. F. Fowler, Jr., M. D. Pratt, K. A. Zug, H. I. Maibach, V. A. DeLeo, J. I. Silverberg, A. R. Atwater, M. J. Reeder and D. L. Holness	2022	Occupational contact dermatitis: Retrospective analysis of North American Contact Dermatitis Group Data, 2001 to 2016	BACKGROUND: Patch testing is an important diagnostic tool for suspected allergic contact dermatitis (ACD) in occupational settings. OBJECTIVE: Provide an overview of occupational skin disease (OSD) and an analysis of occupational ACD in North American patients undergoing patch testing between 2001and 2016. METHODS: Patients with OSD were analyzed for frequency of allergic reactions, by a screening series of allergens, occupations, and industries. RESULTS: Occupational dermatitis was diagnosed in 1,039 patients (mean age 43.2 years, 57.1% male, 42.9% female). Of these, 1,015 (97.7%) had ACD, 15 (1.4%) had irritant contact dermatitis (ICD), and 9 (0.9%) had OSD. The most common occupationally related allergens included rubber accelerators, preservatives, and epoxy resins. Of OSD, 1,015 (97.7%) were common sites of dermatitis. The occupations most affected were service workers and machine operators. LIMITATIONS: Our cohort may not reflect the general working population. CONCLUSION: This study identified common occupational allergens, exposure sources, and occupations/industries at risk. This information may help the clinician evaluate and manage patients with occupational contact dermatitis.	J Am Acad Dermatol. 2022 Apr;86(4):782-790.	10.1016/j.jaad.2021.03.042	33753252	ヒト	皮膚	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0667	D. Degirmencioglu Gok, F. Tugge Okutucu, N. Ozturk and H. A. Ceyhun	2024	Association of bisphenol A with cognitive functions and functionality in adult attention deficit hyperactivity disorder	BACKGROUND: Bisphenol A (BPA) has been linked to attention-deficit/hyperactivity disorder (ADHD) symptoms, but the effects on cognitive functions and functionality in adult ADHD have not been investigated. We investigated the associations between serum BPA with cognitive functions and functionality in adult ADHD patients. METHODS: The levels of BPA were measured in 45 adult ADHD patients and 30 well-matched healthy controls. The relationship between plastic exposure and BPA was also evaluated. Stroop test and Wisconsin Card Sorting Test were applied for neurocognitive evaluation and participants were compared in basic cognitive functions including planning, organization, attention/vs, problem solving, cognitive flexibility, variety of attention, information processing speed, the ability to change perceptual set and response under interference. Sheehan disability scale was applied for functionality. The association of BPA with test scores was analyzed statistically. RESULTS: Serum BPA levels in adult ADHD patients were found significantly higher than healthy controls. Adult ADHD patients were also found to have significantly lower functionality and cognitive test scores. BPA levels showed a significant effect on the Stroop test and Wisconsin Card Sorting Test, indicating significant differences between the groups in terms of cognitive functions. However, no significant correlation was found between BPA levels and cognitive functions. CONCLUSIONS: BPA is associated with ADHD and affects functionality in the field of work, but larger-scale further studies are needed for its effect on cognitive functions.	J Psychiatr Res Vol.169 Pages 64-72	10.1016/j.jpsychires.2023.11.027	38000186	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0668	C. D. de Siqueira, A. G. Ademola, A. C. R. de Moraes and F. B. Filippin-Monteiro	2023	Human body burden of bisphenol A: a case study of lactating mothers in Florianopolis, Brazil	Exclusive breast milk is the diet recommended by the World Health Organization (WHO) until 6 months of age. However, breastfeeding has the potential of transferring certain toxic chemicals from the mother to the infant. Bisphenol A (BPA) is a synthetic chemical used as a monomer in polycarbonate plastics and epoxy resins. Information on BPA concentration in the breast milk of lactating mothers is very limited. Also, this study aimed to determine the concentration of BPA in the colostrum of 50 post-term women at a university-affiliated maternity hospital in South Brazil. The results, obtained for all 50 samples, indicated a high concentration of BPA with a median value of 35.28 ng/mL. Furthermore, the concentration of BPA in mothers was influenced by the consumption of foods packaged in plastic packaging, especially when the plastic is heated (p = 0.0001). Based on the estimated daily intake (EDI) of BPA, the median value of 0.0012 ng/kg bw/day was found to be 1,000 times lower than the tolerable daily intake (TDI) established by the European Authority of Food Safety. These data showed a high concentration of BPA in the breastmilk of the lactating mothers which might be through the use of plastic containers as food/drink packages. This is of public health importance as the high concentration of BPA in their breast milk can be an indicator of potentially serious health problems in these mothers and much more in the babies breastfed with BPA-contaminated breast milk.	Environ Sci Pollut Res Int Vol.30 Issue 1 Pages 1785-1794	10.1007/s11356-022-22349-6	35921009	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0669	D. S. Davis, O. L. M. Scandlen, R. Saboy, M. Ghaffarzadeh, T. G. Hannam, A. Lagunov and L. A. Favetta	2024	High seminal BPA in IVF patients correlates with lower sperm count and up-regulated miR-21 and miR-130a	Bisphenol A (BPA) is a widespread industrial chemical, used as the key monomer of polycarbonate plastics and epoxy resins. BPA has been detected in human seminal fluid and has been correlated with changes in sperm quality and reproductive outcomes. However, the mechanisms underlying these changes remain unclear. Here, we investigated the relationship between seminal BPA and sperm quality in IVF patients. According to WHO guidelines, BPA levels in the seminal plasma were then measured through an enzyme-linked immunosorbent assay (ELISA) and compared to sperm quality metrics. The relative miRNA expression of key genes associated to male reproduction, including androgen receptor, miR-34c, miR-21, miR-130a, was then quantified and compared between groups with high or low BPA content. Our results revealed that BPA levels were increased with age and were negatively correlated with sperm counts (p<0.05). The negative correlation revealed significant correlations between patients over age-matched. No other relationships between seminal BPA and motility, morphology or DNA fragmentation levels were observed. qPCR analysis showed that androgen receptor mRNA expression was significantly greater in sperm with high seminal BPA (p<0.05). Moreover, we found that the expression of miR-21 and miR-130a were also upregulated in the higher BPA group (p<0.05). These results display a relationship between BPA content in the semen and male fertility parameters, and provide insights into the molecular mechanisms through which BPA may be affecting male reproductive capability. Ultimately, this research can potentially drive changes to guidelines and exposure limits for BPA exposure.	Reprod Toxicol Vol.128 Pages 108651	10.1016/j.reprotox.2024.108651	38925230	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0670	Y. Dai, J. Ding, Z. Wang, B. Zhang, Q. Guo, J. Gou, X. Qi, X. Ding, C. Wu, J. Zhang and Z. Zhou	2025	Biomonitoring, dietary predictors, drinking water ingestion of 33 endocrine disrupting chemicals in primary school children in China, towards an exposome approach	Exposure to multiple endocrine disrupting chemicals (EDCs) may have some adverse impacts on child health yet, little data is available on the body burdens, co-exposure patterns, health risks, and possible sources of a wide range of EDCs in children. Urine samples (n = 1,000) from primary school children in China were collected and analyzed for 33 EDCs including bisphenols, parabens, phthalates, and 10 toxic and essential elements were quantified in urine. A 24-hour dietary recall survey was conducted to collect dietary information, and tap water and bottled water were collected accordingly. Multivariable linear regression models were applied to estimate associations of dietary information and drinking water types with urinary EDC concentrations. A total of 31 chemicals were detected in more than 50 % of urinary samples. The median urinary ΣEDCs was 1,100 ng/mL. Children from Shanghai had significantly higher urinary concentrations of ΣEDCs, ΣPhthalates, ΣBisphenols, and ΣParabens than those from Guangzhou, Guiyang, and Lanzhou. Consumption of dairy products was positively associated with urinary ΣEDCs and bisphenol concentrations. Meat and meat products were positively associated with ΣPhthalates concentrations. Rice and rice products were positively associated with urinary concentrations of methyl- and ethyl parabens, respectively. Cereal intakes were positively associated with urinary cadmium, arsenic and cobalt levels, and the consumption of aquatic products was to relation to increases of urinary lead and cadmium concentrations. Children who mainly drank filtered water had lower urinary concentrations of chlorophyl-ate metabolites and bisphenol S, while those with bottled water as the main drinking water source had higher 2,4-dichlorophenol concentrations, and lower cadmium levels. In urine, compared to those who mainly drank tap water. Our findings suggested that children in this area were widely exposed to multiple classes of EDCs, and diet and drinking water were potential exposure sources of the analyzed chemicals.	Environ Int Vol.203 Pages 109725	10.1016/j.envint.2025.109725	40816046	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0671	S. C. D'Cruz, C. Hao, M. Labuschire, V. Mustelier, C. Freire, L. Lagoff, L. Magnaghi-Jaulin, A. Olivas-Martinez, A. Rodriguez-Carrillo, C. Jaulin, A. David, M. F. Fernandez and F. Smagulova	2022	Genome-wide distribution of histone trimethylation reveals a global impact of bisphenol A on telomeric binding proteins and histone acetyltransferase factors: a pilot study with human and in vitro data	OBJECTIVE: To assess the genetic and epigenetic effects promoted by Bisphenol A (BPA) exposure in adolescent males from the Spanish INMA- Granada birth cohort, and in human cells. METHODS: DNA methylation was analyzed using MBDBP. Repeat number variation in genomic DNA was evaluated, along with the analysis of H3K4me3 by using chromatin immunoprecipitation followed by high-throughput sequencing (ChIP-seq). Analyses were performed with maternal urine from a child-based of the adolescents, concentrations in urine measurements by in vitro assessments of human HeLa cells exposed to 10 nM BPA, specifically, immunofluorescence evaluation of protein levels, gene expression analysis and ChIP-qPCR analysis. RESULTS: Adolescents in the high urinary BPA levels group presented a higher level of Satellite III (SATIII) repetitive region copy numbers compared to those in the low BPA group. Differentially methylated regions (DMRs) were identified between the two groups, including genes such as ZNF577, ZNF578, ZNF781, ZNF782, ZNF783, ZNF784, ZNF785, ANGEL, ELOF1 and CERKL and SATIII genes. Genome-wide sequencing revealed increased H3K4me3 occupancy of the promoters of genes, revealing histone acetyltransferase factors, DNA binding factors and DNA repair genes. Results were supported in HeLa cells, especially 10 nM BPA in vitro. In accordance with the data obtained in blood samples, we observed higher H3K4me3 occupancy and lower DNA methylation at some specific regions in HeLa cells. In exposed cells, changes in the expression of genes encoding DNA repair factors, (KTA1, ANGEL1 TEP1) were observed, and increased expression of several genes encoding telomeric DNA binding factors (DAXX1, TERT, TPP1, UPF1, ZBTB48) were also found. Furthermore, an increase in ESRL/ERRα was observed in the nuclei of HeLa cells along with increased binding of ESR1 to KAT8, KAT2A and TERT/TP promoters. CONCLUSIONS: Our results suggest that BPA exposure may affect telomere maintenance and DNA repair mechanisms. Our data also suggest that the effects of BPA exposure in cells may be mediated by ERRα. BPA exposure may affect telomere maintenance and DNA repair mechanisms. Our data also suggest that the effects of BPA exposure in cells may be mediated by ERRα. BPA exposure may affect telomere maintenance and DNA repair mechanisms. Our data also suggest that the effects of BPA exposure in cells may be mediated by ERRα.	Clin Epigenetics. 2022 Dec 26;14(1):186.	10.1186/s13148-022-01408-2	36572933	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0672	E. Czubacka, B. Wielgomas, A. Klimowska, M. Radwan, P. Radwan, A. Kawacka, P. Kałuży and J. Jurewicz	2021	Urinary Bisphenol A Concentrations and Parameters of Ovarian Reserve among Women from a Fertility Clinic	BACKGROUND: Human exposure to environmentally widespread endocrine disruptors, especially bisphenol A (BPA), has been suggested to affect reproductive health. Animal studies indicate that BPA may play a role in ovarian reserve impairment. However, human studies are inconclusive. The aim of the current study was to assess the effects of environmental exposure to BPA on ovarian reserve. METHODS: The study participants comprised 312 women recruited between 2017–18 years old who attended an infertility clinic for diagnosis, due to the couples' infertility. BPA urinary concentrations were assessed by the validated gas chromatography–ion trap mass spectrometry method. The ovarian reserve was assessed using ovarian reserve parameters: the ovarian volume, AFC (antralia), FSH (follicle-stimulating hormone), AMH (anti-Müllerian hormone), and HTC (antral follicle count). RESULTS: In the current study, the negative association between BPA urinary concentrations and AMH (r = -0.02 and AFC (p > 0.05) levels was found. Exposure to BPA was not related to other examined parameters of ovarian reserve (FSH, HCI, CONCLUSIONS: Our results suggest that BPA exposure may affect ovarian reserve parameters and reduce ovarian reserve. As this is one of the first studies of its kind, the findings need confirmation in a further investigation.	Int J Environ Res Public Health Vol.18 Issue 15	10.3390/ijerph18158041	34360336	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0673	Y. Cui, Y. Hong, Y. Xu, Z. Jin, Y. Ji, Y. Liu, L. Zhao and L. Ren	2024	Associations between urinary level of bisphenol A, phthalates, 8-iso-prostaglandin-F2 α , and emotional and behavioral problems among Chinese adolescents	BACKGROUND: Emotional and behavioral problems (EBPs) of adolescents is a worldwide public health problem. Bisphenol A (BPA) and phthalates (PAEs) are prevalent and potentially toxic to human health. Therefore, this study aimed to investigate the associations between urinary BPA, PAEs, 8-iso-PGF2α and EBPs in Chinese adolescents. METHODS: A cross-sectional study was conducted in 2019. EBPs of adolescents were assessed using the Strengths and Difficulties Questionnaire (SDQ). Urinary concentrations of BPA and seven PAEs metabolites in adolescents were determined by high performance liquid chromatography-tandem mass spectrometry. Urinary 8-iso-PGF2α concentration was detected by enzyme-linked immunosorbent assay (ELISA). Spearman rank correlation analysis, multivariate logistic regression analysis, restricted cubic spline functions were used to explore the relationship between the levels of BPA, PAEs, 8-iso-PGF2α and EBPs. RESULTS: BPA and PAEs metabolites were positively associated with EBPs in Chinese adolescents. Both the 8-iso-PGF2α was significantly non-linearly correlated with emotional symptoms, conduct problems, peer problems and total difficulties. Furthermore, 8-iso-PGF2α may partially mediate the association between BPA, PAEs and EBPs. CONCLUSIONS: Our findings suggested that BPA and PAEs exposure were associated with EBPs in Chinese adolescents. Both the 8-iso-PGF2α was significantly non-linearly correlated with emotional symptoms, conduct problems, peer problems and total difficulties. Furthermore, 8-iso-PGF2α may partially mediate the association between BPA, PAEs and EBPs. CONCLUSIONS: Our findings suggested that BPA and PAEs exposure were associated with EBPs in Chinese adolescents. Both the 8-iso-PGF2α was significantly non-linearly correlated with emotional symptoms, conduct problems, peer problems and total difficulties. Furthermore, 8-iso-PGF2α may partially mediate the association between BPA, PAEs and EBPs exposure characterization matter could not represent their long-term exposure level. CONCLUSIONS: High exposure of BPA and PAEs are associated with EBPs, which may be partly mediated by oxidative stress among adolescents. The results of this study could provide certain ideas for subsequent related research.	J Affect Disord Vol.363 Pages 456-464	10.1016/j.jad.2024.07.040	39019230	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

曝露性評価（動物）1：該当、0：該当しない　曝露性評価（疫学）1：該当、0：該当しない　曝露性評価（in vitro）1：該当、0：該当しない　曝露性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに曝露性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原則に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	曝露性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0674	Y. P. Cui, P. Yang, C. Liu, P. P. Chen, Y. L. Deng, Y. Miao, Q. Luo, M. Zhang, W. Q. Lv and Q. Zeng	2021	Urinary bisphenol A and its alternatives among pregnant women: Predictors and risk assessment	BACKGROUND: Exposure to bisphenol A (BPA) has been associated with various adverse health outcomes. Recently, an increasing concern on its alternatives such as bisphenol S (BPS) and bisphenol F (BPF) has been aroused due to the restriction use of BPA. Few studies have identified predictors of exposure to BPA alternatives and assessed their health risks. OBJECTIVE: The aim of this study was to identify predictors of BPA and its alternatives exposure among pregnant women and assess the health risks. METHODS: A total of 1,000 pregnant women were recruited from the Wuhan Maternal and Child Health Hospital Cohort, a prospective cohort established Chinese cohort. A questionnaire was conducted to obtain demographic characteristics, dietary habits, and lifestyles. We examined the predictors of creatinine-adjusted urinary BPA and its alternatives concentrations using multivariable linear regression. Risk assessments of exposure to BPA and its alternatives was calculated based on the estimated of daily intake (EDI). RESULTS: Geometric means of creatinine-adjusted urinary BPA, BPS, and BPF were 0.64 ng/mL, 0.08 ng/mL, and 0.05 ng/mL, respectively. Urinary BPA was positively correlated with BPS (r = 0.19, p < 0.001) and BPF (r = 0.14, p < 0.001). Changes' levels of fried food were related to higher concentrations of BPA, and intake of polyethylene was associated with higher concentrations of BPF and BPS. The mean EDI of BPA, 7.9 % of BPS, and 7.8% ranged from 0.625% to 13.139% tried by body weight/day, which were below the tolerable daily intake (TDI) for BPA defined by the European Food Safety Authority (EFSA) (4 ng/kg body weight/day). The maximum hazard index (HI) value was 0.7439. CONCLUSION: Several predictors identified in this study may inform public recommendations to reduce exposure to BPA and its alternatives.	Sci Total Environ Vol.784 Pages 147184	10.1016/j.scitotenv.2021.147184	33901963	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0675	J. C. Cruz, B. A. Rocha, M. C. O. Sousa, K. Kamran and F. B. Júnior	2025	Co-exposure to multiple endocrine-disrupting chemicals and oxidative stress: Epidemiological evidence of nonmonotonic dose response curves	This study aimed to investigate the effect of multiple exposure to eight classes (parabens, bisphenols, glycolipid ethers, antimicrobials, benzophenones, phthalates, tri and dichlorophenols) of endocrine-disrupting chemicals (EDCs) on oxidative stress biomarkers in pregnant women. A cross-sectional study was conducted with 1,000 pregnant women in the second trimester of pregnancy. Urine samples were collected from each mother-fetal pairs enrolled in the population-based New York University Children's Health and Environment Study (NYU CHES). Bisphenols and phthalates were measured in maternal urine collected repeatedly during pregnancy. Analyses included 25 phthalate metabolites and 9 bisphenols that were detected in 50 % of participants or more. Total biomarkers were summed from electronic ultrasonography records and estimated for each EDC class. Oxidative stress was assessed by 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 8-isoprostane (8-isoPGF2α) concentrations in urine collected during the second trimester of pregnancy. Multivariable linear regression models were used to investigate potential interactions and BKMR was used to explore the joint effects of the mixture. We examined the predictors of creatinine-adjusted urinary BPA and its alternatives concentrations using multivariable linear regression. Risk assessments of exposure to BPA and its alternatives was calculated based on the estimated of daily intake (EDI). RESULTS: Geometric means of creatinine-adjusted urinary BPA, BPS, and BPF were 0.64 ng/mL, 0.08 ng/mL, and 0.05 ng/mL, respectively. Urinary BPA was positively correlated with BPS (r = 0.19, p < 0.001) and BPF (r = 0.14, p < 0.001). Changes' levels of fried food were related to higher concentrations of BPA, and intake of polyethylene was associated with higher concentrations of BPF and BPS. The mean EDI of BPA, 7.9 % of BPS, and 7.8% ranged from 0.625% to 13.139% tried by body weight/day, which were below the tolerable daily intake (TDI) for BPA defined by the European Food Safety Authority (EFSA) (4 ng/kg body weight/day). The maximum hazard index (HI) value was 0.7439. CONCLUSION: Several predictors identified in this study may inform public recommendations to reduce exposure to BPA and its alternatives.	Sci Total Environ Vol.969 Pages 178952	10.1016/j.scitotenv.2025.178952	40010254	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0676	W. Cowell, M. H. Jacobson, S. E. Long, Y. Wang, L. G. Kahn, A. Ghassabian, M. Naidu, G. D. Tordoff, Y. Afanasyeva, M. Liu, S. S. Mehta-Lee, S. G. Brubaker, K. Kannan and L. Trasande	2023	Maternal urinary bisphenols and phthalates in relation to estimated fetal weight across mid to late pregnancy	BACKGROUND: Bisphenols and phthalates are high production volume chemicals used as additives in a variety of plastic consumer products leading to near-ubiquitous human exposure. These chemicals have established endocrine disrupting properties and may impact cardiometabolic health in the early and later stages of life. OBJECTIVES: To examine associations between urinary bisphenol A (BPA), bisphenol S (BPS), and phthalate metabolites in mother-fetal pairs enrolled in the population-based New York University Children's Health and Environment Study (NYU CHES). Bisphenols and phthalates were measured in maternal urine collected repeatedly during pregnancy. Analyses included 25 phthalate metabolites and 9 bisphenols that were detected in 50 % of participants or more. Fetal biometry data were extracted from electronic ultrasonography records and estimated fetal weight (EFW) was calculated using the Hadlock 4 equation. Linear mixed models were used to examine associations between urinary biomarkers and EFW z-score, adjusting for maternal and paternal covariates. We examined sex differences using stratified models. RESULTS: We found no statistically significant associations were observed across chemicals, phthalates, bisphenols, and sexes. However, within gestational timepoints, we found that among females, the molar sums of the phthalates DEHP and DnOP were generally associated with decreases in EFW among smaller babies and increases in EFW among larger babies. Among males, the opposite trend was observed. However, confidence intervals were generally wide at the tails of the distribution. CONCLUSIONS: In this sample, exposure to bisphenols and phthalates was associated with small sex-specific shifts in fetal growth; however, few associations were observed at the median of fetal weight and confidence intervals in the tails were wide. Findings were strongest for DEHP and DnOP, which are increasingly used as replacements for DEHP, supporting the need for future research on these contaminants.	Environ Int. 2023 Apr;174:107922.	10.1016/j.envint.2023.107922	37075581	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0677	S. A. Costa, M. Severo, C. Lopes and D. Torres	2024	Association between bisphenol A exposure and cardiometabolic outcomes: A longitudinal approach	Increased cardiometabolic risk is associated with abnormalities in blood biomarkers profile and adiposity measurements. Some substances found in the food matrix and the environment, called endocrine-disrupting chemicals, may impact cardiometabolic health in the early and later stages of life. Bisphenol A (BPA) is a food contaminant that migrates from food-contact materials and may act as an endocrine disruptor, negatively affecting human health. The present work aims to longitudinally assess the association between BPA exposure and cardiometabolic outcomes, considering data from Portuguese population-based birth cohort Generation XXI. Blood levels (0.69±0.1 IR 14.2-53.8) (1,281 and insulin resistance (0.84±0.1 IR 10.1-22.5) (1,282) were assessed a significant longitudinal association with BPA daily exposure after adjustment for important variables and the Bonferroni correction. Higher BPA exposure (β=0.0001; IR 10.1-22.5) (p=0.0001) and insulin resistance (β=0.0001; IR 10.1-22.5) (p=0.0001) at 7 years old. Higher BPA exposure (β=0.0001; IR 10.1-22.5) (p=0.0001) and triglycerides

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質の段階毒性の原則に基づき除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0687	A. G. Christiansen, O. Carstensen, M. Sommerlund, P. A. Clausen, J. H. Bamkilde, V. Schlünssen, M. Isaksson, S. A. J. Schmidt and H. A. Kolstad	2022	Prevalence of skin sensitization and dermatitis among epoxy-exposed workers in the wind turbine industry	BACKGROUND: A high prevalence of skin sensitization and dermatitis has been reported among workers exposed to epoxy components. OBJECTIVES: To estimate the risk of skin sensitization and dermatitis among workers in the wind turbine industry in Denmark and to identify risk factors for skin sensitization. METHODS: A cross-sectional study among 1,000 randomly selected workers was conducted. A questionnaire-based interview and clinical skin examination, and a nasal wash and blood sample were collected at two wind turbine blade factories in Denmark. Participants underwent a skin examination, were tested with a delayed patch test panel including epoxy-containing products used at the factories, and answered a questionnaire. RESULTS: Screen production workers (EPBs) were sensitized to an epoxy component compared with none of the office workers. Skin sensitization was more frequent among EPBs (odds ratio (OR) 5.3, 95% confidence interval (CI) 1.1-25.5) and laminators (OR 3.2, 95% CI 0.8-12.8) than among office workers. Dermatitis was more frequent among EPBs (OR 3.5, 95% CI 0.9-13.7), blade workers (OR 2.7, 95% confidence interval (CI) 0.8-9.1) and higher among laminators (OR 8.0) than the nonsensitized workers (OR 1.0). Workers sensitized to epoxy components had a higher risk of dermatitis if they had worked more than 5 years in the factories (OR 3.5, 95% CI 1.0-12.7). Nonsensitized workers had a higher risk of dermatitis if they had worked more than 5 years in the factories (OR 2.3, 95% CI 1.0-5.2). Bisphenol A and F were the most frequent sensitizers. One of the four workers sensitized to epoxy components used at the factories did not react to the epoxy resin of the TRIAX mat(TM) panel. CONCLUSIONS: Despite comprehensive skin protection, sensitization and dermatitis are prevalent among highly epoxy-exposed workers in the wind turbine industry in Denmark. Our findings document the need for intensified preventive efforts and emphasize the importance of tailored patch testing. What is already known about this topic? Epoxy components are well-known sensitizers of the skin. A high prevalence of skin sensitization and dermatitis has been reported among workers exposed to epoxy components. Comprehensive protective equipment is recommended when working with epoxy components. What does this study add? Despite comprehensive skin protection, skin sensitization and dermatitis are prevalent among epoxy-exposed workers. We found that 50% of workers sensitized to epoxy products had dermatitis. Only 70% of the sensitized workers were detected by the epoxy mixture the TRIAX test(TM), which emphasizes the importance of tailored testing.	Br J Dermatol Vol.187 Issue 6 Pages 988-996	10.1111/bjd.21830	35972390	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0688	E. U. Chowdhury, H. Banu, M. S. Monshed, I. A. Jahan, S. Khand and M. A. Hassnat	2025	Raised Bisphenol A has a Significant Association with Adverse Reproductive Manifestations Rather than Biochemical or Hormonal Aberrations in Women with Polycystic Ovary Syndrome	BACKGROUND: Bisphenol A (BPA) is a widely used industrial element. Recently it is suspected that BPA may disrupt the endocrine system to influence the manifestations of polycystic ovary syndrome (PCOS). OBJECTIVE: This study aimed to assess serum BPA level and its association with manifestations of PCOS in women. METHODOLOGY: This cross-sectional study included 80 young adults, with PCOS and 80 age-matched healthy controls. BPA, free testosterone, DHEAS, LH, FSH, SHBG, fasting glucose, insulin, and lipid profile were measured. Clinical features, including hirsutism, menstrual irregularities, and glycemic traits, were evaluated. Statistical analyses, including hormone, lipid, biochemical, and hormone receptor binding plastics, dehydroepiandrosterone-sulfate, and BPA. Glucose was measured by glucose oxidase. Subjects by glycemic phosphate dehydrogenase peroxidase, all hormones including SHBG by chemiluminescent immunoassay and BPA by sandwich enzyme-linked immunosorbent assay. Insulin resistance was measured using homeostasis model assessment of insulin resistance. RESULTS: Women with PCOS had significantly higher BPA levels (ng/mL) than the control group (27.30 (19.60, 33.90) vs. 16.0 (13.38, 18.78); median (IQR), p < 0.001). Using the 75th percentile value of the control group, 19 (23.8%) women with PCOS had high BPA levels. Those with high BPA levels had a significantly higher frequency of menstrual irregularities (" abortive among women with PCOS (OR = 3.2, 95% confidence interval (CI) 1.1-9.3, p = 0.032) and hirsutism (OR = 3.5, 95% CI 1.2-10.2, p = 0.021). Women with PCOS and high BPA (OR = 3.2, 95% CI 1.1-9.3, p = 0.032) had higher levels of BPA than those without the features. Serum BPA had no significant association or correlation with any androgenic and metabolic manifestations. CONCLUSION: Raised BPA level may be associated with adverse reproductive features in PCOS.	J ASEAN Fed Endocr Soc Vol.40 Issue 1 Pages 26-31	10.15605/jafes.040.01.14	40416478	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0689	W. C. Chou, J. W. Gaynor, E. M. Graham, B. Kloeppinckx, T. Walker, E. S. Coker, R. F. Wambach and Z. Lin	2025	A Machine Learning-Based Clustering Analysis to Explore Bisphenol A and Phthalate Exposure from Medical Devices in Infants with Congenital Heart Defects	BACKGROUND: Plastic-containing medical devices are commonly used in critical care units and other patient care settings. Patients are often exposed to xenobiotic agents that are leached out from plastic-containing medical devices, including bisphenol A (BPA) and phthalates. Given the potential health implications, there is an urgent need for a comprehensive understanding of this exposure. OBJECTIVES: This multi-institutional study aimed to characterize the exposure to BPA and phthalates from medical devices in infants with congenital heart defects (CHD) undergoing cardiac surgery during the perioperative period. METHODS: We collected daily urine samples from infants with CHD undergoing cardiac surgery during the perioperative period from birth to 6 (1.4) and measured BPA, 402 methoxyphthalate (DEHP) metabolites (MEHP, MEHHP, MEOHP, MECPP), and non-DEHP phthalate metabolites (MBP, MMP, MEP, MCPP, MiBP) using ultra high-performance liquid chromatography-tandem mass spectrometry. Machine learning-based cluster analysis was utilized to analyze these liner dependent data. RESULTS: Utilizing a machine learning-based unsupervised clustering approach, 3 unique clusters of infants undergoing cardiac time series toxicokinetic exposure patterns. These distinct clustering groups correlated with the utilization of extracorporeal membrane oxygenation (ECMO) and cardiopulmonary bypass (CPB) during cardiac surgery. Infants undergoing cardiac surgery with ECMO support had significantly higher urinary concentrations of several BPA and phthalate metabolites compared to those without ECMO use, a trend we observed with non-DEHP metabolites. Moreover, peak concentrations in toxicokinetic profiles demonstrated within the intensity of medical devices. CONCLUSION: Our findings suggest that dynamic changes of urinary BPA and DEHP metabolites corresponded to the type and number of medical devices used in infants. Further studies are needed to investigate the potential toxicological risks of infants with CHD undergoing cardiac surgery exposed to these chemicals in medical devices. https://doi.org/10.1289/EHP14056.	Environ Health Perspect. 2025 Jun;133(6):67016.	10.1289/ehp15034	40338266	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0690	Y. J. Choi, Y. A. Lee, Y. C. Hong, J. Cho, K. S. Lee, C. H. Shin, B. N. Kim, J. I. Kim, S. J. Park, N. Bhagwat, K. Bannerjee and Y. H. Lin	2020	Effect of prenatal bisphenol A exposure on early childhood body mass index through epigenetic influence on the insulin-like growth factor 2 receptor (IGF2R) gene	OBJECTIVES: Epigenetic mechanisms have been suggested to play a role in the link between in utero exposure to bisphenol A (BPA) and pediatric obesity; however, there is little evidence regarding this mechanism in humans. We obtained data on obesity-associated CpG sites from a previous epigenome-wide association study, and then examined whether methylation at these CpG sites was influenced by prenatal BPA exposure. We then evaluated the relationship between CpG methylation status and body mass index (BMI) in a prospective children's cohort at ages 2, 4, 6, and 8 years. METHODS: Methylation profiles of 59 children were longitudinally analyzed at ages 2 and 8 years using the Infinium Human Methylation BeadChip. A total of 956 CpG sites known to be associated with BMI or obesity-associated risk were tested for prenatal BPA levels, repeated-measures linear and logit regression groups based on the BMI percentile of maternal BPA levels (2 ≥6 µg/g creatinine) followed by an analysis of the association between DNA methylation and BMI trajectories. RESULTS: Methylation at cg07600487 (IGF2R) at age 2 years was significantly associated with maternal BPA level (β = 0.004, p = 0.0011, false discovery rate [FDR] = 0.0011). Moreover, the increase of methylation at cg07600487 (IGF2R) at age 2 years, the linear mixed model analysis revealed that BMI during ages 2-8 years significantly increased by 0.49 (95% confidence interval [CI]: 0.082 to 0.91, p = 0.02) kg/m2 in boys. The indirect effect of prenatal BPA exposure on early childhood BMI through methylation at cg07600487 (IGF2R) at age 2 years was marginally significant. CONCLUSIONS: Prenatal exposure to BPA may influence differential methylation of IGF2R at age 2. This result indicates that a possible sensitive period of DNA methylation occurs earlier during development, which may affect BMI and later childhood in a sex-specific manner.	Environ Int. 2020 Oct:143:105929.	10.1016/j.envint.2020.105929	32644488	ヒト	疫学	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0691	Y. Choi, S. J. Lee, J. Jeon, K. J. Jung and S. H. Jee	2019	Inverse associations of bisphenol A and phthalate metabolites with serum bilirubin levels in Korean population	Bisphenol A (BPA) and phthalates are endocrine disruptors that can induce oxidative stress. Serum bilirubin has antioxidant properties and may serve as a biomarker of oxidative stress. The objective of this study was to explore the relationship of BPA and phthalates with serum bilirubin levels in a Korean population. Urinary concentrations of BPA and six phthalates [mono-n-butyl phthalate (MnBP), mono-iso-butyl phthalate (MiBP), mono-(2-ethyl-5-carboxyl) phthalate (MECPP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-benzyl phthalate (MBzP)] were measured in 709 participants. Serum concentrations of BPA and three phthalate metabolites (MnBP, MiBP, and mono-(2-ethylhexyl) phthalate (MEHP)) were measured in 702 participants. After multivariate adjustment, including confounding variables, associations between above chemicals and serum bilirubin levels were analyzed using multivariate linear regression with age, sex, BMI, SGOT, SGPT, GFR, and alcohol intake adjustment. Participants were further stratified by sex. Among the urinary BPA and phthalate metabolites, MnBP, MiBP, MECPP, and MEHHP were detected in more than 95% of the subjects. MnBP, MiBP, MECPP, MEHHP, and MEOHP were positively associated with serum bilirubin levels (β = 0.011, P = 0.003; β = 0.010, P = 0.003; β = 0.008, P = 0.010; β = 0.008, P = 0.010; β = 0.006, P = 0.031, respectively). After stratification by sex, the associations of urinary BPA remained both in male and female, of which urinary phthalates disappeared in female. The association of serum MiBP was disappeared after stratification. Urinary BPA and phthalate metabolites were inversely associated with serum bilirubin levels, whereas serum MiBP showed positive association with bilirubin. These results could provide clues for understanding the mechanisms of endocrine disruptor from oxidative stress to excretion from our body.	Environ Sci Pollut Res Int Vol.26 Issue 26 Pages 26685-26695	10.1007/s11356-019-05205-y	31292880	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0692	S. Chu, M. J. Kim, Y. J. Park, S. Kim, K. Choi, G. J. Cheon, Y. H. Cho, H. L. Jeon, J. Yoon and J. Park	2020	Thyroxine-binding globulin, peripheral deiodinase activity, and thyroid autoantibody status in association of phthalates and phenolic compounds with thyroid hormones in adult population	Exposure to consumer chemicals such as phthalates and phenolic compounds has been associated with thyroid hormone disruption in humans. However, information related to factors that may influence such associations is limited. We investigated the effects of thyroid autoantibody status and thyroxine-binding globulin (TBG) on the associations between urinary phthalate and phenol biomarkers and thyroid hormones. Environmental Health Survey (KoNEHS) 2015-2017, and measured urinary concentrations of major phthalate metabolites, bisphenol A (BPA), and triclosan, with thyroid hormone related measures, including free and total T3 and T4, TSH, thyroxine-binding globulin (TBG), calculated peripheral deiodinase (DIO) activity, and thyroid autoantibodies of thyroperoxidase (TPO) and thyroglobulin (Tg). Phthalate metabolites were negatively associated with free T3 and positively associated with total T3. These observations could be explained by TBG levels and calculated peripheral DIO activity that were also associated with phthalate exposure. In contrast, BPA was positively associated with total T4 and negatively associated with total T3, without any changes in TBG concentration. Serum TPO and Tg antibodies were not associated with urinary biomarker concentrations. Our results suggest that phthalates and BPA may disrupt thyroid hormone homeostasis via different pathways, and TBG may play a role in phthalate exposure. The results of our observation-level potential underlying mechanisms of phthalates-induced thyroid hormone disruption, and suggests the importance of consideration of thyroid autoimmunity status in association studies for thyroid-disrupting chemicals.	Environ Int Vol.140 Pages 105783	10.1016/j.envint.2020.105783	32464474	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0693	J. Y. Choi, J. Lee, D. A. Huh and K. W. Moon	2022	Urinary bisphenol concentrations and its association with metabolic disorders in the US and Korean populations	Bisphenol A (BPA) is a representative endocrine-disrupting compound used in a vast array of consumer products, and are being frequently substituted by its analogues, bisphenol S (BPS) and bisphenol F (BPF). We aimed to investigate the urinary concentrations of BPA, BPS, and BPF in the US and Korean populations, and to compare the exposure levels between the two countries. We used data from the US National Health and Nutrition Examination Survey (2013-2014) and 2008 Korean adults from the Korean National Environmental Health Survey (2015-2017) cycle and analyzed. We examined the exposure levels of bisphenols, and determined their associations with obesity, high obesity (superobesity threshold (ST)), CC and triglycerides (TG) levels, and hypercholesterolemia prevalence through multiple linear, and binary (ordinal) logistic regression models. In both populations, high BPA levels (several tertiles vs. 2nd, Schindler) showed corresponding associations with (typically) favorable obesity. BPA levels were associated with decreased HDL-C levels (Q3: β = -0.063, p = 0.00 3.01; Q3: β = -0.032, p = 0.02), increased TG levels (Q3: β = 0.221, p = 0.029 [US]; Q3: β = 0.089, p = 0.02), and higher odds for obesity (Q3: OR = 1.58, 95% CI: 1.06, 2.35 [US]; Q3: OR = 1.52, 95% CI: 1.03, 2.24 [Korea]). Similar results were observed for BPS and BPF. Urinary BPA, BPS, and BPF concentrations were significantly associated with metabolic disorders in the US and Korean populations. Increases in HDL-C (Q3: β = -0.048, p = 0.02) and elevated odds for obesity at higher BPF levels (Q3: OR = 1.48, 95% CI: 1.02, 2.15) was observed in US women. The findings of our study indicated that BPS and its analogues, BPS and BPF, are associated with lipid metabolism disorders. In addition to obesity in adults. Given the increase in exposure to BPA alternatives, continuous biomonitoring, and further investigation of their health effects through prospective cohort studies are warranted.	Environ Pollut Vol.295 Pages 118679	10.1016/j.envpol.2021.118679	34915096	ヒト	疫学	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0694	J. W. Choi, H. Jang, J. R. Kuiper, D. H. Bennett, R. J. Schmidt and H. M. Shin	2025	Gestational exposures to mixtures of multiple chemical classes and autism spectrum disorder in the MARBLES study	BACKGROUND: Previous epidemiologic studies on gestational chemical exposures and autism spectrum disorder (ASD) often lack analysis of chemical mixtures or are limited to investigating certain chemical classes. OBJECTIVE: We examined the impact of multi-class chemical mixtures on ASD risk, using data from the MARBLES (Markers of Autism Risk in Babies Learning Early Signs) study. METHODS: Children were clinically assessed at age 3 and classified as ASD, typical development (TD), or non-TD with other neurodevelopmental concerns. In blood or urine from 235 pregnant mothers, we quantified 32 biomarkers across 5 chemical classes: per- and polyfluoroalkyl substances (PFAS), parabens, phthalates, and organophosphate esters (OPFRs). We only analyzed 18 biomarkers detected in >50% of the sample. After identifying clusters with similar chemical profiles via hierarchical clustering, we applied linear discriminant analysis (LDA) to compare ASD exposure summary scores. In covariate-adjusted models, we used LDA scores to assess co-exposure associations with ASD risk and neurodevelopmental scores. RESULTS: Among 220 children (ASD: 51, TD: 116, non-TD: 53), we identified four clusters: Cluster 1 (PFAS), Cluster 2 (parabens), Cluster 3 (PFAS, Cluster 2), and Cluster 4 (phthalates and OPFRs). Clusters 2 and 3 were associated with non-TD (1.07 [1.01, 1.14] and 1.12 [1.05, 1.19], respectively). Cumulative exposure across the four clusters was linked to increased risk of both ASD and non-TD. Postnatal biomarkers within and between clusters were observed. CONCLUSION: This study shows that considering multiple chemical classes resulted in stronger associations with ASD and non-TD risk, compared to when investigated separately in our previous studies.	Environ Res. 2025 Aug 1:278:121646.	10.1016/j.envres.2025.121646	40250579	ヒト	疫学	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0695	J. E. Choi, E. J. Choi, S. Lee, B. Park, H. A. Lee, Y. S. Hong, E. Ha, H. S. Kim and H. Park	2025	Relationship of urinary bisphenol A in childhood on thyroid hormone function in adolescents: a cohort study	BACKGROUND: Bisphenol A (BPA) is a type of endocrine-disrupting chemical utilized in the production of plastics. Soy epoxy resins and polycarbonate polymers. BPA exhibits weak estrogenic and potent anti-androgenic effects, and prior research has linked it to disturbances in thyroid function. This study aims to assess the potential association between early childhood exposure to urinary bisphenol A and thyroid hormone levels in adolescence. METHODS: We analyzed data from 1,128 participants in the Mothers and Children's Environmental Health (MOCEH) birth cohort study. Urinary BPA levels were measured at ages 6 months, 1, 2, 3, 4, 5, and 6 years. The concentration of urinary BPA was repeatedly measured for each subject at ages 2-3 years and 7-9 years. Serum levels of free triiodothyronine (T3), free thyroxine (T4), and thyroid-stimulating hormone (TSH) were measured at ages 10-12 years in a subgroup of 128 out of 166 subjects, who had undergone repeated BPA concentration measurements. We utilized the GAS program to analyze possible links between childhood exposure to BPA and thyroid hormone function in adolescents. Additionally, we explored how exposure to BPA during key specific periods influenced changes in thyroid hormone levels. RESULTS: The study found that urinary BPA levels at ages 2-3 years were not notably linked to thyroid hormone levels in adolescents aged 10-12 years. However, BPA levels at ages 7-9 years were significantly associated with free T3 levels in girls aged 10-12 years. Specifically, a 10-fold increase in urinary BPA concentration at ages 7-9 years was associated with a 0.26 pg/mL decrease in free T3 levels in girls aged 10-12 years (95% CI: -0.44, -0.08). However, specifically T3H and free T3. There was a significant decrease in the concentration of free T3 in girls with higher BPA concentrations. CONCLUSIONS: BPA exposure in childhood affects thyroid function in adolescent girls. This relationship may contribute to an increased prevalence of thyroid disorders in adolescents due to environmental influences.	PLoS One. 2025 May 22;20(5):e0322658.	10.1371/journal.pone.0322658	40403006	ヒト	疫学	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0696	Y. Chow, K. N. Kim, Y. J. Lee, J. I. Kim, B. N. Kim, Y. H. Lim, Y. C. Hong, C. H. Shin and Y. A. Lee	2024	Prenatal and childhood exposure to endocrine-disrupting chemicals and early thelarche in 8-year-old girls: A prospective study using Bayesian kernel regression	BACKGROUND: Studies on the combined effects of persistent and non-persistent endocrine-disrupting chemicals (EDCs) on puberty are insufficient. To date, no studies have analyzed breast development at age 8 years, a key criterion for determining precocious puberty. We investigated the relationship between prenatal or childhood exposure to EDC mixtures and early thelarche, defined as breast development before age 8 years in girls. METHODS: This prospective study included 211 girls, who had undergone an prenatal and 8-year ultrasound examination. Urinary concentrations of 11 EDCs (5 cat, heat, mercury, bisphenol A (BPA), 3 dimethylarsinic acid, and three phthalate metabolites) from the Environment and Development of Children cohort. Prenatal exposure was assessed through samples from pregnant women at 12-27th weeks of gestation. Tanner staging was assessed by a pediatric endocrinologist. The Bayesian kernel machine regression (BKMR) model was used to estimate the overall effect of the mixture and the individual contribution of each EDC to early thelarche. RESULTS: Early thelarche was observed in 63 (29.9%) girls at age 8 years. In the logistic regression models, the risk of early thelarche increased with increasing prenatal exposure to Cd (an inverse relationship was observed for urinary BPA levels (odds ratio (OR) = 1.86, 95% confidence interval [CI] 1.29-2.68) but decreased with prenatal BPA exposure (aOR per IQR = 0.57, 95% CI 0.35-0.92). Some of the 8-year-old chemical exposures were associated with early thelarche. In the BKMR models, an increase in the mixture of prenatal EDCs was associated with a higher risk of early thelarche, with prenatal Cd and inversely associated with prenatal BPA exposure (p = 0.004 for Cd and p = 0.004 for BPA). In the BKMR models, an increase in the mixture of 8-year-old EDCs was associated with a higher risk of early thelarche, with 8-year-old Cd and BPA showing positive associations

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0700	Z. H. Chi, L. Liu, J. Zheng, L. Tian, J. Chevrier, R. Bornman, M. Obida, C. G. Goodyer, B. F. Hales and S. Bayen	2024	Biomonitoring of bisphenol A (BPA) and bisphenol analogues in human milk from South Africa and Canada using a modified QuEChERS extraction method	A novel but modified [pH]CHERS extraction method was developed to assess the levels of free and conjugated bisphenols (BPs) in human milk collected between 2018 and 2019 from two regions of South Africa (the Limpopo Province Sheshe district, n = 39; Pretoria, n = 19) and Canada (Montreal, n = 20). Total BPA (free and conjugated) and BPS were the predominant bisphenols detected in samples from Sheshe and Pretoria, with median concentrations of 0.19 and 0.16 ng/mL, respectively. Conjugated BPA and BPS were detected in 100 % and 97 % of the samples from Sheshe, with median levels of 1.03 ng/mL and 0.48 ng/mL, and detection frequencies of 73 % and 89 %, respectively. The free-association analysis of BPA revealed a predominantly conjugated form in the African samples. In contrast, total BPA was detected in only one milk sample from Montreal. Total BPS levels were lower than BPA in South Africa, with detection frequencies of 73 % and 21 % in Sheshe and Pretoria, respectively. In contrast, total BPS was the major BP detected (50 %) in Montreal (up to 3.07 ng/mL). BPAF was found exclusively in South Africa, with detection frequencies for total BPAF of 46 % and 84 % in Sheshe (<MDL–3.01 ng/mL) and Pretoria (<MDL–0.14 ng/mL), respectively. To our knowledge, this is one of the first studies to detect bisphenols in human milk from data-scarce countries such as South Africa and to highlight the notable disparities in the types and levels of bisphenols detected across two distinct countries (Canada and South Africa).	Environ Pollut Vol.348 Pages 123730	10.1016/j.envpol.2024.123730	38458524	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0701	Z. Chen, J. He and W. Shi	2023	Association between urinary environmental phenols and the prevalence of cardiovascular diseases in US adults	Environmental phenols, as endocrine disruptors, are used widely in personal care and consumer products. However, few studies have examined the association between phenol exposure, including bisphenol A (BPA), bisphenol S (BPS), and triclosan (TCS), and cardiovascular disease (CVD). We aimed to investigate the association between urinary phenols and the prevalence of CVD. A total of 3004 participants were measured with liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). The CVD was defined as a composite of 5 self-reported cardiovascular outcomes, including congestive heart failure, coronary heart disease, angina pectoris, heart attack or stroke. Multivariable logistic regression models were used to examine the association between phenols and the prevalence of CVD. A total of 3004 participants were enrolled, and 720 (16.5%) were diagnosed of CVD. The average levels of BPA, BP-3, and triclosan concentrations were 0.38, 0.30, 0.05, and 19.27 ng/mL, respectively. After multivariate-adjusted logistic regression models with increased risk of CVD after adjusting all covariates (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.01 to 1.11, P = 0.01). Compared with the lowest quartile (<1.15), the highest quartile (≥3.09 ng/mL) of BPA was associated with increased risk of CVD (OR 1.31, 95% CI 1.02 to 1.68, P = 0.04). Restricted cubic models confirmed that the association between BPA and the risk of CVD was non-linear (P = 0.005). Only BPA was associated with the risk of CVD, following a J-curve-shaped relationship.	Environ Sci Pollut Res Int Vol.29 Issue 28 Pages 42947-42954	10.1007/s11356-021-18323-3	35091943	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0702	Y. M. Chen, Z. Y. Liu, S. Chen, X. T. Lu, Z. H. Huang, M. Wu-Intan, B. X. Huang, Q. Y. Lan, T. Wu, R. Z. Huang, S. Y. Huang, L. L. Lu, Y. Y. Jian and H. L. Zhu	2023	Mitigating the impact of bisphenol A exposure on mortality: Is diet the key? A cohort study based on NHANES	Bisphenol A (BPA) is a widespread environmental pollutant linked to detrimental effects on human health and reduced life expectancy following chronic exposure. This prospective cohort study aimed to examine the association between BPA exposure and mortality risk, and to investigate the potential mediating role of dietary factors in this relationship. The study included 2,579 participants from the 2003-2016 National Health and Nutrition Examination Survey (NHANES). Urinary BPA levels were employed to assess BPA exposure, and dietary quality was evaluated using the Healthy Eating Index (2015-HEI-2015). All-cause, cardiovascular disease (CVD), and cancer mortality statuses were determined until December 31, 2019, resulting in a cumulative follow-up of 80,066 person-years. The results showed that the highest tertile of urinary BPA levels corresponded to a 39% increase in all-cause mortality and a 42% increase in CVD mortality compared to the lowest tertile. In contrast, the highest HEI-2015 scores was associated with a 29% reduction in all-cause mortality relative to the lowest tertile. Although no significant interaction was found between HEI-2015 scores and urinary BPA levels concerning mortality, the association between HEI-2015 scores and both all-cause and CVD mortality was statistically significant at low urinary BPA levels. Continuous monitoring of BPA exposure is crucial for evaluating its long-term adverse health effects. Improving dietary quality can ward off cause mortality and decrease the risk of all-cause and CVD mortality at low BPA exposure levels. However, due to the limited protective effect of dietary quality against BPA exposure, minimizing BPA exposure remains a vital goal.	Ecotoxicol Environ Saf. 2023 Nov 15:267:115629.	10.1016/j.ecoenv.2023.115629	37890258	ヒト	その他(死亡率)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0703	Y. Chen, Z. Zhang, G. He, H. Liang, X. Song, J. Xi, S. Wei, W. Yuan, Z. Wang and M. Miao	2024	Associations of prenatal exposure to bisphenols with infant anthropometry: A prospective cohort study	BACKGROUND: Bisphenols (BPs) have been shown to exhibit developmental toxicities. Epidemiological evidence on prenatal BPs exposure and infant growth primarily confined scope to specific BPs and birth outcomes, with few studies focusing on infant growth and reporting inconsistent findings. The joint effects of prenatal exposure to BPs mixture on infant growth was rarely studied. OBJECTIVE: This study examined associations of prenatal exposure to individual bisphenol A (BPA) and its analogues: Bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), and tetrachlorobisphenol A (TCBPA) and their mixture with infant growth. METHODS: Between 2018 and 2020, 1,010 pregnant women were recruited from Wuhan Maternal and Child Health Hospital. Maternal urine samples were collected in each trimester. Infant weight, length, and head circumference were measured at birth, 6 months, and 12 months. Linear mixed-effects models and Bayesian kernel machine regression models (BKMR) were used to analyze associations of exposure to individual BPs and BPs mixture with infants' anthropometric measurements, and to identify the important components among mixture. The risks for rapid growth and overweight of each BP were determined using modified Poisson regression models. RESULTS: The 6 general profile of higher prenatal BPs exposure (mainly BPS, BPF, and BPS) associated with higher anthropometric measurements and higher risks of overweight during infancy was found. We also observed higher risks of rapid growth in infants following prenatal BPs exposure, with risk ratios ranging from 1.40 to 1.95. The joint effects of BPs mixture and single effect of each BP from the BKMR models were consistent with the above findings. Prenatal exposure to BPs was associated with greater weight, length, and head circumference at birth, while it was mainly by BPF. CONCLUSIONS: Prenatal exposure to BPs and their mixture could increase anthropometric measurements of offspring during infancy, with implications of altered growth trajectory in future.	Sci Total Environ. 2024 Jun 20:930:172409.	10.1016/j.scitotenv.2024.172409	38636856	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0704	Y. Chen, C. Xu, Y. Huang, Z. Liu, J. Zou and H. Zhu	2024	The Adverse Impact of Bisphenol A Exposure on Optimal Cardiovascular Health as Measured by Life's Essential 8 in U.S. Adults: Evidence from NHANES 2005 to 2016	Background/Objectives: Cardiovascular diseases are the primary cause of global morbidity and mortality, with cardiovascular health (CVH) remaining well below the ideal level and showing minimal improvement in the U.S. population over recent years. Bisphenol A (BPA), a pervasive environmental contaminant, has emerged as a potential contributor to adverse cardiovascular outcomes. This cross-sectional study delves into the impact of BPA exposure on achieving optimal CVH, as assessed by the Life's Essential 8 metric, among U.S. adults. Methods: Analyzing data from 6889 participants in the National Health and Nutrition Examination Survey (NHANES) collected between 2005 and 2016, BPA exposure was quantified through urine BPA levels, while optimal CVH was determined using the American Heart Association's Essential 8 criteria, encompassing behavioral and biological factors. Multivariable logistic regression and propensity score matching were employed to evaluate the association between BPA exposure and CVH. Results: This study reveals that individuals in the highest tertile of BPA exposure (≥2.64 ng/mL) had significantly lower odds of achieving optimal CVH (OR = 0.74, 95% CI: 0.60–0.92, p = 0.006) compared to those in the lowest tertile (<1.15 ng/mL). This association was also identified when urinary BPA was analyzed as a continuous variable and was mirrored in the link between urinary BPA levels and health factor scores. Conclusions: The findings underscore the potential benefits of reducing BPA exposure in enhancing the prevalence of optimal CVH and mitigating the burden of cardiovascular disease. Given the widespread use of BPA, ongoing monitoring of BPA's impact on CVH is essential. Further studies are necessary to elucidate the long-term and causative connections between BPA and CVH. These insights contribute to understanding the complex interplay between environmental factors and CVH outcomes, informing targeted interventions to mitigate cardiovascular disease risk within the population.	Nutrients Vol.16 Issue 19	10.3390/nu16193253	39408220	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0705	Y. Chen, H. Xiao, A. Namat, J. Liu, F. Ruan, S. Xu, R. Li and W. Xia	2022	Association between trimester-specific exposure to thirteen endocrine disrupting chemicals and preterm birth: Comparison of three statistical models	BACKGROUND: Growing evidence indicated that maternal exposure to some endocrine disrupting chemicals (EDCs) may increase the risk of preterm birth (PTB). However, few studies have evaluated the joint effect of EDCs on PTB. OBJECTIVES: This study aimed to evaluate the associations of maternal EDCs mixture in the 1st, 2nd, and 3rd trimesters during pregnancy with PTB, and identify the vital components that mainly contribute to PTB. METHODS: This study included 847 pregnant women that provided urine samples for all three trimesters. Urinary concentrations of thirteen EDC metabolites (three phenols, one phthalate, and four benzoic acids and benzothiazole) were examined. Logistic regression model, quantile g-computation and Bayesian kernel machine regression (BKMR) models were applied to study the associations. RESULTS: Higher urinary concentrations of 2,5-dichlorophenol, 2,4-dichlorophenol, and 3-phenoxybenzoic acid in the 1st trimester were positively associated with PTB (OR (95% CI): 1.38 (1.02, 1.86), 1.36 (1.02, 1.82), and 1.34 (1.02, 1.76), respectively). Quantile g-computation identified that urinary EDCs mixture in the 1st trimester were positively associated with PTB (OR (95 % CI): 1.48 (1.02, 2.16)), and the most heavily weighted component for PTB was BPS (28.7%). Followed by mono-2-ethylhexyl phthalate (MEHP) (17.5%). BKMR model determined a significant association between EDCs mixture in the 1st trimester and PTB when all EDC concentrations were at or above their 55th percentile compared to the median. The BKMR model found that BPS and MEHP were associated with an increase in the estimated probability of PTB, when the other EDCs were held in their 55th and 75th percentiles, respectively, in the 1st trimester. CONCLUSIONS: The results of mixture analysis models indicated that exposure to higher EDCs mixture in the 1st trimester may increase the risk of PTB. BPS was considered as the most contributing factor to PTB among the detected EDCs.	Sci Total Environ. 2022 Dec 10:851(Pt 2):158236.	10.1016/j.scitotenv.2022.158236	36041600	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0706	Y. Chen, J. Wu, R. Li, W. Kang, A. Zhao, Y. Yin, S. Tong, J. Yuan and S. Li	2023	Individual and joint association of phenols, parabens, and phthalates with childhood lung function: Exploring the mediating role of peripheral immune responses	The functioning of the respiratory system can be interfered with by exposure to mixtures of environmental chemicals, however, the evidence is still ambiguous. We evaluated the association of exposure to mixtures of 15 chemicals, including 2 phenols, 2 parabens, and 11phthalates, with the lung function metrics. Based on data from the National Health and Nutrition Examination Survey (NEF-2021), this analysis was conducted among 1,582 children aged 6-18 years. Linear regression, Bayesian kernel machine regression, quantile-based g-computation regression, and a generalized additive model were performed to estimate the associations. Stratification analyses were performed to investigate possible biological pathways mediated by immune cells. Our results indicated that the phenols, parabens, and phthalates mixture was negatively related to lung function parameters. Ben and PP1 were identified as important contributors to negative associations with FEV1/CI, FVC, and PEF, with non-linear relationships observed between BP3 and those outcomes. The most influential chemical was MiBP, followed by MnBP, MEP, and Ben. Additionally, the negative associations between the mixture of PP1 and FEV1/FVC were mediated by eosinophils and monocytes. The findings offer insights into the associations of chemical mixtures with respiratory health and the possible driving mechanisms, which would be of significance in adding novel evidence of the role of peripheral immune responses, as well as calling for remediation actions to be prioritized during childhood.	J Hazard Mater Vol.454 Pages 131457	10.1016/j.jhazmat.2023.131457	37099904	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0707	Y. Chen, M. Miao, Z. Wang, H. Ji, Y. Zhou, H. Liang, G. He and W. Yuan	2023	Prenatal bisphenol exposure and intelligence quotient in children at six years of age: A prospective cohort study	The effects of prenatal bisphenol A (BPA) exposure on children's cognitive development have been reported; however, relevant evidence on BPA analogues was limited, with no consideration of the joint effect of their mixtures. We aimed to investigate the associations of prenatal exposure to BPA and its analogues, including bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF), with children's intelligence quotient (IQ) at six years of age. We assessed the associations of prenatal exposure to individual BPs with children's intelligence quotient (IQ) and evaluated the joint effects using the Quantile g-computation model (QGC) and Bayesian kernel machine regression model (BKMR). QGC models showed that higher maternal urinary BPs mixture concentrations were associated with lower scores among boys in a non-linear way; however, no associations were observed in girls. For individual effects, BPA and BPF were associated with decreased IQ scores in boys and some identified as important contributors to the joint effect of BPs. However, associations of BPs with increased IQ scores in girls, and FSIQM with increased IQ scores in both sexes were observed. Our findings suggested prenatal exposure to BPs mixture may affect children's cognitive function in a sex-specific pattern and provided evidence of the neurotoxicity of BPA and BPF.	Chemosphere. 2023 Sep:334:139023.	10.1016/j.chemosphere.2023.139023	37230300	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0708	X. Chen, S. Zhang, M. Zhang, W. Zhong, S. Bai, Y. Zhao, C. Li, S. Lu and W. Li	2021	Urinary parabens, bisphenol A and triclosan in primiparas from Shenzhen, China: Implications for exposure and health risks	The usage of parabens, bisphenol A and triclosan in diverse consumer products is in widespread. Nevertheless, there are limited data concerning exposure to these chemicals, in human being, especially in primiparas. Biomonitoring of chemicals in primiparas is useful for the estimation of chemical exposure risks for both primiparas and their offspring. This study aims to investigate urinary levels of parabens, bisphenol A and triclosan of 80 primiparas from Shenzhen, China and to evaluate their potential health risks. Methyl, ethyl, and n-propyl parabens (bisphenol A and triclosan exhibited high detection rates (DRs, ≥ 97%) in urine samples, suggesting that primiparas are exposed to them widely. The median concentrations of methyl, ethyl, and n-propyl parabens, bisphenol A and triclosan in urine were 2.16, 0.65, 0.08, 1.30 and 3.00 μg/L, respectively. Ethyl paraben was the predominant paraben in urine samples. Urinary concentrations of methyl paraben were significantly higher than those of ethyl paraben, n-propyl paraben, bisphenol A and triclosan. Personal care products, plastic containers and urinary concentrations of ethyl paraben or PPL industrial products containers might be an important factor influencing primipara exposure to these four chemicals. Urinary concentrations of methyl paraben were positively associated (p < 0.05) with the time of computer use by participant, suggesting that indoor dust might constitute an important source of parabens. The estimated daily intake of parabens, bisphenol A and triclosan contained with the acceptable daily intakes in a comparatively low level. The based-quotients (HQs) of these chemicals were all less than 1, suggesting no health risks for primiparas from South China. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s10311-020-00989-1.	J Environ Health Sci Eng Vol.19 Issue 1 Pages 251-259	10.1007/s40201-020-00599-1	34150233	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0709	W. J. Chen, C. Robledo, E. M. Davis, J. R. Goodman, C. Xu, J. Hwang, A. E. Jenks, T. Ganea, A. M. Calafat and J. D. Peck	2022	Assessing urinary phenol and paraben mixtures in pregnant women with and without gestational diabetes mellitus: A case-control study	Prior studies have identified the associations between environmental phenol and paraben exposures and increased risk of gestational diabetes mellitus (GDM), but no study addressed these exposures as mixtures. As methods have emerged to better assess exposures to multiple chemicals, our study aimed to apply Bayesian kernel machine regression (BKMR) to evaluate the association between phenol and paraben mixtures and GDM. This study included 600 GDM cases and 737 obstetric patient controls from the University of California Medical Center, San Francisco's late 2000s pregnancy urine samples were retrospectively assayed to quantify concentrations of bisphenol A (BPA), benzophenone-3, triclosan, 2,4-dichlorophenol, 2,5-dichlorophenol, butylparaben, methylparaben, and propylparaben. Multivariable logistic regression was used to evaluate the associations between individual chemical exposures and GDM, adjusting for maternal age, race/ethnicity, pre-pregnancy body mass index, and nulliparity. BKMR was used to evaluate the associations between chemical mixtures and GDM, and to identify the most influential phenol and paraben mixtures within each grouping for the cumulative association among the chemical biomarkers. When analyzing individual chemicals using logistic regression, benzophenone-3 was associated with GDM (adjusted odds ratio (aOR) per interquartile range (IQR) = 1.16, 95% confidence interval (CI) 1.13, 1.18), while BPA was negatively associated with GDM (aOR 0.82, 95% CI 0.77, 0.90). In parallel BKMR analysis, an increase in a combination of all phenol and paraben exposures at the 60th percentile, compared to the 50th percentile, was associated with an increase in the estimated difference in the probability of GDM (0.07, 95% Credible Interval (CrI): 0.00, 0.14). Among other chemicals, butylparaben, followed by triclosan, were identified as the most influential chemicals in the chemical mixture. Benzophenone-3 and triclosan were identified as important contributors to the positive association when accounting for correlated phenols and parabens, suggesting the importance of addressing chemical mixtures in perinatal environmental exposure studies. Additional prospective investigations will increase the understanding of the relationship between benzophenone-3 exposure and GDM development.	Environ Res. 2022 Nov:214(Pt 2):113897.	10.1016/j.envres.2022.113897	35839910	ヒト	生殖発生	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0710	S. Chen, Y. Tao, P. Wang, D. Li, R. Sher, G. Fu, T. Wei and W. Zhang	2023	Association of urinary bisphenol A with cardiovascular and all-cause mortality: National Health and Nutrition Examination Survey (NHANES) 2003-2016	Bisphenol A (BPA), one of the most widely consumed endocrine disrupting chemicals, has been found to be associated with a variety of diseases, especially cardiovascular diseases. However, few studies have investigated the association of BPA with long-term health outcomes. This study analyzed data from the National Health and Nutrition Examination Survey (NHANES) 2003-2016. The NHANES data were linked to mortality records through December 31, 2019. Urinary BPA was measured using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Survey-weighted Cox proportional hazards models were used to compare the hazard ratios (HRs) of cardiovascular disease (CVD) and all-cause mortality among participants with different urinary BPA concentrations. This study included 9,852 adults and seven hundred and fifty-six deaths were recorded during the follow-up duration was 9.1 years. During this period, 1,550 all-cause deaths occurred, of which 391 were cardiovascular deaths. Compared to the lowest BPA/Cr quartile group, the adjusted HRs of the highest BPA/Cr quartile group were 1.79 (95% CI: 1.33-2.42) for cardiovascular mortality and 1.21 (95% CI: 1.00-1.47) for all-cause mortality. In addition, there was a significant interaction between sex and BPA/Cr in the CVD-related mortality (P for interaction = 0.044). For the female participants, the adjusted HR for cardiovascular mortality in female participants was 2.82 (95% CI: 1.56-5.10), while that in male participants was only 1.34 (95% CI: 0.79-2.26). Higher urinary BPA is associated with an increased risk of cardiovascular mortality among US adults. The effects of BPA on cardiovascular mortality may be more pronounced in women than in men.	Environ Sci Pollut Res Int. 2023 Apr;30(17):51217-51227.	10.1007/s11356-023-25924-7	36807039	ヒト	その他(死亡率)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0711	Q. Chen, Q. Deng, Q. Liao, Y. Liu, Z. Zhang, D. Wu, Y. Lu, J. Qin, Q. Liu, S. Li, Z. Long, X. Xing, Q. Wang, X. Zeng, G. Dong, M. Hou and Y. Xiao	2024	8-OHdG mediates the association of co-exposure to fifty-five typical endocrine-disrupting chemicals with renal function: a cross-section investigation in Southern Chinese adults	Individual typical endocrine-disrupting chemicals (EDCs), including organophosphate triesters (OPEs), parabens, triclosan (TCS), bisphenols, benzophenone (BPs), phthalates (PAEs), and synthetic phenolic antioxidants (SPAs), are associated with renal dysfunction. However, the combined effects and underlying mechanisms of mixed EDC exposure on renal function remain unclear. Two hundred ninety-nine adult participants were recruited from Guangzhou, China, between 2018 and 2019. Fifty-five EDCs and 8-hydroxy-2'-deoxyguanosine (8-OHdG) were measured in urine samples. Renal function was assessed by estimated glomerular filtration rate (eGFR). Multivariate linear regression models and Bayesian kernel machine regression (BKMR) were used to analyze associations of exposure to individual EDCs and their mixtures with renal function. Results: Individual EDCs, including OPEs, parabens, TCS, bisphenols, BPs, PAEs, and SPAs, were widely detected in urine samples. Multivariate linear regression models revealed that exposure to mixtures of individual EDCs was associated with a 3.8% reduction in eGFR. Bisphenol A (BPA) and bisphenol S (BPS) were identified as the primary contributors to this effect. Moreover, 8-OHdG mediated the eGFR decline associated with EDC mixtures, with a mediation proportion of 26.39%. A sex-modified effect was also observed (P = 0.004), indicating that exposure to the mixture of EDCs was linked to more pronounced renal dysfunction in females. Our novel findings suggest that exposure to a typical mixture of EDCs is associated with renal dysfunction in the general adult population of Southern China. Furthermore, 8-OHdG may play a role in the pathogenesis of EDC-induced renal dysfunction.	Environ Sci Pollut Res Int Vol.31 Issue 21 Pages 30779-30792	10.1007/s11356-024-33266-1	38613763	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0712	P. P. Chen, P. Yang, C. Liu, Y. L. Deng, Q. Luo, Y. Miao, M. Zhang, F. P. Cui, J. Y. Zeng, T. Shi, T. T. Lu, D. Chen, L. Q. Wang, C. P. Liu, M. Jiang and Q. Zeng	2022	Urinary concentrations of phenols, oxidative stress biomarkers and thyroid cancer: Exploring associations and mediation effects	Phenols have been shown to influence the cellular proliferation and function of thyroid in experimental models. However, few human studies have investigated the association between phenol exposure and thyroid cancer, and the underlying mechanisms are also poorly understood. We conducted a case-control study by age- and sex-matching 1319 thyroid cancer and 1319 controls to investigate the associations between phenol exposures and the risk of thyroid cancer, and further to explore the mediating role of oxidative stress. We found that elevated urinary triclosan (TCS), bisphenol A (BPA) and bisphenol S (BPS) levels were associated with increased risk of thyroid cancer, with the odds ratios (ORs) and 95% confidence intervals (CIs) of 1.30 (1.04, 1.62), 1.30 (1.04, 1.62) and 1.29 (1.03, 1.61) for the highest versus the lowest quartile (Q4 vs. Q1), respectively. Positive associations were also observed between urinary TCS, BPA and BPS and three oxidative stress biomarkers measured by 8-hydroxy-2'-deoxyguanosine (8-OHdG), 8-iso-prostaglandin F2α (8-iso-PGF2α) and 2-nitro-tyrosine (2-nitro-Tyr) (all P < 0.05). Moreover, 8-iso-PGF2α and 8-OHdG were also associated with thyroid cancer risk (all P < 0.05). Mediation analysis showed that urinary 8-iso-PGF2α mediated 28.99%, 47.66% and 31.38% of the associations between TCS, BPA and BPS exposures and the risk of thyroid cancer, respectively (all P < 0.05). Our results suggest that exposure to TCS, BPA and BPS may be associated with increased risk of thyroid cancer and lipid peroxidation may be an intermediate mechanism. Further studies are warranted to confirm the findings.	J Environ Sci (China). 2022 Oct:120:30-40.	10.1016/j.jes.2022.01.009	35623770	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0713	P. P. Chen, C. Liu, M. Zhang, Y. Miao, F. P. Cui, Y. L. Deng, Q. Luo, J. Y. Zeng, T. Shi, T. T. Lu, W. J. Yin, W. Q. Liu, G. L. Yi, G. Qiu and Q. Zeng	2022	Associations between urinary bisphenol A and its analogues and semen quality: A cross-sectional study among Chinese men from an infertility clinic	Human studies on association between bisphenol A (BPA) exposure and semen quality, mostly based on single urinary measurement, are inconsistent. There is limited human evidence on BPA analogues such as bisphenol F (BPF) and bisphenol S (BPS). We aimed to investigate the associations of urinary BPA, BPF and BPS with semen quality in a cross-sectional study among Chinese men from an infertility clinic. We found that urinary concentrations of BPA, BPF and BPS were associated with semen quality among 968 Chinese men from an infertility clinic. We found that higher BPA exposure was associated with increased odds, while 10% of having below reference semen concentration, low sperm count, progressive motility and total motility (≥75th vs trends < 0.05). Higher BPS exposure was associated with increased 19% of having below reference progressive motility and total motility (both P for trends < 0.05). Use 25% competing extreme quartiles were 1.42 (95% CI: 1.07, 2.02) and 1.67 (95% CI: 1.18, 2.35), respectively. Elevated risks for motility outcomes were also observed when bisphenol mixtures were at a 75th percentile. For semen quality parameters, modest or continuous outcomes, inverse associations with individual BPA and BPS and bisphenol mixtures were still maintained. Our results suggested that higher exposure to individual BPA and BPS and bisphenol mixtures were associated with impaired semen quality.	Environ Int Vol.161 Pages 107132	10.1016/j.envint.2022.107132	35149449	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0714	M. Chen, Y. Yang, K. Barat, Y. Fu, Y. Meng, Y. Zhang, F. Su and M. Zhao	2023	Relationship between bisphenol A and the cardiovascular disease metabolic risk factors in American adults: A population-based study	BACKGROUND: Bisphenol A (BPA) is widely used in personal care and consumer products. However, no study has reported a specific relationship between BPA concentrations and metabolic hazardous elements for cardiovascular diseases (CVDs). Consequently, in this study, we used a 6-years of population-based NHANES data (2011-2016) to analyze the association between BPA concentrations and metabolic risk factors for CVDs. METHODS: A total of 1667 participants were enrolled in our project. The participants in the study were divided into quartiles based on BPA levels (Q1: <0.4 ng/mL; Q2: 0.7-1.3 ng/mL; Q3: 1.4-3.0 ng/mL; Q4: >3.0 ng/mL). This study used multiple linear and multivariate logistic regression models to determine the association among BPA concentrations and CVD metabolic risk factors. RESULTS: When the concentration of BPA was increased by 0.3 ng/mL, the diastolic blood pressure was increased by 0.28 mmHg. In the same time, compared to participants in the first quartile (Q1), those in the fourth quartile (Q4) of BPA concentrations had decreased by 0.13 mg/dL and diastolic blood pressure was increased by 2.08 mmHg. In the same time, compared to participants in the first quartile (Q1), those in the fourth quartile (Q4) of BPA concentrations had 21% higher odds of hypertension, 38% higher odds of obesity, 82.3% higher odds of central obesity, 33% higher odds of elevated HbA1c, 17% higher odds of elevated non-HDL cholesterol, and 60.8% higher odds of diabetes. Compared to the lowest quartile, Q2- CONCLUSIONS: We found that higher concentrations of BPA were associated with a higher metabolic risk for CVDs. Further regulation of BPA may need to be considered for the prevention of CVDs in adults.	Chemosphere Vol.324 Pages 138289	10.1016/j.chemosphere.2023.138289	36870620	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0715	M. Chen, C. Lu, S. Zhang, L. A. Tse, X. Hong, K. Liu, Y. Ding, P. Xiao, Y. Tian and Y. Gao	2023	Bisphenol A substitutes and childhood obesity at 7 years: a cross-sectional study in Shandong, China	Bisphenol A (BPA) substitutes, such as bisphenol S (BPS) and bisphenol AF (BPAF), are increasingly used due to restrictions on BPA usage, a known endocrine disrupting chemical and putative obesogen. However, little is known about the potential health effects of BPA substitutes in children. We investigated the associations of urinary BPA, BPS, and BPAF concentrations with childhood obesity at 7 years. A total of 1,793 participants in the 2019-2020 survey. Urinary BPA and its substitutes including BPS, BPAF, bisphenol B (BPB), bisphenol AP (BPAP), bisphenol Z (BPZ), and bisphenol F (BPF) were determined. Anthropometric measures including height, weight, waist circumference, and body fat percentage were assessed, and overweight/obesity was defined as BMI ≥ score ≥ 85th percentile. Linear and logistic regressions were used to continuous and categorical outcomes, respectively. Restricted cubic spline (RCS) models were used to explore the dose-response relationships between BPA substitutes and childhood obesity. The BPA substitutes were widely detected (> 75%) in children's urine samples. A positive association with obesity measures was consistently observed for urinary BPS and BPAF, i.e., BMI z-score, waist circumference, and overweight/obesity. Further analysis from the WQS regression model demonstrated a positive association between bisphenol mixtures and all measures of obesity, with BPAF contributing the greatest weighting to the observed associations. Sex differences might exist as the positive associations were only significant in boys. No significant association was found between obesity and BPA or other BPA substitutes. Our study adds to mounting evidence that BPA substitutes (BPS and BPAF are linked to obesity in children, especially in boys. Further longitudinal studies with larger sample size with continued biomonitoring these chemicals and their obesogenic effects are necessary.	Environ Sci Pollut Res Int Vol.30 Issue 29 Pages 73174-73184	10.1007/s11356-023-27578-x	37188933	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0716	J. J. Chen, C. F. Wu, S. S. Li, C. C. Chen, Y. H. Wang, C. J. Hsieh, S. L. Wang, M. L. Chan and M. T. Wu	2025	Association of multiple environmental toxicants with markers of early kidney injury in pregnant women: an exposome approach	Pregnant women are regularly exposed to a variety of environmental toxicants in daily life, posing a potential threat of kidney injury before presence of clinical manifestations. As there is a paucity of studies employing an exposome-based approach of kidney health in pregnant women, this study utilizes the above-mentioned strategy to identify the most significant environmental toxicants associated with early kidney injury in pregnant women. A total of 1,000 pregnant women were recruited from 2012 to 2015 in the Taiwan Maternal Cohort Study. Urine samples collected in the first trimester were successfully collected for study. Sixteen biomarkers of exposure to environmental toxicants, including creatinine measurements of melamine, 8 phthalate metabolites, bisphenol A (BPA), methylparaben (MeP), ethylparaben (EP), propylparaben (PP), and butylparaben (BP), and outcome measurements of NGAL for early² 2- of glycosaminoglycan) and albumin to creatinine ratio (ACR). A two-tier strategy of statistical analysis was employed and data was randomly and evenly split to both training (n = 500) and validation (n = 500) sets. Using an elevated quantile score (EQS) regression in the training set and subsequently a multivariate regression in the validation set, we found that NP was the most important chemical to link with early markers of kidney injury, both ACR and NAG. Our findings indicate that short-term exposure to NP is associated with markers of subclinical kidney injury in pregnant women in Taiwan. Further research is warranted to determine whether NP exposure is linked to clinically-relevant kidney outcomes.	Environ Health Vol.24 Issue 1 Pages 47	10.1186/s12940-025-01201-7	40635015	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0717	J. Chen, H. Zhu, Y. Chen, S. Pan, H. Liang, X. Song, Q. Wu, W. Yuan, M. Miao and Z. Wang	2024	The Role of Placental DNA Methylation at Reproduction-Related Genes in Associations between Prenatal Bisphenol Analogues Exposure and the Digit Ratio in Children at Age 4: A Birth Cohort Study	Placental DNA methylation (DNAm) may be a potential mechanism underlying the effects of prenatal bisphenol analogues (BPA) exposure on reproductive health. Based on the Shanghai Minhang Birth Cohort Study (SMBCS), this study investigated associations of placental DNAm on reproduction-related genes with prenatal BPA exposure and children's digit ratio at age 4 using multivariate linear regression models, and mediation analysis was further used to examine the mediating role of placental DNAm in the associations between prenatal BPA exposure and digit ratio among 305 mother−child pairs. Prenatal exposure to bisphenol A (BPA) was associated with increased 2D:4D ratio in boys, 4D:5D (ring finger) and 2D:5D (index finger) in girls, and 2D:4D (index finger) in children with higher BMI at 4 years old. Placental DNAm of Peroxisomal Biogenesis Factor 13 (PEX13) - Coumestrol pathway were found to associations between higher DNAm at the 5 genes and increased digit ratios. Further mediation analysis showed that about 10% of the effect of BPF exposure on increased digit ratios was mediated by placental PEX13 methylation. In conclusion, the altered placental DNAm status might be a mediator underlying the feminizing effect of prenatal BPs exposure.	Environ Sci Technol. 2024 Jul 2;58(26):11320-11330.	10.1021/acs.est.4c03764	38898774	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0718	J. Chen, M. Miao, X. Song, H. Ji, H. Lian, Y. Chen, W. Yuan and Z. Wang	2025	Tracing impacts of prenatal exposure to bisphenol analogues on child anogenital distance development: A birth-cohort study	Prenatal exposure to bisphenol analogues (BPs) is increasingly common and may affect children's reproductive development. However, human evidence is limited and inconsistent. Based on the Shanghai Minhang Birth Cohort Study that enrolled participants in 2010 at Minhang Maternal and Child Health Hospital in Shanghai, China, we measured BPs in maternal urine samples collected during pregnancy and children's anogenital distance (AGD) boys, AGD3(P) (anus-penis), AGD2(S) (anus-scrotum) girls, AGD2(C) (anus-clitoris), AGD3(P) (anus-fourchette) from birth to 48 months as an indicator of reproductive development. A total of 565 mother−child pairs were included. Boys with detected maternal bisphenol S (BPS), bisphenol F (BPF), bisphenol Z (BPZ) and bisphenol AF (BPAF) tended to have increased AGD3(P) at 3 months, while at 12 months, BPS, BPF, and BPAF were associated with a marginal decrease in AGD3(P). In girls, higher levels of BPS, BPF and BPZ were associated with longer AGD at 48 months, and higher risks of rapid AGD growth. Bayesian kernel machine regression (BKMR) models revealed consistent associations of BPs mixtures with AGD in both sexes, with BPF and BPS identified as major contributors. Our study revealed the lasting, sex-specific impacts of prenatal exposure to BPA and its alternatives on children's reproductive development.	J Hazard Mater. 2025 Jun 15:490:137730.	10.1016/j.jhazmat.2025.137730	40022929	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-
統合_0719	H. Chen, W. Zhang, X. Sun, Y. Zhou, J. Li, H. Zhao, W. Xia, S. Xu, Z. Cai and Y. Li	2024	Prenatal exposure to multiple environmental chemicals and birth size	BACKGROUND: Epidemiological studies addressing the combined effects of exposure to chemical mixtures at different stages of pregnancy on birth size are scarce. OBJECTIVE: To evaluate the association between prenatal exposure to multiple chemicals and birth size. METHODS: We measured 12 chemicals in urine samples collected from 1,000 pregnant women in the third trimester. Principal component analysis was used to create clusters of exposed populations and to decrease correlated components of exposed chemicals. In each trimester, for this study, we assessed the associations of these exposure profiles with birth weight, birth length, and ponderal index using multivariable linear regression. RESULTS: We found that compared with women in cluster 1 (lower urinary chemical concentrations), women in cluster 2 (higher urinary concentrations of metals, biomethanols, bisphenols, and some phenols), and women in cluster 3 (higher urinary concentrations of phthalates) were more likely to give birth to children with higher birth weight (0.23 (95% CI: 0.03, 0.43) lb in the 1st trimester; 0.22 (95% CI: 0.02, 0.42) lb in the 2nd trimester; 0.20 (95% CI: 0.00, 0.40) lb in the 3rd trimester). In addition, prenatal exposure to PCD higher benzophenones (ludwig) was associated with reduced birth length across pregnancy. Compared with women in cluster 1, those in cluster 2 had a 0.11 cm (95% CI: 0.01, 0.21) shorter birth length in the 1st trimester, a 0.12 cm (95% CI: 0.02, 0.22) shorter birth length in the 2nd trimester, and a 0.11 cm (95% CI: 0.01, 0.21) shorter birth length in the 3rd trimester. Exposure to multiple chemicals simultaneously, the actual exposure situation of pregnant women, was associated with birth size, indicating that chemical mixtures should be taken more seriously when studying the health effects of pollutants.	J Expo Sci Environ Epidemiol. 2024 Jul;34(4):629-636.	10.1038/s41370-023-00568-4	37422589	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-
統合_0720	C. Y. Chen, C. C. Lee, H. J. Hsu, I. W. Wu, Y. C. Chen, H. C. Pan, Y. T. Chen, C. K. Hsu and C. Y. Sun	2024	Long-term impacts of endocrine-disrupting chemicals exposure on kidney function: A community-based cohort study	This study explores the extended renal effects of endocrine-disrupting chemicals (EDCs) exposure, a linkage already established with adverse health outcomes, notably chronic kidney disease. To delve deeper, the Chiayi County Community Research Center conducted a longitudinal study on 687 participants, monitoring them for three years. Urine samples from individuals were scrutinized between 2017 and 2019, scores, analyzing 11 EDCs and renal function. Findings revealed elevated mono (2-ethylhexyl) phthalate (MEHP) and bisphenol A levels in higher-dose EDC exposure cases. MEHP notably correlated with increased urinary albumin-to-creatinine ratio (UACR), predicting a ~ 16% decline in estimated glomerular filtration rate. Higher MEHP levels also hinted at declining renal function. UACR escalation linked significantly with specific EDCs. MEHP, methylparaben, nonylphenol, and 4-tert-octylphenol. This research underscores enduring renal hazards tied to environmental EDC exposure, particularly MEHP, emphasizing the urgent call for robust preventive public health strategies.	Environ Toxicol Pharmacol. 2024 Mar:106:104379.	10.1016/j.etap.2024.104379	38307303	ヒト	腎	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0721	M. Charlton, E. Seek, Y. Wang, S. S. Mehta-Lee, R. Gordon, M. Liu, L. Trevande and L. G. Kahn	2024	Evaluating associations of bisphenol and phthalate exposure with time to pregnancy and subfecundity in a New York City pregnancy cohort	It is important to understand the impact of consumer chemical exposure and fecundity, a couple's measure of probability of successful conception, given approximately 15% of couples experience infertility. Prior research has generally found null associations between bisphenol and phthalate exposure and fecundability, measured as time to pregnancy (TTP). However, this research has not been paired with current chemical exposures and have often lacked diversity in their study populations. We evaluated the associations between common bisphenol and phthalate chemical exposure groups and TTP as well as subfecundity (TTP>12 months) in the New York City Fertility Study, a preconception cohort study enrolling participants from 2017-2020 who were actively trying to conceive and not using contraception. Using questionnaires, we observed a significant adverse association between total bisphenol exposure and certain phthalate groups on TTP and odds of subfecundity. Furthermore, no evidence exists to examine the joint effects of the chemical groups on the outcomes, we found evidence of a potential interaction between total bisphenol exposure and low molecular weight phthalates on TTP. Future research should continue to update knowledge regarding the complex and potentially interacting effects of these chemicals on reproductive health.	Environ Pollut. 2024 Sep 1:356:124281.	10.1016/j.envpol.2024.124281	38830524	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0722	C. H. Chang, C. T. Lu, T. L. Chen, W. T. Huang, P. C. Tseng, C. W. Chang, Y. C. Chen, Y. L. Yu and Y. N. Chiang	2023	The association of bisphenol A and paraben exposure with sensorineural hearing loss in children	Bisphenol A (BPA) and parabens (PBs) are chemicals that are extensively used in personal care products (PCPs). In early childhood development, hearing is critical to speech and language development, communication, and learning. In vitro and in vivo, BPA/PBs exhibited neurotoxicity through elevated levels of oxidative stress. BPA also has the potential to be an ototoxicant. Therefore, this study aimed to determine the association of BPA/PBs with sensorineural hearing loss in children. We recruited 1,000 children aged 6-12 years from 2016 to 2017 in Taiwan and collected their urine samples and pure-tone audiometry data. Urinary BPA and PB concentrations were analyzed by using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Logistic regression models were developed to determine the BPA/PB exposure with sensorineural hearing loss. Children with sensorineural hearing loss had higher BPA concentrations than normal hearing children (0.22 ng/mL vs. 0.12 ng/mL; p = 0.05). After adjustment for covariates, the risk of hearing loss at middle frequencies reached 2.85-fold (95% CI: 1.12-7.99) when BPA concentrations increased by 1 log10. The risk of slight hearing loss reached 2.33-fold (95% CI: 1.09-5.19) when children had a methyl paraben (MP) concentration. This study clarifies the role of exposure to BPA/PBs in hearing loss in children. Future research needs to be expanded to include cohort designs and nationwide studies to identify causality.	Environ Sci Pollut Res Int Vol.30 Issue 45 Pages 100552-100561	10.1007/s11356-023-29426-4	37635162	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0723	C. H. Chang, C. T. Lu, T. L. Chen, H. C. Chen, W. C. Pan, C. W. Chang, Y. C. Chen and Y. L. Yu	2024	Relationships between bisphenol A and paraben exposure, oxidative stress, and the activity of outer hair cells in the cochlea in children with hearing loss	This study aimed to determine the associations of childhood exposure to bisphenol A (BPA) and parabens (PBs) with oxidative stress and the activity of outer hair cells (OHCs) in the cochlea of children with hearing loss. In 2, A total of 621 children were enrolled from two communities. Urinary concentrations of BPA and four PBs including methyl paraben (MP), ethyl paraben (EP), propyl paraben (PP), and butyl paraben (BP) were quantified by using liquid chromatography-tandem mass spectrometry (LC/MS/MS). Four urinary biomarkers of oxidative stress, 8-hydroxy-2′-deoxyguanosine (8-OHdG), 8-isoprostane (8-iso-PGF2α), 4-hydroxynonenal mercapturic acid (HNE-MA), and 8-nitroguanosine (8-nitro-G) were measured using high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry. Hearing tests were conducted by audiologists in the audiometric test room, and the results were confirmed by an otolaryngologist. The activity of OHCs in the cochlea was measured by distortion product otoacoustic emissions (DPOAEs). The associations of BPA/PBs with oxidative stress and the activity of OHCs in children with hearing loss were investigated by using multivariate logistic regression models. The prevalence of hearing loss was 12.7%. There was a significant negative association between the presence of 8-OHdG (AOR, 0.94; 95% CI: 0.90, 0.98) and the activity of OHCs in the left ear. Significant results were also observed for BPA (24 Hz), MP (1 kHz, 1.5 kHz, 2 kHz), EP (2-8 Hz), and 8-OHdG (2 kHz) in the right ear. This study revealed that exposure to BPA/PBs reduces the activity of OHCs, especially at middle frequencies, in children.	Ecotoxicol Environ Saf Vol.287 Pages 117310	10.1016/j.ecoenv.2024.117310	39536565	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0724	A. Chang, A. Ridpath, J. Carpenter, S. Kieszak, K Sircar, A. Espinosa-Bode, D. Nelson and C. Martin	2020	Urine Bisphenol A and Arsenic Levels in Residents of the Cheyenne River Sioux Tribe, South Dakota, with and without Diabetes	INTRODUCTION: Diabetes disproportionately affects American Indians/Alaskan Natives (AI/AN). Bisphenol A (BPA) and arsenic (As), environmental toxicants which may be associated with diabetes, have not been well-studied in this population. Our objectives were to determine if urinary BPA and As are associated with diabetes among adults in the Cheyenne River Sioux Tribe (CRST), and to compare their urinary levels with the general U.S. population. METHODS: We conducted a cross-sectional study of CRST adults ≥ 18 years old in 2013-2014. Urinary BPA and As were measured using high-performance liquid chromatography and inductively coupled plasma mass spectrometry, respectively. We used spot urine samples which were tested for BPA and normalized to urinary creatinine. Multivariate linear and logistic regression models were used to examine associations between urine arsenic species and BPA and diabetes, and linear regression to assess the association between self-reported exposures and BPA and As levels. We used conditional logistic regression to investigate the association between urine arsenic species and BPA and As levels among participants who were discordant with respect to diabetes status. RESULTS: Of the 1,011 CRST participants, 19% had diabetes. The unadjusted geometric mean urine BPA was identified as 0.91 ng/mL for CRST and 1.65 ng/mL for total As, BPA geometric means of CRST participants were higher than NHANES participants within total As geometric means were lower. BPA and As were not associated with case status. CONCLUSION: The results of this study are consistent with others that have reported an association between diabetes and exposure to BPA or As.	J Med Toxicol. 2020 Jul;16(3):276-283.	10.1007/s13181-019-00748-5	31848906	ヒト	代謝	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_0725	A. Chandrakanth, S. Findus, R. Vasantharekha, W. Santosh and B. Seetharaman	2024	Exploring the Effects of Endocrine-Disrupting Chemicals and miRNA Expression in the Pathogenesis of Endometriosis by Unveiling the Pathways: a Systematic Review	Endometriosis, characterized by endometrial-like mucosal tissue outside the uterine cavity, is a reproductive disorder affecting about 10% of women within the reproductive age. The pathogenesis of endometriosis has been associated with endocrine-disrupting chemicals (EDCs) and microRNA (miRNA) expression. However, the exact mechanisms underlying these associations remain unclear. This systematic review aims to explore the same. The investigation focused on studies delineating the correlation between endocrine disruptors, microRNAs, and endometriosis. To optimize the search scope, keywords and subject headings were used as search terms. Then, two authors rigorously screened studies using criteria, selecting 27 studies from various databases. Notably, dioxins, organochlorine pesticides, and polychlorinated biphenyls exhibited a solid connection to endometriosis, while bisphenol A and phthalates yielded conflicting results. The heightened presence of bisphenol A, polychlorinated biphenyls, and phthalates was linked to altered gene expression, including genes like MIR663, MIR21, and MIR886. MicroRNAs like miRNA-31, miRNA-182, and miRNA-183 emerged as vital factors in the onset of endometriosis and progression. Furthermore, elevated expressions of miR-155 by miR-146a were observed in endometriosis patients. Our review underscores the significance of EDCs and miRNAs in endometriosis. Further research is crucial to unravel the intricate molecular mechanisms and to reduce the disruptive exposure and endometriosis and behavior microRNA dysregulation and endometriosis. However, research lacks the combination of all these factors. The review delves into the effects of endocrine-disruptors and microRNAs on the pathogenesis of endometriosis to improve our understanding of the disorder and in finding therapies.	Reprod Sci Vol.31 Issue 4 Pages 932-941	10.1007/s43032-023-01412-8	38036864	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは除外候補性評価へ進め、当該時点評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0726	A. L. Cathey, V. K. Nguyen, J. A. Colacino, T. J. Woodruff, P. Ravindra and M. T. Aung	2023	Exploratory profiles of phenols, parabens, and per- and poly-fluoroalkyl substances among NHANES study participants in association with previous cancer diagnoses	BACKGROUND: Some hormonally active cancers have low survival rates, but a large proportion of their incidence remains unexplained. Endocrine-disrupting chemicals may affect hormone pathways in the pathology of these cancers. OBJECTIVE: To evaluate cross-sectional associations between per- and polyfluoroalkyl substances (PFAS), phenols, and parabens and self-reported previous cancer diagnoses in the National Health and Nutrition Examination Survey (NHANES). METHODS: We extracted concentrations of 7 PFAS and 12 phenols/parabens and self-reported diagnoses of melanoma and cancers of the thyroid, breast, ovary, uterus, and testes from NHANES cycles between 2005 and 2016. We used multivariable logistic regression models to estimate associations between chemicals and cancers, adjusting for sociodemographic covariates. We conceptualized race as a social construct proxy of structural racial/ethnic inequities and stratified models by race/ethnicity (Non-Hispanic Black, Mexican American, and other Hispanic participants separately compared to White participants). RESULTS: Previous melanoma in women was associated with higher PFOS (OR:1.27; 95% CI: 1.04, 1.55), PFNA (OR:1.73; 95% CI: 1.09, 2.73), PFHxS (OR:1.76; 95% CI: 1.09, 2.84), BPS (OR: 1.61; 95% CI: 1.07, 2.42), and MeP (OR: 1.61; 95% CI: 1.07, 2.42) exposure. Previous thyroid cancer was associated with higher PFOS (OR:1.74; 95% CI: 1.00, 3.04), PFNA (OR:2.26; 95% CI: 1.30, 3.93), PFHxS (OR:2.29; 95% CI: 1.30, 4.04), PFDeA (OR:1.93; 95% CI: 1.02, 3.65), and BPS (OR: 1.74; 95% CI: 1.00, 3.04). Previous uterine cancer was associated with increased PFOA (OR: 1.43; 95% CI: 1.02, 2.02), while higher ethylparaben was inversely associated (OR: 0.51; 95% CI: 0.27, 0.97). Previous PFAS exposure associated with previous ovarian and uterine cancers in White women, while BPS/4-n-BPP was associated with previous breast cancer among non-White women. IMPACT STATEMENT: Biomarkers across a range of exposure categories (phenols, parabens, and per- and poly- fluoroalkyl substances) were cross-sectionally associated with increased odds of previous melanoma diagnoses in women, and increased odds of previous ovarian cancer was associated with several phenols and parabens. Some associations differed by racial group, which is particularly impactful given the established racial disparities in distributions of exposure to these chemicals. This is the first epidemiological study to investigate exposure to phenols in relation to previous cancer diagnoses, and the first NHANES study to explore racial/ethnic disparities in associations between environmental phenol, paraben, and PFAS exposures and historical cancer diagnosis.	J Expo Sci Environ Epidemiol Vol.33 Issue 5 Pages 687-698	10.1038/s41370-023-00601-6	37718377	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0727	J. Castro, R. Arroyo, M. Aparicio, M. Martínez, J. Rovira, S. Arce, S. C. Cunha, S. Casal, J. Oliveira Fernandes, M. Schuhmacher, M. Nadal, J. M. Rodríguez and L. Fernández	2021	Dietary Habits and Relationship with the Presence of Main and Trace Elements, Bisphenol A, Tetrabromobisphenol A, and the Lipid, Microbiological and Immunological Profiles of Breast Milk	Breastfeeding is the best way to feed an infant, although it can also be a source of abiotic contaminants, such as heavy metals or bisphenol A (BPA). The early life exposure to these compounds can lead to various toxic effects in both the short and long term. These substances can reach breast milk through the mother's habits, diet, being one of the main routes of exposure. The aim of the present work was to analyze possible associations between the dietary habits of women and the content of major trace elements, BPA, fatty acids, and lipids, and the microbiological and immunological profiles of human milk. Possible associations between the concentrations of BPA in the milk samples and the concentrations of major trace elements in human milk were also studied. The results obtained showed that the consumption of canned drinks is related to the presence of BPA in human milk. Furthermore, some relationships were found between the amount of major trace elements and the microbiological and immunological profile of the milk samples. Finally, the presence of BPA was associated with changes in the immunological profile of human milk.	Nutrients Vol.13 Issue 12	10.3390/nu13124346	34959899	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0728	J. Castilleno-Rosales, N. E. Alvarado-González, V. Nuño-Samudio, B. Suárez, N. Olea and L. M. Iribarne-Durán	2024	Exposure to bisphenols, parabens, and benzophenones in colostrum breast milk of Panamanian women: A pilot study from the PA-MAMI cohort	BACKGROUND: Breast milk is the optimal source of nutrition for infants, but can also expose them to endocrine-disrupting chemicals (EDCs), among other environmental contaminants. AIM: To determine concentrations of bisphenols (BPs), parabens (PBs), and benzophenones (BP-1, BP-2, BP-3, BP-8, and 4-hydroxy BP in colostrum milk samples from 30 mothers. And two questionnaire was used to collect data on potential influentially variables, and multiple linear and logistic regression analyses were conducted. RESULTS: Twelve chemicals (100 %) were found in the colostrum samples (BP-3, and bisphenol A (BPA) were detected in all 30 samples (11.1 %). The most frequently detected compounds were BPA (90.7 %), BP-8 (63.0 %), MeP (57.7 %), and BPF (51.7 %). The median concentrations was 3.83 ng/mL for BP-3 and 2.37 ng/mL for BPA. No significant associations were found between the presence of BPs, PBs, and BP-3 in colostrum and maternal factors, including age, BMI, education, and parity. However, the consumption of chewy food, yogurt and chocolate, intake of nutritional supplements, and application of some personal care products, CONCLUSION: Bisphenols, parabens, and benzophenones were widely present in colostrum milk samples from Panamanian women. Preventive measures are needed to maximize the benefits of breastfeeding.	Sci Total Environ Vol.954 Pages 176677	10.1016/j.scitotenv.2024.176677	39374701	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0729	C. Cantelmi, M. Muselli, A. Parisi, M. Totaro, D. Tiribelli, G. Corbacchi, M. Giorgio-Barani, M. Maccarrone, S. Nacciarone, S. Francavilla and A. Barbonetti	2022	Association between urinary bisphenol A concentrations and semen quality: A meta-analytic study	Although preclinical research has revealed disrupting effects on male reproductive functions of bisphenol A (BPA), as yet clinical studies have led to inconsistent results. The present meta-analysis aims to establish the existence and the extent of the association between BPA exposure and semen quality. A thorough search of PubMed, Scopus and Web of Science databases was carried out. Only studies reporting data from multivariate analyses were included. Pooled effect sizes (ES) were calculated using a random-effects model. Eight studies were included in the meta-analysis, involving a total sample of 2,386 men. Only the expected association between BPA levels and sperm motility reached statistical significance (pooled ES coefficient = -0.82; 95% CI: -1.53 to -0.11; p = 0.02). Pthe heterogeneity I2 (I2 = 63.9%). Yet, such a significance was lost after data adjustment for publication bias, as well as at the sensitivity analysis, when each of the two studies that contributed most to the overall estimate was excluded. In conclusion, the overall estimates of data produced by clinical studies point to a clinically negligible, if any, association between urinary BPA concentrations and semen quality. Further studies in centers at high risk of occupational exposure are warranted to corroborate the herein revealed weak correlation with a more sperm motility.	Biochem Pharmacol. 2022 Mar;197:114896.	10.1016/j.bcp.2021.114896	34968490	ヒト	精子(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0730	J. E. Carroll, H. E. Gunst, D. March, K. F. Acues, C. Huret, R. Balasubramanian, D. Kontos and S. R. Sturgeon	2025	Urinary Levels of Endocrine-Disrupting Chemicals and Breast Density in Young Women	BACKGROUND: Endocrine disrupting chemicals (EDC) found in many household and personal care products have hormonal properties and effects on the mammary gland. It is unclear whether urinary concentrations of EDCs are associated with higher percent breast density, a major risk factor of breast cancer. METHODS: We conducted a cross-sectional study of 97 college-aged women. We quantified individual levels of bisphenol A (BPA), parabens (MeP, EtP, PrP, BuP), benzophenone-3 (BP3), triclosan (TCS), and dichlorophenols (2,4-DCP, 2,5-DCP) in first morning urine samples. Percent breast density was measured from mammograms that had been retrieved (89% success) per each breast density. Associations between urinary concentrations of individual EDCs and percent breast density were assessed using linear regression. RESULTS: There was no evidence of a statistically significant increase in mean percent breast density in the middle or highest tertile for any EDC measured. There was a suggestion that the mean percent breast density was elevated in individuals in the middle and highest tertile levels of ethyl paraben compared with those in the lowest tertile, with a similar increase in mean percent breast density of 3.6% (1.1, 6.1) and 3.2% (0.7, 5.8) for tertile 2 and 3 (p = 0.24). Similar trends in percent breast density were observed for methylparaben, propylparaben, and butylparaben. CONCLUSIONS: Urinary levels of EDCs were not associated with percent breast density in college-aged women. IMPACT: The estimated effect of EDCs on the breast tissue of young women is unclear and warrants larger studies.	Cancer Epidemiol Biomarkers Prev Vol.34 Issue 8 Pages 1306-1313	10.1158/1055-9965.Epi-24-1694	40377690	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0731	F. Ceriì, S. Tieli, L. Buiarri, D. Ciociaro, V. Della Latta, A. P. Pala, A. Daudoi, A. Raffaelli, F. Pratesi, R. Corte, F. Marenghi, R. Tassinari, E. Fabbiz, G. Toffoi, S. Ciardiani, C. La Rocca, A. Gastaldelli and G. Life Persuaded Project	2022	Exposure to Endocrine Disruptors (DiI(2-Ethylhexyl)phthalate (DEHP) and Bisphenol A (BPA)) in Women from Different Residing Areas in Italy: Data from the LIFE PERSUADED Project	Phthalates and bisphenol A (BPA) are plasticizers used in many industrial products that can act as endocrine disrupters and lead to metabolic diseases. During the LIFE PERSUADED project, we measured the urinary concentrations of BPA and DiI-ethylhexylphthalate (DEHP) metabolites in 980 Italian women representative of the Italian female adult population (living in the north, centre, south of Italy in both rural and urban areas). The whole cohort was exposed to DEHP and BPA with measurable levels above limit of detection in more than 90% and 95% of the samples, respectively. The exposure patterns differed for the two chemicals in relation to the different residing areas. Women living in urban areas showed higher exposure to DEHP than women living in rural areas (median 19.8 vs. 14.1 µg/kg bw/day, $p < 0.001$), whereas, no difference between areas was observed for BPA. The estimated daily intake of BPA was 0.11 µg/kg bw per day, about 30 fold below the current temporary tolerable daily intake of 4 µg/kg bw per day established by the EFSA in 2015. The analysis of cumulative exposure showed a positive correlation between DEHP and BPA. Further, the reduction of exposure to DEHP and BPA, through specific legislative measures, is necessary to limit the harmfulness of these substances.	Int J Mol Sci Vol.23 Issue 24	10.3390/ijms232416012	36555656	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0732	F. Ceri, D. Ciociaro and A. Gastaldelli	2022	Assessment of Exposure to Di-(2-ethylhexyl) Phthalate (DEHP) Metabolites and Bisphenol A (BPA) and Its Importance for the Prevention of Cardiometabolic Diseases	Exposomics analyses have highlighted the importance of biomonitoring of human exposure to pollutants, soon non-persistent, for the prevention of non-communicable diseases such as: obesity, diabetes, non-alcoholic fatty liver disease, atherosclerosis, and cardiovascular diseases. Phthalates and bisphenol A (BPA) are endocrine disrupting chemicals (EDCs) widely used in industry and in a large range of daily life products that humans are exposed to. Exposure to these chemicals is widespread, and it is important to assess the patterns of exposure in diverse subgroups, to implement non-invasive strategies for the prevention of exposure in these subgroups, to prevent non-communicable diseases, such as obesity and diabetes, in childhood and adulthood. This is the goal of the LIFE PERSUADED project that measured the urine concentrations of phthalates, DEHP metabolites, MEHP, MEHHP, MEOHP and MEP. A faster method for the urinary metabolites of BPA was developed. In this paper we describe the method that was set up for the LIFE PERSUADED project and validated during the preliminary test. CONCLUSIONS: Knowing the accurate determination of urinary phthalates and BPA can be achieved running from small sample size (50 mL) using two SID techniques applied in cascade on the same deconjugated matrix.	Metabolites Vol.12 Issue 2	10.3390/metabo12020167	35208241	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0733	L. Caporossi, P. Viganò, E. Paci, S. Capanna, A. Alteri, D. Pigini, G. Tranfo and B. Papaleo	2022	A Case-Control Study on the Effects of Plasticizers Exposure on Male Fertility	Male infertility is a serious concern for public health, and the possible role of exposure to plasticizers such as phthalates and bisphenol A in contributing to the condition is widely debated. We have herein enrolled 135 infertility cases attending an infertility center and 211 controls (fathers of a spontaneously conceived newborn) to investigate this issue. The urinary levels of seven phthalates and BPA were analyzed through HPLC-MS/MS. Semen quality was assessed according to the World Health Organization (WHO) guidelines. Associations between urinary concentrations of chemicals and parameters of semen volume, sperm concentration, sperm motility, and sperm morphology were investigated through multivariate logistic regression models. Results showed significantly higher urinary concentrations for all the phthalates in cases, compared to controls, except for monoethyl phthalate (MEP). In cases, MEP, the major urinary metabolite of diethyl phthalate (DEP), was found 3.6-fold higher than in controls (median values: 54.9 ng/mL vs. 15.1 ng/mL, $p < 0.001$). Similarly, the urinary concentrations of the DEHP metabolites were 1.5–2.0-fold higher in cases than in controls. Sperm motility was found to be significantly lower in cases than in controls ($p < 0.001$), while no significant differences between cases and controls were observed for sperm volume, concentration, and morphology. Multivariate logistic regression models showed that the urinary concentrations of MEP, MEHP, MEHHP, MEOHP, and MEP were associated with a significantly higher risk of male infertility, with adjusted odds ratios (ORs) ranging from 1.5 to 2.0 for the highest vs. the lowest tertile. Urinary BPA was not significantly associated with male infertility. Our results suggest that the exposure to DEHP, but not to BPA, may be a risk factor for male infertility.	Int J Environ Res Public Health. 2022 Dec 23;20(1):235.	10.3390/ijerph20010235	36612557	ヒト	精子	-	-	-	-	-	-	症例対照研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0734	L. Caporossi, P. Viganò, E. Paci, S. Capanna, A. Alteri, G. Campo, D. Pigini, M. De Rosa, G. Tranfo and B. Papaleo	2021	Female Reproductive Health and Exposure to Phthalates and Bisphenol A: A Cross Sectional Study	The ensemble toxicity of some plasticizers (phthalates and bisphenol A) is documented in the literature and may pose a risk to female reproductive health. The aim of this study was to assess exposure to six phthalates. This was achieved by measuring their respective metabolites (mono-ethylphthalate (MEP), mono-n-butylphthalate (MnBP), mono-n-octylphthalate (MnOP), and monobenzylphthalate (MBzP)), as well as the sum of two of the diethyl hexyl phthalate metabolites (∑ DEHP) and bisphenol A (BPA) via female population with infertility problems, and by conducting a correlation analysis between infertility factors, work activities, and lifestyle habits. The study was carried out on a sample of 150 women who attended a fertility center and 150 women who were recruited among the hospital staff and were used as controls. The urine samples of 286 women was given used to quantify xenobiotics and a questionnaire was collected. Phthalate metabolites and bisphenol A were normalized by HPLC/MS/MS. The data showed significantly higher mean values for MEP in women with recurrent pregnancy loss (RPL) (526.5 ± 1439.3 µg/g of creatinine) and idiopathic infertility (290.0 ± 1962 µg/g of creatinine) than in women with other infertility factors (76.9 ± 115.8 µg/g of creatinine). Similarly, for MnBP levels, women with idiopathic infertility (0.90 ± 3.66 µg/g of creatinine) showed significantly higher values than women with the other infertility factors together (0.35 ± 1.08 µg/g of creatinine). Women with tubal factors of infertility, RPL, and endocrine dysfunctions, show higher values of ∑DEHP (p < 0.022). Considering occupations, women working in commerce showed more than twice as much BPA (0.66 ± 1.08 µg/g of creatinine) than women working in other sectors (0.29 ± 0.46 µg/g of creatinine). Women in the healthcare sector showed the lowest values (0.06 ± 0.16 µg/g of creatinine). The presence of significant correlations between some of these phthalates, DEHP metabolites especially in women with RPL and idiopathic infertility, suggests a possible involvement of these compounds as competing factors in reproductive issues. The study of sources of exposure suggested that the working activity intends, as a cofactor in particular, represents a major one for BPA (p < 0.015).	Toxics Vol.9 Issue 11	10.3390/toxics9110299	34822691	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0735	L. Caporossi, A. Alteri, G. Campo, E. Paci, G. Tranfo, S. Capanna, E. Papaleo, D. Pigini, P. Viganò and B. Papaleo	2020	Cross Sectional Study on Exposure to BPA and Phthalates and Semen Parameters in Men Attending a Fertility Center	Among the possible risk factors for male reproduction, exposure to phthalates and alkylphenols is widely documented. This study evaluated the possible association between chemical exposure and the quality of the seminal fluid of 150 subjects in a fertility clinic. The urinary levels of seven phthalate metabolites (monoethylphthalate, MEP; monobenzylphthalate, MBzP; mono-n-butylphthalate, MnBP; mono-(2-ethylhexyl) phthalate, MEHP; mono-(2-ethyl-5-hydroxyhexyl) phthalate, MEHHP; mono-n-octylphthalate, MnOP; mono-(carboxyheptyl)phthalate, MCPP) and bisphenol A (BPA), were analyzed by high-performance liquid chromatography tandem mass spectrometry (HPLC/MS/MS). Sperm quality was assessed according to World Health Organization (WHO) guidelines. Associations between urinary concentrations of chemicals and parameters of semen volume, sperm concentration, sperm motility, and sperm morphology were investigated through multivariate logistic regression models. Results showed significantly higher urinary concentrations for all the phthalates in cases, compared to controls, except for monoethyl phthalate (MEP). In cases, MEP, the major urinary metabolite of diethyl phthalate (DEP), was found 3.6-fold higher than in controls (median values: 54.9 ng/mL vs. 15.1 ng/mL, $p < 0.001$). Similarly, the urinary concentrations of the DEHP metabolites were 1.5–2.0-fold higher in cases than in controls. Sperm motility was found to be significantly lower in cases than in controls ($p < 0.001$), while no significant differences between cases and controls were observed for sperm volume, concentration, and morphology. Multivariate logistic regression models showed that the urinary concentrations of MEP, MEHP, MEHHP, MEOHP, and MEP were associated with a significantly higher risk of male infertility, with adjusted odds ratios (ORs) ranging from 1.5 to 2.0 for the highest vs. the lowest tertile. Urinary BPA was not significantly associated with male infertility. A negative association was found between the use of plastic containers for food storage ($p < 0.027$) and semen volume (2.56 vs. 2.36 mL as average values, mean vs. daily). A significant positive correlation emerged ($p < 0.009$) between the consumption of canned food and the levels of MEP (3.81 vs. 6.51 µg/g creat as average values, daily vs. never) and between the use of perfumes and levels of MEP (MEHP vs. BMA µg/g creat, as average values, daily vs. never). To further statistically significant associations were found, even considering the working activity. Some evidence emerged about the possible link between exposure and seminal fluid quality further searched on prospective studies will allow us to confirm the casually hypothesis.	Int J Environ Res Public Health Vol.17 Issue 2	10.3390/ijerph17020489	31940982	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0736	X. L. Cao, N. K. Xu, K. Y. Zhou and C. M. Xu	2022	Association of urinary bisphenol A concentrations with in vitro fertilisation outcomes: a systematic review and meta-analysis protocol	INTRODUCTION: Bisphenol A (BPA) is a common environmental endocrine disruptor. BPA has been reported to be associated with female infertility, which may not only affect natural pregnancy and natural fertility but also affect the outcomes of in vitro fertilisation (IVF). BPA exposure may help to partly explain the unsatisfactory IVF outcomes, but the relationship between the urinary BPA concentrations and IVF outcomes remains controversial. Therefore, we will perform a meta-analysis to identify and review the relationship between urinary BPA concentrations and IVF outcomes. METHODS AND ANALYSIS: A comprehensive literature search on PubMed, Embase, Web of Science, Cochrane Library and Chinese databases (CNKI, Wanfang and VIP) will be performed from the inception to 1 October 2022. Only English and Chinese articles will be included. Two researchers will independently screen the articles, extract the data and assess the quality of the included studies. Any disagreements will be resolved through discussion with a third researcher. In addition, the references of the included literature will also be traced to supplement our search results and to obtain all relevant literature. The Newcastle-Ottawa Scale will be used to assess the methodological quality of the included studies using a star rating system ranging from 0 to 9 stars. Heterogeneity in estimates from different articles will be quantified, and publication bias will be investigated using funnel plots. Finally, a sensitivity analysis will also be conducted to estimate whether our results could have been markedly affected by a single included study. ETHICS AND DISSEMINATION: Ethical approval is not required for this protocol, as participants are not included. Findings will be disseminated through peer-reviewed publications and conference presentations.	BMJ Open. 2022 Nov 1;12(11):e063930.	10.1136/bmjopen-2022-063930	36319056	ヒト	体外受精(メタアナリシス)	-	-	-	-	-	-	メタアナリシス（プロトコール論文）	1	1	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_0737	G. Cambien, A. Dupuis, M. Belmouaz, M. Bauwens, A. Bacle, S. Ragot, V. Migani, M. Allioux and S. Ayrault-Thevenot	2024	Bisphenol A and chlorinated derivatives of bisphenol A assessment in end stage renal disease patients: Impact of dialysis therapy	Patients with end stage kidney disease treated by dialysis (ESKDD) procure dialysis sessions to remove molecules usually excreted by kidneys. However, dialysis therapy could also contribute to endocrine disruptors (ED) exposure. Bisphenol A (BPA) and chlorinated derivatives of bisphenol A (ClxBPA) are suspected ED. The aim of this study was to compare BPA and ClxBPA exposure between ESKDD patients and healthy volunteers. This is a monocentric, cross-sectional, observational study. We compared BPA and ClxBPA exposure between ESKDD patients, patients with stage 5 chronic kidney disease (CKD5D) on dialysis and healthy volunteers. We also describe the impact of a single dialysis session according to dialysis modalities: Hemodialysis (hemo), online hemodiafiltration therapy (HDF) and materials used with per-post BPA and ClxBPA concentrations. The plasma levels of BPA and four ClxBPA were measured for 60 ESKDD patients, in pre and post dialysis sessions (hemo and HDF) and 15 healthy volunteers. BPA plasma concentrations were 10 times higher for ESKDD patients versus healthy volunteers (median [IQR]: 2.0 [1.0–3.0] ng/mL versus 0.2 [0.1–0.3] ng/mL, $p < 0.001$). ClxBPA plasma concentrations were 30 times higher for CKD5 patients versus healthy volunteers (median [IQR]: 0.3 [0.2–0.4] ng/mL versus 0.01 [0.01–0.02] ng/mL, $p < 0.001$). Post-dialysis BPA concentrations were 50% lower than pre-dialysis ones (1.0 [0.5–1.5] ng/mL versus 2.0 [1.0–3.0] ng/mL, $p < 0.001$). For healthy volunteers, ClxBPA were never detected, or quantified under the CKD5 and ESKDD validation limits. Similar results have been observed on quantified ratio (2 patients: 28.8%) and 2 patients: 57.1%), respectively. Dialysis therapy was ineffective to remove BPA either for HD (-1.96 ± 6.82 ng/mL in pre-dialysis versus 3.4% ± 6.63 ng/mL in post-dialysis) or HDF (1.00 ± 1.63 ng/mL in pre-dialysis versus 1.62 ± 15.98 ng/mL in post-dialysis) regarding per post BPA concentrations ($p > 0.05$). The same result was observed regarding ClxBPA analysis. Presence of polysulfone in dialyzer fibers, unexposed ESKDD patients to BPA in pre-dialysis samples, with 3.0% ± 4.73% for ESKDD patients treated with a polysulfone dialyzer versus 0.78% ± 0.63% ($p = 0.048$) for ESKDD patients treated with another dialyzer membrane. Conclusion: ESKDD patients are highly exposed to BPA and ClxBPA, and dialysis therapy is ineffective to remove BPA and ClxBPA, without a polysulfone dialyzer. This work is to our knowledge the first to investigate the impact of a dialysis session and materials used on BPA and ClxBPA plasma concentrations and to compare these concentrations to those found in CKD5 patients and in healthy volunteers.	Ecotoxicol Environ Saf Vol.270 Pages 115880	10.1016/j.ecoenv.2023.115880	38159342	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0738	L. R. Camara, T. E. Arbuckle, H. Trottier and W. D. Fraser	2019	Associations between Maternal Exposure to Bisphenol A or Triclosan and Gestational Hypertension and Preeclampsia: The MIREC Study	BACKGROUND: Little is known about the association between bisphenol A (BPA) or triclosan (TCS) exposure and hypertension in pregnancy. OBJECTIVE: To investigate potential associations between maternal urinary concentrations of BPA and TCS and gestational hypertension and preeclampsia. METHODS: We conducted a nested case-control study within the Maternal-Infant Research on Environmental Chemicals (MIREC) study, a cohort of pregnant women recruited in the first trimester in South Western Ontario (2008–2011). Urinary BPA and TCS were measured in the first trimester by liquid chromatography–tandem mass spectrometry using a single-void urine sample. Blood pressure was measured during each trimester. Multinomial regression was performed to estimate the adjusted odds ratio (aOR) and 95% confidence intervals (CI) for the associations between these phenols and GH and preeclampsia. RESULTS: BPA and TCS were not associated with GH or preeclampsia. However, in nulliparous women, BPA (0.50–1.30 µg/L) was associated with decreased risk of GH (aOR: 0.43; 95%CI: 0.21–0.88) while creatinine-adjusted BPA was associated with an increased risk of GH (1.50–3.50 µg/L: aOR = 2.58; 95% CI: 1.09–6.13; and > 3.50 µg/L: aOR = 2.76; 95% CI: 1.18–6.45). CONCLUSION: BPA and TCS urinary concentrations were not associated with GH or preeclampsia; however, our results suggest an association between TCS and GH in nulliparous women. Additional studies are required to confirm our results.	Am J Perinatol Vol.36 Issue 11 Pages 1127-1135	10.1055/s-0038-1676489	30551231	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通格性評価（動物）1：該当、0：該当しない　通格性評価（疫学）1：該当、0：該当しない　通格性評価（in vitro）1：該当、0：該当しない　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階評価へ進め、当該性評価段階で排除に基づき排除。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0739	W. Cai, Q. Yan, Y. Deng and Y. Guo	2025	The correlation of bisphenol A exposure on inflammatory cytokines in preschool children	OBJECTIVE: Based on current evidence suggesting that bisphenol A (BPA) may contribute to obesity through the modulation of inflammatory markers, this study aims to investigate the correlation between BPA exposure and cellular inflammatory factors in preschool children. METHODS: A total of 136 preschool children aged 4-6 years were included. Urine and blood samples were collected. BPA exposure was detected by liquid chromatography-tandem mass spectrometry (LC-MS/MS), and cytokines were detected by flow cytometry. Spearman correlation analysis was used to assess the correlation between urinary BPA exposure and cellular inflammatory factors was analyzed using Spearman's correlation and respectively stratified by gender and BMI. RESULTS: The detection rate of BPA in urine samples was 100 %. The median urinary BPA concentration was 5.08 μg/L (QR:3.21-7.82 μg/L), and the creatinine-adjusted BPA concentration was 3.96 μg/g(QR:2.67-5.68 μg/g). BPA level was negatively correlated with IL-10 (r = -0.167, P = 0.049) and positively correlated with IL-6 (r = 0.176, P = 0.040). After stratification by gender, a significant association between BPA exposure and IL-10 was found in females (r = -0.307, P = 0.003), while no associations was found in males. According to BMI classification, BPA exposure had a significant correlation with IL-6 (r = 0.264, P = 0.041) in children with normal weight. Children in the highest BPA exposure group (Q4) showed a decrease in levels of IL-10, and this effect was significantly expressed in girls. In addition, BPA exposure in overweight/obese children was correlated with increased levels of IL-6. However, the mechanism between BPA and inflammatory factors remains to be further explored.	Cytokine Vol.186 Pages 156835	10.1016/j.cyto.2024.156835	39689452	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0740	S. Cai, X. Rao, J. Ye, Y. Ling, S. Mi, H. Chen, C. Fan and Y. Li	2020	Relationship between urinary bisphenol a levels and cardiovascular diseases in the U.S. adult population, 2003-2014	BACKGROUND: Emerging evidence has identified cardiovascular system as a potential target of Bisphenol A (BPA). Although a few studies have revealed the relationship between BPA and the risk of several cardiovascular diseases (CVD) outcome, and CVD risk factors, no published studies have investigated the link between urinary BPA and the risk of stroke. METHODS: Data were derived from the United States National Health and Nutrition Examination Survey (NHANES), with a representative sample ages ≥ 18 years from 2003 to 2014. We performed multivariable logistic regression models to examine associations between quantiles and natural logarithm-transformed urinary BPA concentrations and five specific CVD outcomes and total CVD. RESULTS: In quantile analysis, highest level of urinary BPA was associated with increased prevalence of CVD (OR = 1.37, 95% CI: 1.03, 1.82), CHD (OR = 1.57, 95% CI: 1.08, 2.28), and stroke (OR = 1.70, 95% CI: 1.03, 2.80) after adjusting for confounders. When BPA was transformed BPA concentration was shown to be significantly associated with 39%, 31%, 25%, 29%, 26%, and 15% increased odds ratios of prevalence of congestive heart failure, coronary heart disease (CHD), angina pectoris, MI, stroke and total CVD among total participants, respectively. Similar associations were found in males rather than in females. CONCLUSION: We provided the premier evidence of positive relationship between urinary BPA concentration and stroke in U.S. POPULATION. Urinary BPA levels were also positively correlated with congestive heart failure, CHD, angina pectoris, MI, as well as total CVD. These associations were more evident in males. Well-coordinated and prospective studies are warranted to gain the human effects of BPA on CVD.	Ecotoxicol Environ Saf Vol.192 Pages 110300	10.1016/j.ecoenv.2020.110300	32058166	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0741	M. Büyükeser	2023	Comparison of urine bisphenol A levels in transient tachypnea of the newborn and healthy newborns	BACKGROUND: To investigate the relationship between neonatal urine bisphenol A (BPA) levels and the prevalence and prognosis of transient tachypnea of the newborn (TTN). METHODS: This prospective study was conducted between January and April 2020 in the Neonatal Intensive Care Unit (NICU) of Gaziantep Cengiz Gökçek Maternity and Children Diseases Hospital and Pediatric Hospital. The study group consisted of patients diagnosed with TTN and the control group was made up of healthy neonates housed together with their mothers. Urine samples were collected from the neonates within the first 3 hours postnatally. RESULTS: Urine BPA levels and urine BPA/creatinine ratios were found to be significantly higher in the TTN group than in the control group (p < 0.001 and p = 0.001, respectively). The area under the curve (AUC) was 0.727 (95% confidence interval (CI): 0.647-0.808) with a sensitivity of 76.5% and specificity of 61.5%, and the cut-off value of urine BPA/creatinine to be 3.05 μg/g (95% CI: 2.727-3.333), sensitivity 85.3%, and specificity 96.2%) and the cut-off value for BPA/creatinine was 29.15 μg/g (95% CI: 0.771-1.538), sensitivity 61.5%, and specificity 84.6%) among the 77 TTN patients. CONCLUSIONS: BPA and BPA/creatinine values were higher in the urine of newborns diagnosed with TTN which is a fairly common cause of NICU hospitalization. In samples collected within the first 6 hours after birth, which may be a reflection of intrauterine factors.	Turk J Pediatr. 2023;65(1):35-45.	10.24953/turkjped.2022.304	36866983	ヒト	-	-	-	-	-	-	呼吸器系	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0742	M. Buke Sahin, M. Cagar, A. Yisar, A. Baki Ozyurt, S. B. Eskenti Aksa, I. Iqbal, M. Celik, O. Doyuma, F. Erkekoglu and C. I. Yavuz	2024	Bisphenol derivatives in cord blood and association between thyroid hormones and potential exposure sources	Endocrine-disrupting environmental chemicals are a public health concern, particularly fetal exposure to Bisphenol derivatives. This study aimed to assess fetal exposure to Bisphenol derivatives (BPA, BPF, and BPS) by measuring their levels in umbilical cord blood and investigating their correlations with plastic material used in daily life as well as cord blood TSH and free-L thyroxine (FT4) levels. In the descriptive study, a questionnaire was used to face-to-face interview was administered before birth, and cord blood samples were taken immediately after delivery. The mean levels of BPA, BPF, TSH, and FT4 were measured as 10.69 ± 2.39 ng/mL 3.80 ± 0.46 ng/mL 3.76 ± 0.21 μIU/mL, and 1.19 ± 0.03 ng/dL, respectively. Statistical analysis revealed a positive association between birth weight and cord blood BPA concentration (β = 0.36, p = 0.03). Further research on maternal exposure during the fetal and neonatal period is critical for public health.	Int J Environ Health Res Vol.34 Issue 8 Pages 3036-3045	10.1080/09603123.2023.2286016	38007699	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0743	J. P. Buckley, H. Kim, E. Wong and C. M. Rebholz	2019	Ultra-processed food consumption and exposure to phthalates and bisphenols in the US National Health and Nutrition Examination Survey, 2013-2014	BACKGROUND: Ultra-processed food has low nutritional quality, is associated with development of chronic diseases, and may increase exposure to chemicals used in food packaging and production. OBJECTIVES: To examine associations between consumption of ultra-processed food and urinary concentrations of phthalates and bisphenols. METHODS: We used data from the National Health and Nutrition Examination Survey (NHANES) 2013-2014 participants (≥18 years), our visualized dataset reported in a 2019 dietary recall according to the NOVA food processing classification system and calculated energy intake from ultra-processed food. Urinary concentrations of mono-benzyl (MBzP), mono-(2-ethylhexyl) (MEHP), mono-(carboxynonyl) (MCNP), mono-(carboxyoctyl) (MCOP), and four metabolites of di(2-ethylhexyl) (1)(3)(4) phthalates and bisphenols A, F, and S were measured in spot urine samples. We estimated percentage of energy intake from ultra-processed food and created tertiles of consumption. We used survey-weighted linear regression models to examine associations between consumption and creatinine-adjusted molar/molar (log) urinary concentrations. We examined effect measure modification by age group, race/ethnicity, and poverty-income ratio and assessed associations with minimally processed food. RESULTS: Ultra-processed food consumption was associated with higher urinary concentrations of MBzP, MEHP, MCNP, MCOP, and BPA. Participants in the highest tertile of energy from ultra-processed food was associated with 81% (95% CI: 54%, 113%) higher urinary MCOP concentrations, with a stronger association among children than adolescents or adults. Ultra-processed sandwiches/hamburgers, French fries/other potato products, and ice cream/popsicles were associated with higher concentrations of multiple chemicals. Higher energy from minimally processed food was associated with lower concentrations of MCPP, MCNP, MCOP, and bisphenols A and F. DISCUSSION: Ultra-processed food consumption may increase exposure to currently used phthalates. Additional research is needed to determine whether minimally processed food diets or changes in food production practices can reduce phthalate and bisphenol exposures, and related health effects, particularly among children who are more vulnerable to toxicants and tend to consume more ultra-processed food than adults.	Environ Int Vol.131 Pages 105057	10.1016/j.envint.2019.105057	31398592	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0744	M. L. Brandi, F. Marini, S. Parri, S. Bandinelli, T. Iantomasi, F. Giusti, E. Tatì, G. Gini, F. Nannipieri, S. Battaglia, G. Tripepi, C. G. Egan and L. Ferrucci	2024	Association of vitamin D and bisphenol A levels with cardiovascular risk in an elderly Italian population: results from the InCHIANTI study	Few studies have evaluated the association between circulating levels of 25-hydroxyvitamin D (25(OH)D), 1,25-dihydroxyvitamin D (1,25(OH)2D), and the endocrine disruptor bisphenol A (BPA), with risk of cardiovascular disease (CVD). We investigated the association of 25(OH)D, 1,25(OH)2D, and BPA with CVD risk factors and with the presence of subclinical atherosclerosis. Serum vitamin D metabolites, 1,25(OH)2D, 25(OH)D, and the endocrine-disrupting agent BPA, with an estimated 17-y risk score and the European Society of Cardiology-based 10-year CV risk SCORE2/SCORE2-OP using univariate and multiple regression. In 298 individuals, blood samples were tested for serum values of 25(OH)D, 1,25(OH)2D and urinary BPA levels. One hundred eighty individuals (60.2%) were deficient (< 30 ng/ml) in 25(OH)D. Levels of 25(OH)D were inversely correlated with CV risk score (β = -0.0281 for both as well as SCORE2/SCORE2-OP (β = -0.030) for both) while BPA levels were positively correlated with both CV risk scores (p = 0.0003 for both). In a logistic regression model, male gender (odds ratio (OR) 2.1, 95% CI 1.1-3.8, p = 0.022), obesity (OR 2.8, 95% CI 1.2-6.5, p = 0.016) and BPA tertile 3 (23 ng/ml) (OR 2.9, 95% CI 1.4-6.1, p = 0.006) were significantly associated with the presence of subclinical atherosclerosis. Similar results were found for SCORE2/SCORE2-OP. Finally, 25(OH)D and BPA levels were associated with 1,25(OH)2D (OR 1.01 and 1.39, p = 0.008 respectively and 1.25(OH)2D levels (-21 ng/ml were associated with SCORE2/SCORE2-OP at +25% (95% CI 98, 156%; CI 7-43, p = 0.0001). In this cross-sectional analysis, BPA exposure was associated with significantly reduced levels of vitamin D that in turn were significantly associated with increased CV risk.	Geroscience Vol.46 Issue 6 Pages 6141-6156	10.1007/s11357-024-01193-1	38837025	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0745	M. L. Brandi, S. Bardelli, T. Iantomasi, F. Giusti, E. Tatì, G. Gini, F. Nannipieri, S. Battaglia, R. Giusti, C. G. Egan and L. Ferrucci	2022	Association between vitamin D and bisphenol A levels in an elderly Italian population: results from the InCHIANTI study	OBJECTIVE: This study aimed to evaluate the association between the endocrine-disrupting chemical, bisphenol A (BPA) on circulating levels of 25-hydroxy vitamin D (25(OH)D) and other vitamin D metabolites in an elderly population in Italy. METHODS: This was a retrospective analysis of the InCHIANTI Bisheal-In Italy. The association between vitamin D metabolites, namely 1,25(OH)2D, 25(OH)D, quantified between 1990 and BPA levels were evaluated. Multiple regression models were used to examine the association between predictor variables with 1,25(OH)2D or 25(OH)D levels. RESULTS: Samples from 298 individuals aged 72.8 ± 15.7 years, were evaluated. Of these, 180 (60.2%) were deficient (< 30 ng/ml) in 25(OH)D. Levels of 25(OH)D were inversely correlated with CV risk score (β = -0.0281 for both as well as SCORE2/SCORE2-OP (β = -0.030) for both) while BPA levels were positively correlated with both CV risk scores (p = 0.0003 for both). In a logistic regression model, male gender (odds ratio (OR) 2.1, 95% CI 1.1-3.8, p = 0.022), obesity (OR 2.8, 95% CI 1.2-6.5, p = 0.016) and BPA tertile 3 (23 ng/ml) (OR 2.9, 95% CI 1.4-6.1, p = 0.006) were significantly associated with the presence of subclinical atherosclerosis. Similar results were found for SCORE2/SCORE2-OP. Finally, 25(OH)D and BPA levels were associated with 1,25(OH)2D (OR 1.01 and 1.39, p = 0.008 respectively and 1.25(OH)2D levels (-21 ng/ml were associated with SCORE2/SCORE2-OP at +25% (95% CI 98, 156%; CI 7-43, p = 0.0001). In this cross-sectional analysis, BPA exposure was associated with significantly reduced levels of vitamin D that in turn were significantly associated with increased CV risk.	Endocr Connect Vol.11 Issue 3	10.1530/ec-21-0571	35148277	ヒト	-	-	-	-	-	-	観察研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0746	C. G. Bunsell-g, E. Ergdahl, M. Unenge Hallerbäck, S. Wikström, C. Lindh, J. Ruegg, E. Tanner and C. Gennings	2021	Prenatal exposure to bisphenols and cognitive function in children at 7 years of age in the Swedish SELMA study	BACKGROUND: Experimental evidence demonstrates that exposure to bisphenol A (BPA), and the recently introduced alternatives bisphenol S (BPS) and bisphenol F (BPF) alter normal neurodevelopment. More research is needed to evaluate the associations between exposure to individual BPA alternatives, and neurodevelopmental outcomes in humans. OBJECTIVE: The present study examined the individual associations between prenatal BPA, BPS and BPF exposure and cognitive outcomes in children at age 7 years. METHODS: Women were enrolled in the Swedish Environmental Longitudinal Mother and Child, Asthma and Allergy (SELMA) study, at an antenatal median week 10.5, and their children were examined for cognitive function at 7 years of age (N = 800). Maternal urine BPA, BPS, and BPF concentrations were measured in samples collected from children's cognitive function at the age of 7 years was measured using the Wechsler Intelligence Scale for Children-IV (WISC-IV). RESULTS: At three bisphenols were detected in over 90% of the women, where BPA had the highest detection frequency (98%). Maternal urine BPA, BPS, and BPF concentrations were not correlated with each other (Spearman's ρ ≤ 0.2). Higher maternal urine BPA, but not BPS or BPF, was associated with a decrease in all four sub-scales assessing verbal comprehension, perceptual reasoning, working memory and processing speed. This association corresponded to a 2.8 point decrease in the full scale IQ score for an interquartile range (IQR) change in prenatal BPF exposure (IQR: -0.094-0.960 ng/mL). In sex-stratified analyses, significant associations with full scale IQ were found to boys (β = -3.86, 95%CI: -6.56, -1.16), while the associations for girls did not reach significance (β = -1.36, 95%CI: -3.97, 0.22). No significant associations between BPA nor BPS and cognitive were found. DISCUSSION: Prenatal exposure to BPF was significantly associated with childhood cognitive function at 7 years. Since BPF is replacing BPA in numerous consumer products globally, this finding urgently call for further studies.	Environ Int. 2021 May;150:106433.	10.1016/j.envint.2021.106433	33637302	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0747	M. M. Borghese, R. Huang, S. MacPherson, E. Gaudreau, S. Gagné, J. Ashby-Mantin, M. Fisher, L. Bouj, M. F. Bouchard and T. E. Arbuckle	2023	A descriptive analysis of first trimester urinary concentrations of 14 bisphenol analogues in the MIREC Canadian pregnancy cohort	BACKGROUND: Concern over the health effects of BPA, particularly for the developing fetus, has led to an increasing use of bisphenol analogues in industrial and consumer products, which may be as hormonally active as BPA. Biomonitoring data for many bisphenol analogues, especially in pregnant populations, are limited. METHODS: We measured concentrations of 13 bisphenol analogues in 1(st) trimester urine samples (n = 1891) from participants in the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort. Bisphenol concentrations were compared between participant characteristics using Spearman correlations, Kruskal-Wallis tests, and multivariable linear regression models. We also examined associations between bisphenol concentrations and maternal occupational and healthcare exposures. RESULTS: Bisphenol A (BPA) was detected in 89% of participants with a specific gravity-standardized geometric mean concentration of 0.88 μg/L. Bisphenol AP (AP), 4,4'-(1-phenylethylidene) bisphenol (BPAP), and bisphenol AF (BPAF) were detected in <5% of participants. Bisphenol F (BPF) and bisphenol S (BPS) were detected in >50% of participants. Specific gravity-standardized geometric mean concentrations of these 5 compounds ranged from 0.053 to 0.168 μg/L. Urine bisphenol analogue concentrations were detected in <5% of participants. Concentrations of BPF (0.134 ng/mL) and BPS were higher in younger women and those with higher pre-pregnancy BMI, lower household income, lower education, and among smokers. We found a similar pattern of differences in BPF by age, education, and smoking status, but not BMI. Bisphenol concentrations were not related to maternal occupational exposures. Bisphenol S was higher among participants who reported working in healthcare, education, or an office setting. Canned food consumption was not related to bisphenol analogue concentrations. CONCLUSION: BP (A, S)(AP, BPC, BPF, and BPS) were frequently detected in 1(st) trimester urine samples in this large pan-Canadian pregnancy cohort. This suggests widespread exposure to these analogues around 2008-2011 and warrants further investigation into associations with health outcomes.	Int J Hyg Environ Health. 2023 Aug;253:114225.	10.1016/j.ijheh.2023.114225	37542835	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0748	R. Boro, V. Ballicaño, R. Tanzirai, G. Soulikidi, I. Mamela, M. Bugliari, E. Migliore and P. Piccioni	2019	Bisphenol A, Tobacco Smoke, and Age as Predictors of Oxidative Stress in Children and Adolescents	OBJECTIVES: The purpose of this study was to investigate bisphenol A (BPA) and its role in the induction of oxidative stress, and confirm the same for tobacco smoke. METHODS: A total of 135 young, healthy students (7-19 years old) were recruited in Chisenso, Italy. A spot of urine of each subject was analyzed to quantify BPA, cotinine, and 15(S)-isoprostane (8-iso-PGF2α). RESULTS: BPA showed a slight increase of concentration proportional with age, whereas cotinine and 8-iso-PGF2α showed a decrease. Cotinine and 8-iso-PGF2α showed a similar shape. The lower trend was observed for 15(S)-isoprostane and cotinine. The result of Spearman's linear correlation test between these 3 levels and of the effect of BPA on 8-iso-PGF2α (multivariate and log-log OLS) is a U-shape. Therefore, BPA—isoprostane relations are represented inaccurately; even their threshold for each one by set of BPA. An increase of oxidative stress due to BPA was observed, but only from 6 ng/mg of CREA up. Passive tobacco smoke is also able to induce an increase in oxidative stress. CONCLUSION: Preventive regime BPA and passive tobacco smoke represents an important tool for promoting the highest health standard.	Int J Environ Res Public Health Vol.16 Issue 11	10.3390/ijerph16112025	31174388	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0749	P. A. Bommarito, S. M. Blaauwendraad, D. R. Stevens, M. A. van den Dries, S. Spaan, A. Pronk, H. Tiemeier, R. Gaillard, L. Trasande, V. W. V. Jaddoe and K. K. Ferguson	2024	Prenatal Exposure to Nonpersistent Chemicals and Fetal-to-childhood Growth Trajectories	INTRODUCTION: Prenatal exposure to nonpersistent chemicals, including organophosphate pesticides, phthalates, and bisphenols, is associated with altered fetal and childhood growth. Few studies have examined these associations using longitudinal growth trajectories or considering exposure to chemical mixtures. METHODS: Among 777 participants from the Generation R Study, we used growth models to identify weight and body mass index trajectories using weight and height measures collected from the prenatal period to age 10. We measured exposure biomarkers for organophosphate pesticides, phthalates, and bisphenols, in maternal urine at three timepoints during pregnancy. Multinomial logistic regression was used to estimate associations between averaged exposure biomarker concentrations during pregnancy and growth trajectory membership. We used quantile g-computation to estimate joint associations with growth trajectories. RESULTS: 76 (Median) and DAP-1 (-0.90% CI: -1.32, -0.50) and bisphenol A (DP-1 (-0.90% CI: -1.3, -0.22) were associated with higher odds of a growth trajectory characterized by lower prenatal and higher childhood weight, while exposure to organophosphate pesticides was negatively associated with a trajectory of average prenatal and lower childhood weight. This study is consistent with the hypothesis that nonpersistent chemical exposures disrupt growth trajectories from the prenatal period through childhood.	Epidemiology. 2024 Nov 1;35(6):874-884.	10.1097/ede.0000000000001772	39042458	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0750	M. S. Bloom, S. Upadhyaya, A. W. Kongsu, J. R. Kuiper, J. P. Buckley, J. Aschner, D. Barr, E. S. Barrett, D. H. Bennett, D. Dabelea, A. L. Dunlop, A. Fichet, M. Kerkez, D. Liang, J. Meeker, R. Miller, T. G. O'Connor, M. E. Romano, S. Sathyanarayana, A. P. Starling, A. Stroustrup and D. J. Watkins	2025	Racial and ethnic differences in prenatal exposure to environmental phenols and parabens in the ECHO Cohort	BACKGROUND: Research suggests racial/ethnic disparities in prenatal exposure to endocrine disrupting environmental phenols (EPs) in United populations. However, no studies have investigated racial/ethnic disparities in prenatal EP exposure across the U.S. OBJECTIVES: To estimate demographic differences in prenatal urinary EPs among participants in the Environmental Influences on Child Health Outcomes (ECHO) Cohort. METHODS: An analysis of 6588 pregnant ECHO participants was performed, with 7868 specimens collected from 1999-2020. Racial/ethnic identity was self-reported. Urinary levels of 11 chemicals (2,4-DCP1, 2,5-dichlorophenol (2,5-DCP), benzophenone-3 (BP-3), bisphenols A (BPA), F (BPF), and S (BPS), and methyl- (MeP), ethyl- (EtP), propyl- (PrP), and butyl- (BuP) parabens were measured in one or more visits during pregnancy. Ethnic/racial means were adjusted for age, pre-pregnancy body mass index, educational level, gestational age and season at urine collection, and ECHO cohort. RESULTS: Participants were classified as Asian (5%), Black (20%), Hispanic (29%), White (41%), and Multiracial (5%). Asian participants had higher urinary levels of BPA (+0.19 log10 ng/mL), BPF (+0.27 log10 ng/mL), and 2,5-DCP (+0.17 log10 ng/mL) than White participants. Black participants had higher urinary levels of MeP (+0.41 log10 ng/mL), PrP (+0.34 log10 ng/mL), and BuP (+0.29 log10 ng/mL) than White participants. Hispanic participants had higher urinary levels of MeP (+0.24 log10 ng/mL), PrP (+0.24 log10 ng/mL), and BuP (+0.21 log10 ng/mL) than White participants. Multiracial participants had higher urinary levels of MeP (+0.21 log10 ng/mL), PrP (+0.21 log10 ng/mL), and BuP (+0.19 log10 ng/mL) than White participants. EtP was higher among Black (95% CI: 1.7-3.7) and non-Hispanic Other (95% CI: 1.1-3.1) participants. EPs were higher among Asian (95% CI: 1.3-2.1), Black (95% CI: 1.7-2.3), and non-Hispanic Other (95% CI: 1.1-2.1) participants. BPA was higher among Asian (95% CI: 1.3-2.1), Black (95% CI: 1.7-2.3), and non-Hispanic Other (95% CI: 1.1-2.1) participants. BPS was higher among Asian (95% CI: 1.3-2.1) participants. Urinary BuPA, BPA, BPF, and BPS were similar across groups. IMPACT STATEMENT: This multiethnic, observational cohort study investigated whether there are racial and ethnic differences in prenatal exposure to endocrine disrupting environmental phenols and parabens. Among 6588 participants from multiple U.S. cohorts, who provided urine specimens during pregnancy, those who self-reported a racial and ethnic identity other than non-Hispanic White had higher urinary concentrations of 2,5-dichlorophenol, 2,5-dichlorophenol, methyl paraben, ethyl paraben, and propyl paraben and lower urinary concentrations of benzophenone-3 than those reporting as non-Hispanic White. These data show differences in prenatal concentrations of endocrine disrupting environmental phenols and parabens by racial and ethnic identity.	J Expo Sci Environ Epidemiol	10.1038/s41370-025-00750-w	39955434	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0751	S. M. Blaauwendraad, E. Voerman, L. Trasande, K. Kannan, S. Santos, G. J. G. Ruijter, C. M. Sol, L. Manchini, E. Shoaby, B. Kvalebo, V. W. V. Jaddoe and R. Gaillard	2021	Associations of maternal bisphenol urine concentrations during pregnancy with neonatal metabolomic profiles	BACKGROUND: Fetal exposure to bisphenols is associated with altered fetal growth, adverse birth outcomes and childhood cardio-metabolic risk factors. Metabolomics may serve as a tool to identify the mechanisms underlying these associations. We examined the associations of maternal bisphenol urinary concentrations, in pregnancy with neonatal metabolite profiles from cord blood. METHODS: In a population-based prospective cohort study, we measured bisphenol A, F and S concentrations in urine samples collected in mid-pregnancy (median 20.4 weeks of gestation). We measured 158 metabolites in cord blood serum samples, including acylcarnitines, amino acids, non-esterified fatty acids (NEFA), phosphatidylcholines (PC) and sphingomyelins in cord blood. RESULTS: The associations of maternal total bisphenol concentrations with neonatal metabolite profiles were present. Higher maternal average BPA concentrations were associated with higher neonatal mono-unsaturated alkyl/acyl-phosphatidylcholine concentrations, whereas higher maternal average BPS was associated with lower neonatal overall and saturated alkyl/acyl-phosphatidylcholine (p-values < 0.05). Trimester-specific analyses showed that higher maternal BPA, BPF and BPS were associated with alterations in neonatal NEFA, diacyl-phosphatidylcholine, acyl-alkyl phosphatidylcholine, alkyl/acyl-phosphatidylcholine, sphingomyelins and acyl-carnitines, with the strongest effects for third trimester maternal bisphenol and neonatal diacyl-phosphatidylcholine concentrations (p-values < 0.05). Associations were mostly present in girls and were not explained by maternal diet, lifestyle or socio-demographic factors. CONCLUSIONS: Higher maternal bisphenol A, F and S concentrations, in pregnancy are associated with alterations in neonatal metabolite profile, mainly in NEFA, PL and carnitines concentrations. These findings provide novel insight into potential mechanisms underlying associations of maternal bisphenol exposure during pregnancy with adverse offspring outcomes, but need to be replicated among larger, diverse populations.	Metabolomics. 2021 Sep 13;17(9):84.	10.1007/s11306-021-01836-w	34518915	ヒト	代謝(脂質代謝)	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0752	S. M. Blaauwendraad, S. Strahm, C. Duh-Leong, M. -J.u, K. Kanner, L. G. Kahn, V. W. V. Jaddoe, A. Ghassabian and L. Trasande	2024	Fetal bisphenol and phthalate exposure and early childhood growth in a New York City birth cohort	BACKGROUND: Exposure to endocrine-disrupting chemicals such as bisphenols and phthalates during pregnancy may disrupt fetal developmental programming and influence early life growth. We hypothesized that prenatal bisphenol and phthalate exposure was associated with alterations in adiposity through 5 years. This association might change over time. METHODS: Among 1091 mother-child pairs in a New York City birth cohort study, we measured maternal urinary concentrations of bisphenols and phthalates at three time points in pregnancy and child weight, height, and triceps and subscapular skinfold thickness at ages 1, 2, 3, and 5 years. We used multivariable linear regression models to examine associations of prenatal exposure to individual chemicals and a chemical mixture with child growth outcomes. RESULTS: We observed associations of higher maternal urinary second trimester total bisphenol and bisphenol A concentrations in pregnancy and overall child weight between birth and 5 years only (Beta 0.02 SD (95% confidence interval: 0.00, 0.04) and 0.07 (0.02, 0.12) standard deviation score (SDS) change in weight-for-age(-sex) (kg increase in exposure). We reported an interaction of the exposure with time, and analysis showed associations of higher prenatal bisphenol exposure with greater weight-for-age(-sex) SDS at 1 year (0.07 (0.01, 0.13) SDS) and 2 years (0.06 (0.00, 0.12) SDS) but not at 3 or 5 years. Associations of higher prenatal bisphenol S, bisphenol F, phthalate, mono-(2-carboxymethyl) phthalate, and mono-(2-ethyl-5-carboxypentyl) phthalate, mono-(2-ethyl-5-hydroxyhexyl) phthalate, and mono-(2-ethyl-5-oxohexyl) phthalate concentrations were associated with higher child BMI at 5 years (0.20 (0.05, 0.35), 0.28 (0.06, 0.50), 0.31 (0.07, 0.54), 0.25 (0.01, 0.49), 0.26 (0.03, 0.50), 0.26 (0.03, 0.50), 0.25 (0.02, 0.48), 0.26 (0.03, 0.50), 0.26 (0.03, 0.50) SDS). For a doubled thickness, we observed no associations. DISCUSSION: This study contributes to the evidence suggesting associations of prenatal exposure to bisphenols, and high molecular-weight phthalates, on childhood weight and BMI.	Environ Int. 2024 May;187:108726.	10.1016/j.envint.2024.108726	38733764	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0753	S. M. Blaauwendraad, R. Gaillard, S. Santos, C. M. Sol, K. Kannan, L. Trasande and V. W. V. Jaddoe	2022	Maternal Phthalate and Bisphenol Urine Concentrations during Pregnancy and Early Markers of Arterial Health in Children	BACKGROUND: Fetal exposure to endocrine-disrupting chemicals such as phthalates and bisphenols might lead to fetal cardiovascular developmental adaptations and predispose individuals to cardiovascular disease in later life. OBJECTIVE: We examined the associations of maternal urinary bisphenol and phthalate concentrations in pregnancy with offspring carotid intima-media thickness and distensibility at the age of 10 y. METHODS: We measured urinary bisphenol A (BPA) and phthalate metabolites in 2 trimesters of pregnancy in 1,550 mothers participating in a population-based birth cohort. Carotid intima-media thickness and distensibility in the children at age 10 y using ultrasound. RESULTS: Maternal urinary bisphenol A concentrations were not associated with child carotid intima-media thickness at age 10 y. Higher maternal average concentrations of total bisphenol, especially bisphenol S, were associated with a lower carotid intima-media thickness [difference: -0.15 standard deviation score (SD) SD; 95% confidence interval (CI): -0.31, -0.00 and -0.23 (95% CI: -0.37, -0.08) per interquartile range (IQR) increase in maternal urinary total bisphenol and bisphenol S concentrations]. Trimester-specific analysis showed that higher maternal third trimester total bisphenol and bisphenol S concentrations were associated with lower child carotid intima-media thickness [difference: -0.23 (95% CI: -0.37, -0.09) and -0.19 (95% CI: -0.33, -0.04) SD per IQR increase in exposure, respectively]. Higher maternal urinary bisphenol S concentrations were associated with lower child carotid distensibility [difference: -0.19 (95% CI: -0.33, -0.04) SD per IQR increase in exposure]. Higher maternal urinary bisphenol concentrations were associated with smaller childhood carotid intima-media thickness. Further studies are needed to replicate this association and to identify potential underlying mechanisms. https://doi.org/10.1289/EHP12093.	Environ Health Perspect. 2022 Apr;130(4):47007.	10.1289/ehp10293	35471947	ヒト	心血管	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0754	S. M. Blaauwendraad, R. H. M. Dykgraaf, R. Gaillard, M. Liu, I. S. Lasen, V. W. V. Jaddoe and L. Trasande	2024	Associations of bisphenol and phthalate exposure and anti-Müllerian hormone levels in women of reproductive age	BACKGROUND: In women, exposure to endocrine-disrupting chemicals might accelerate the depletion of the ovarian reserve and might be associated with an accelerated reproductive aging and fertility. We examined the longitudinal associations of exposure to bisphenols and phthalates, with anti-Müllerian hormone concentrations. METHODS: Pregnant women of 18 years or older that resided in Rotterdam between 2002 and 2006 were eligible for participation in this longitudinal prospective cohort study. We measured urinary bisphenol and phthalate concentrations at three time points: in pregnancy among 1,620 women, of whom 1,321 women had serum anti-Müllerian hormone (AMH) measurements 6 and/or 9 years postpartum. Serum anti-Müllerian hormone regression models to assess the association of urinary bisphenol and phthalate concentrations with AMH after 6 and/or 9 years, and linear mixed effect model to assess the association with AMH over time. Models were adjusted for sociodemographic and lifestyle factors. FINDINGS: In our multivariable linear regression models we observed associations of higher urinary bisphenol A (BPA) concentrations with lower AMH levels after 6 years (-0.07 [95% confidence interval (CI): -0.13, -0.01] ng/mL per interquartile range increase in exposure) and after 9 years (-0.07 [95% CI: -0.13, -0.01] ng/mL per interquartile range increase in exposure). However, these associations did not remain after adjustment for multiple testing. No significant associations of bisphenol S with AMH at present in our models. In our linear mixed effect models, higher mono (2-ethyl-5-hydroxyhexyl) phthalate (mEHHP), mEHHP and mEHP were associated with lower overall AMH levels [difference: -0.07 (95% CI: -0.13, -0.01), -0.09 (-0.16, -0.02), -0.08 (95% CI: -0.14, -0.02), and -0.06 (-0.11, -0.01) μg/L per doubling in mEHP, mEHHP, and mEHP respectively] (all False Discovery Rate-adjusted p-values < 0.05). INTERPRETATION: We identify decreases in indices of ovarian reserve in relationship to prenatal phthalate exposures. Studies are needed replicating our results among large multi-ethnic non-pregnant populations and assessing transgenerational effects of exposure on ovarian reserve. FUNDING: This work was supported by the Dutch Organization for Health Research and Development, the European Union's Seventh Framework Program, the European Research Council, the Netherlands Organization for Scientific Research, the Sophia Children's Hospital Foundation, the Dutch Diabetes Foundation, the European Union's Horizon 2020 Research and Innovation Program, the National Institutes of Health, Erick Lasko Bolster, and the Royal Netherlands Academy of Arts and Sciences.	EClinicalMedicine. 2024 Jul 17;74:102734.	10.1016/j.eclinm.2024.102734	39114272	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0755	F. M. Bigambo, M. Zhang, J. Zhang, X. Yang, Q. Yu, D. Wu, X. Wang and Y. Xia	2022	Exposure to a mixture of personal care product and plasticizing chemicals in relation to reproductive hormones and menarche timing among 12-19 years old girls in NHANES 2013-2016	The effects of co-exposure to personal care product and plasticizing chemicals (PCPPCs) on reproductive hormones and menarche timing has rarely been studied. We used Bayesian kernel machine regression (BKMR), adaptive best subset shrinkage and selection operator (adaptive LASSO), and generalized linear model (GLM) to explore the mixture effects of 16 PCPPCs, on reproductive hormones and early menarche among 397 girls aged 12-19 years in the National Health and Nutrition Examination Survey (NHANES) 2013-2016. In the BKMR and adaptive LASSO models, we examined the mixture effects of PCPPCs, two environmental phenols (bisphenol A (BPA) and triclosan (TCS)), four phthalate metabolites (mono-ethyl phthalate (MEP), mono-benzyl phthalate (MBzP), mono-isobutyl phthalate (MiBP), mono-(carboxyoctyl) phthalate (MCOP), and Mono-benzyl phthalate (MBzP)) were positively associated with estradiol (E2), and the mixture of PCPPCs was positively associated with testosterone (T). Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP) were inversely associated with SHBG. In GLM, testosterone (T) (MCP and MECPP) were negatively associated with TT, whereas 2,2-dichlorophenol (2,2-DCP) revealed a positive association with early menarche onset. In conclusion, PCPPCs in the mixture and individually are associated with reproductive hormones and early menarche onset in girls.	Food Chem Toxicol Vol.170 Pages 113463	10.1016/j.fct.2022.113463	36220617	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0756	F. M. Bigambo, D. Wang, J. Sun, X. Ding, X. Li, B. Gao, D. Wu, W. Gu, M. Zhang and X. Wang	2023	Association between Urinary BPA Substitutes and Precocious Puberty among Girls: A Single-Exposure and Mixed Exposure Approach from a Chinese Case-Control Study	There is an argument that BPA substitutes may have the same or more deleterious health effects as BPA due to their structural similarity. This study explored the association between urinary BPA substitutes and precocious puberty among girls by including 120 girls with precocious puberty (cases) aged 6-10 years and 120 girls without (controls) from Shenzhen Children's Hospital Department of child endocrine genetic metabolism, China, between 2021 and 165 healthy girls (controls) recruited from a primary school. Logistic regression was used to evaluate the effect of single exposures, and Bayesian kernel machine regression (BKMR) and quantile-based g-computation models were used to assess the effect of mixed exposures. The BKMR and quantile-based g-computation models revealed a positive association between the mixture of BPA substitutes and precocious puberty. The odds ratio (OR) = 1.75 95% confidence interval (CI): 1.16, 2.76, p = 0.010, OR = 1.46, CI: 1.06, 2.06, p = 0.020, and OR = 1.67, CI: 1.18, 2.36, p = 0.007, respectively. The BKMR and quantile-based g-computation models revealed consistent associations for single-exposure and their non-insufficient evidence for the associations of the mixed exposure of bisphenols with precocious puberty. In conclusion, BPA substitutes such as BPS, TBBPA, and BPF, may be associated with an increased risk of precocious puberty in girls.	Toxics. 2023 Nov 6;11(11):905.	10.3390/toxics11110905	37995557	ヒト	生殖(思春期発達)	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0757	F. M. Bigambo, J. Sun, C. Zhu, S. Zhang, Y. Xu, D. Wu, Y. Xia and X. Wang	2024	Gender- and Obesity-Specific Association of Co-Exposure to Personal Care Product and Plasticizing Chemicals and Short Sleep Duration among Adults: Evidence from the National Health and Nutrition Examination Survey 2011-2016	There is limited evidence about the gender- and obesity-specific effects of personal care product and plasticizing chemicals (PCPPCs) on short sleep duration in adults. We evaluated the gender- and obesity-specific association of co-exposure to PCPPCs and short sleep duration among adults aged 20-60 years using the National Health and Nutrition Examination Survey (NHANES) 2011-2016, a secondary data source from the United States. Seventeen PCPPCs, including five phenols, two parabens, and ten phthalates, were detected, and sleep duration was assessed among 3132 adults. Logistic regression, weighted quantile sum (WQS) regression and Bayesian kernel machine regression (BKMR) were employed. We found that bisphenol A (BPA), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), and mono (3-carboxypropyl) phthalate (MCPP) were consistently positively associated with short sleep duration in both females and males, regardless of obesity status, except for BPA with general obesity. In particular, mono-benzyl phthalate (MBzP) revealed a positive association in females, while mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) revealed a positive association in males. Mixture models revealed consistent positive associations in females and males. Our study highlights that PCPPCs are independently associated with an increasing risk of short sleep duration in adults both individually and as a mixture; however, gender- and obesity-specific differences may have little effect on certain individual PCPPCs on short sleep duration.	Toxics Vol.12 Issue 7	10.3390/toxics12070503	39058155	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0758	F. M. Bigambo, H. Sun, W. Yan, D. Wu, Y. Xia, X. Wang and X. Wang	2020	Association between phenols exposure and earlier puberty in children: A systematic review and meta-analysis	OBJECTIVE: To identify the association between phenolic chemicals and the risk of earlier puberty based on the available evidence by systematic review and meta-analysis. METHODS: Databases PubMed, Web of Science, and Cochrane Library were searched and retrieved appropriate journal articles, on the association between phenols exposure and earlier puberty in children published before February 10, 2020. Data software Review Manager 5.3 and Stata/SE 15.1 were used for analysis. RESULTS: Eight articles were included in the meta-analysis, which involved 3,884 children. Bisphenol A has shown the association between 2, 5- dichlorophenol exposure, and earlier puberty in children with either sex (RR: 1.12, 95% CI: 1.06, 1.18). Exposed to children with other phenols such as bisphenol S, Triclosan, Benzophenone-3 were not statistically significant associated with the risk of earlier puberty in children with the overall pooled outcomes of RR of 1.09 (95%CI: 0.88, 1.35), 1.15 (95% CI: 0.98, 1.35), and 1.10 (95% CI: 0.88, 1.38) respectively. CONCLUSION: Our results portray that phenols particularly 2, 5- dichlorophenol exposure might be associated with the risk of earlier puberty in children. Also, caution should be taken to other type of phenolic chemicals since in subgroup analysis some individual studies have shown a positive relationship between bisphenol A, Triclosan and Benzophenone-3 exposures, and the risk of earlier puberty in children. Future cohort studies should be conducted with more sample sizes to determine the relationship between 2, 5- dichlorophenol, and the risk of earlier puberty in children of all genders.	Environ Res. 2020 Nov;190:110056.	10.1016/j.envres.2020.110056	32805251	ヒト	生殖発生(メタアナリシス)	-	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0759	F. M. Bigambo, Z. Chen, W. Yang, Q. Huang and X. Wang	2024	The effect of bisphenols on sex and thyroid hormone concentrations in cord blood among newborns	This study aims to investigate the associations of bisphenols, with sex and thyroid hormones in cord blood among newborns. Four bisphenols, three hormones related to gonadal function, and four parameters related to thyroid function were measured in umbilical cord blood in 339 mother-newborn pairs. Multivariable linear regression, quantile-based g-computation (QGC), and Bayesian kernel machine regression were used. In the multivariable linear regression, bisphenol S (BPS) was associated with increased testosterone (T) (regression coefficient, β = 0.009, 95% confidence interval, CI: 0.003,0.015), p = 0.007) and free-T- (adsorption-FT4) (β = 0.009, 95% CI: 0.002, 0.016, p = 0.009) in male newborns. Bisphenol A (BPA) (β = 0.007, 95% CI: 0.001, 0.013, p = 0.027) and BPS (β = 0.007, 95% CI: 0.001, 0.013, p = 0.027) was observed in females, and bisphenol AF (BPAF) was associated with decreased follicle-stimulating hormone (FSH) in females. These associations were also observed in mixture of bisphenols. Moreover, we observed maternal prepregnancy body mass index (BMI) and delivery mode disparity in the relationship between bisphenols and sex and thyroid hormones. This study suggests that bisphenols may exert effects on sex and thyroid hormones. In newborns, the effect may vary with sex differences, maternal prepregnancy BMI, and delivery mode.	Food Chem Toxicol Vol.189 Pages 114750	10.1016/j.fct.2024.114750	38777166	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0760	L. Bidga, T. Csonka, G. Mihes, C. Markóth, D. Hubai and I. Mátyus	2025	Case Report: Toxic tubulointerstitial nephropathy with lipofuscin deposition - the potential cause of occupational Bisphenol-A exposition	This case study delves into the link between exposure to Bisphenol A (BPA) and kidney issues.Filling a gap in human focused research found in studies. The individual, a 72-year-man with a history of BPA exposure in a plastics manufacturing facility experienced a gradual decline in kidney function over 18 months. Medical tests showed kidney disease with a buildup of lipofuscin in renal tubular cells upon examination. This discovery suggests a connection between BPA exposure and kidney damage underscoring the need for investigation. The lack of human based evidence highlights the importance of research to understand the toxic effects of BPA on the kidneys. In addition, to its implications this case emphasizes the importance of improving safety protocols and raising awareness among healthcare professionals. It relevant work environments to reduce potential health risks associated with BPA exposure.	Pathol Oncol Res. 2025 Jul 7;31:1612046.	10.3389/pore.2025.1612046	40692724	ヒト	腎	-	-	-	-	-	-	-	症例報告	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0761	J. Bi, F. Wang, Y. Wei, Y. Zhang, C. Jia, J. He, J. Yao, Z. Zhang, Z. Li, P. Li and M. He	2022	Association of serum bisphenol A levels with incident overweight and obesity risk and the mediating effect of adiponectin	BACKGROUND: Existing cross-sectional studies indicated a positive association of bisphenol A (BPA) with overweight and obesity. However, the relationship and potential mechanisms underlying this association remain to be elucidated in prospective studies. OBJECTIVE: This study was designed to explore whether serum BPA is associated with incident overweight and obesity risk, and to further explore whether adiponectin plays a mediating role in the association. METHODS: We measured blood BPA and adiponectin in Chinese populations. The association of serum BPA with overweight and obesity risk was evaluated using multivariable logistic regression models. We further examined the mediating effects of adiponectin by causal mediation analysis. RESULTS: Among 796 participants free of overweight and obesity at baseline, 320 individuals developed overweight and obesity during the follow-up period. Compared with those in the lowest quartile of serum BPA, those in the second and third quartiles were positively associated with incident overweight and obesity risk after adjustment for confounders [OR (95% CI): 1.60 (1.04, 2.46) and 1.66 (1.08, 2.56), respectively]. Adiponectin mediated 18.8% (95% CI: 2.1%, 35.5%) of the association between BPA and overweight and obesity. Furthermore, each unit of serum lg(10)-transformed BPA levels was associated with higher changes in waist-to-height ratio and body mass index (all P-values < 0.05). Mediation analysis indicated significant indirect effects of adiponectin on the associations of BPA with overweight and obesity prevalence (mediation proportion: 66.88%, P = 0.027, and 38.8% levels (mediation proportion: 30.31%, P = 0.031). CONCLUSION: Serum BPA displayed a positive association with incident overweight and obesity risk in our menopausal women, and adiponectin might mediate the association. Further mechanistic studies are warranted.	Chemosphere. 2022 Dec;308(Pt 2):136287.	10.1016/j.chemosphere.2022.136287	36084821	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0762	K. Belut, O. Tuby, B. T. Neelihan, O. Mustafa and T. Nurat	2022	The effect of training about environmental toxicant Bisphenol-A exposure in pregnancy on maternal urine Bisphenol-A level	PURPOSE: Bisphenol A (BPA) is an environmental toxic, clearly capable of initiating epigenetic modifications, leading to the development of numerous human illnesses such as; metabolic, reproductive, and behavioral abnormalities. It also causes oxidative stress, which has been shown to be alleviated by selenium supplementation. The purpose of this study was to determine the effect of training of BPA exposure during pregnancy on urine BPA levels. METHODS: This research enrolled 30 pregnant women who were in their first trimester and were free of chronic illness. Women were asked questions on their sociodemographic features, anthropometric measures, obstetric characteristics, BPA awareness level, BPA exposure and the Health Practices in Pregnancy Exercise Scale as a "Pre-test and Post-Test." Then, the participants were taken to women in their first trimester and stored in BPA free bags. Then, training was delivered to encourage BPA exposure reduction and maternal health awareness. Prior trimester face-to-face instruction and brochure distribution were used to provide training. Urine samples were collected from participants before training and one month after training. Urine BPA concentrations were measured using the liquid chromatography mass spectrometry-mass spectrometry (LC-MS/MS) method. Each person's urine concentration was calculated and compared to the BPA content. RESULTS: Our study shows that BPA exposure may be lowered by training. It has been demonstrated that reducing BPA exposure and increasing knowledge can result in an improvement in health status. Additionally, it has been demonstrated that trainings greatly minimize exposure-causing behaviours. CONCLUSION: It was discovered that while the duration of a single training does not make a meaningful effect, the continuing of reminder trainings did make a substantial difference in the urine BPA level.	Heliyon Vol.8 Issue 12 Pages e12495	10.1016/j.heliyon.2022.e12495	36590557	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0763	T. N. Bethea, A. K. Wesselink, J. Weuve, M. D. McClean, R. Hauser, P. L. Williams, X. Yu, A. M. Calafat, D. D. Baird and L. A. Wise	2020	Correlates of exposure to phenols, parabens, and triclocarban in the Study of Environment, Lifestyle and Fibroids	We performed a cross-sectional analysis to identify correlates of urinary concentrations of seven phenols (bisphenols A, F, and S; 2,5-dichlorophenol; 2,4-dichlorophenol; benzophenone-3; triclosan), triclocarban, and four parabens (butyl, ethyl, methyl, and propyl). We analyzed baseline data from 784 participants in the Study of Environment, Lifestyle, and Fibroids, a prospective cohort study of 1693 Black women aged 23-35 years enrolled in Detroit, Michigan (2010-2012). We collected data on demographic, behavioral, and anthropometric factors via telephone interviews, clinic visits, and self-administered questionnaires. For each biomarker, we used multivariable linear regression to estimate percent differences in geometric mean concentrations comparing participants in each category of correlates to the reference group. Urinary concentrations were highest for methyl paraben (1424 μg/g creatinine), propyl paraben (244 μg/g creatinine), and benzophenone-3 (112 μg/g creatinine). Sociodemographic correlates of biomarker concentrations included season of urine collection, education, and body mass index (BMI). BMI was positively associated with bisphenol A and S and triclocarban concentrations and inversely associated with butyl and methyl paraben concentrations. In this cohort of Black women, exposure to phenols, parabens, and triclocarban was prevalent and several factors were associated with biomarker concentrations.	Expo Sci Environ Epidemiol Vol.30 Issue 1 Pages 117-136	10.1038/s41370-019-0114-9	30692588	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0764	K. Berger, C. Hyland, J. L. Ames, A. M. Mora, K. Huen, B. Eskenazi, N. Holland and K. G. Harley	2021	Prenatal Exposure to Mixtures of Phthalates, Parabens, and Other Phenols and Obesity in Five-Year-Olds in the CHAMACOS Cohort	Exposures to phthalates, parabens, and other phenols are often correlated due to their ubiquitous use in personal care products and plastics. Examining these compounds as a complex mixture may clarify inconsistent relationships between individual chemicals and childhood adiposity. Using data from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, a longitudinal cohort of children in Salinas Valley, California (n = 309), we examined biomarkers of 11 phthalate metabolites and 9 phenols, including several parabens and bisphenol A, measured in maternal urine at two time points during pregnancy. We measured child height and weight at age five to calculate the body mass index (BMI) z-scores and overweight/obesity status. The association between prenatal urinary concentrations of biomarkers with the childhood BMI z-score and overweight/obesity status was analyzed using single-pollutant models and two mixture methods: Bayesian hierarchical modeling (BHM) and Bayesian kernel machine regression (BKMR). Urinary biomarkers were associated with higher BMI z-score and overweight/obesity status in girls, but not boys. Positive associations were observed between the sum of medium-chain phthalates and BMI z-score and overweight/obesity status across all modeling approaches. Higher prenatal exposures to the cumulative biomarker mixture also trended with greater childhood adiposity. These results, robust across two methods that control for co-pollutant confounding, suggest that prenatal exposure to certain phthalates and parabens may increase the risk for obesity in early childhood.	Int J Environ Res Public Health. 2021 Feb 12;18(4):1796.	10.3390/ijerph18041796	33673219	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則として除外。

引用評価機関
●：該当

通格性評価（動物）1：該当、0：該当しない　通格性評価（疫学）1：該当、0：該当しない　通格性評価（in vitro）1：該当、0：該当しない　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原則1基づく除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合論文（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0765	K. Berger, E. Coker, S. Rauch, B. Eskenazi, J. Balmes, K. Kogut, N. Holland, A. M. Calafat and K. Harley	2020	Prenatal phthalate, paraben, and phenol exposure and childhood allergic and respiratory outcomes: Evaluating exposure to chemical mixtures	MACHADINUNG: Chemicals found in personal care products and plastics have been associated with asthma, allergies, and lung function, but methods to address real-life exposure to mixtures of these chemicals have not been applied in these associations. METHODS: We quantified urinary concentrations of eleven phthalate metabolites, four parabens, and five other phenols in mothers twice during pregnancy and assessed probable asthma, allergies, and lung function in their children at 3 and 5 years of age in the CHAMACOS cohort (Salinas Valley, California). We used quantile g-computation to estimate associations between exposure mixtures and outcomes measurements. We used Bayesian Kernel Machine Regression (BKMR) to fit exposure-response functions. We ran models for each independent variables. RESULTS: BPA showed inconsistent associations with outcomes. Some associations were observed between patterns of personal care product and plastic use, though there were no significant differences in outcomes across clusters. BKMR showed that monoethyloxoheptyl phthalate and 2,5-dichlorophenol were associated with wheeze at 5 years of age. Specifically, a joint increase per IQR of biomarker + score (standard deviation) = 0.89 (0.68, and 0.11 (0.22), respectively) and across lung function (predicted probability per IQR = -0.02 (-0.04, and -0.07 -0.06), respectively) and that mostly contributed by BPA. Phthalate and bisphenol A were associated with wheezing for (predicted probability per IQR = -0.11 (0.04) and 0.11 (0.06), respectively). Several biomarkers demonstrated positive additive effects on other associations. CONCLUSIONS: BPA and BKMR are useful tools to evaluate associations of biomarker concentrations within a mixture of exposure and should supplement single-chemical regression models when data allow.	Sci Total Environ. 2020 Jul 10:725:138418.	10.1016/j.scitotenv.2020.138418	32302842	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0766	T. L. L. Berge, G. B. Lygre, S. A. Lie, C. H. Lindh and L. Björkman	2019	Bisphenol A in human saliva and urine before and after treatment with dental polymer-based restorative materials	The aim of this study was to quantify bisphenol A (BPA) concentrations in saliva and urine before and after treatment with dental polymer based restorative materials to assess if placement of this material is associated with increased BPA levels in saliva and urine. Twenty individuals in need of at least one dental restoration received composite resin restorative material were included in the study. The participants were instructed to abstain from eating, drinking, and brushing their teeth for at least 12 h prior to sampling. Saliva and urine were collected before and 10 min (saliva only), 1 h, 24 h, and 1 wk after treatment. Samples were stored at -80° C before analysis. BPA in saliva and urine was determined with liquid chromatography-mass spectrometry. Linear mixed-effects regression models were used for statistical analyses. There was a statistically significant increase of salivary BPA concentrations shortly after placement of the dental polymer-based restorations. Following placement, the concentrations of BPA decreased exponentially with time. One week after treatment the BPA level in saliva was only marginally higher than before treatment. In urine, no statistically significant change of the BPA concentration was detected after treatment.	Eur J Oral Sci Vol.127 Issue 5 Pages 435-444	10.1111/eos.12647	31392814	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0767	T. E. Bærug, A. Gami-Sørensen, A. Ernst, N. Brix, K. S. Hougaard, K. K. Hærvig, J. P. Ebbehøj-Bonde, S. S. Tattenborg, C. H. Lindh, C. H. Ramlau-Hansen and G. Toft	2021	Urinary Bisphenol A, F and S Levels and Semen Quality in Young Adult Danish Men	Bisphenol A (BPA) is considered an endocrine disruptor and has been associated with deleterious effects on spermatogenesis and male fertility. Bisphenol F (BPF) and S (BPS) are structurally similar to BPA, but knowledge of their effects on male fertility remains limited. In this cross-sectional study, we investigated the associations between exposure to BPA, BPF, and BPS and semen quality in 904 men (18-29 years of age from the general Danish population. Urinary BPA, BPF, and BPS concentrations were measured by liquid chromatography-tandem mass spectrometry. Semen quality was assessed by standard semen analysis (sperm concentration, total sperm count, sperm motility, and sperm morphology). Associations between urinary bisphenol levels (continuous and quartiles) and semen quality were estimated using a negative binomial regression model adjusting for urine creatinine concentration, alcohol intake, smoking status, body mass index (BMI), fever, sexual abstinence time, maternal pre-pregnancy BMI, and first trimester smoking, and highest parental education during first trimester. We found no associations between urinary bisphenol of semen quality in a sample of young men from the general Danish population	Int J Environ Res Public Health Vol.18 Issue 4	10.3390/ijerph18041742	33670148	ヒト	-	1	1	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0768	V. Bellisario, E. Cocchi, R. Tassinari, G. Squillacioti, T. Munno, S. Settembre, M. Zorzi, P. Dalmasso, A. Cascio, C. Medana and R. Bono	2021	Bisphenol A and S in the Urine of Newborns: Plastic for Non-Food Use Still without Rules	The aim of the present study was to assess the effects of bisphenol (BP) exposure on pregnancy and neonatal life. We had 1st determined BP (BPA and BPS) concentration levels in a group of newborns and their mothers living in Turin (Italy). Urine samples were collected from 100 mothers (T1, T2, and T3) and from their newborns (cord blood and urine). Urinary BP concentrations were determined by solid-phase extraction and liquid chromatography–tandem mass spectrometry. Concentration levels, in newborns, positive correlations between cord blood and BPS (r-sq = 0.33) and between BPS (r = 0.43) concentrations were detected. A significant correlation between cord blood BPS concentrations and administration and concentration levels of liver BPS (p < 0.05). Our study points to a central role of lifestyle, hospital procedures, and neonatal devices in inducing BP exposure, especially during the perinatal period. This is the first report of BP contamination in newborns due to elderly-care alimentary products designed for newborn care, such as glucose-solution containers for BPA and pacifiers for BPS. Further studies are advocated in order to clarify both the impact of other BP forms on human health and development, as well as potential BPS exposure sources during neonatal and childhood life.	Biology (Basel) Vol.10 Issue 3	10.3390/biology10030188	33802301	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0769	A. L. Back, E. V. Bilsteer, C. S. Uldbjerg, Y. H. Lim, H. Bogh, H. Frederiksen, A. M. Andersson and T. K. Jensen	2025	Maternal urinary concentrations of bisphenol A during pregnancy and birth size in children from the Odense Child Cohort	MACHADINUNG: Bisphenol A (BPA) is widely used in the manufacturing of plastics. BPA can pass the placental barrier and influence fetal development. Due to its estrogenic and anti-androgenic properties, BPA may contribute to sex-specific differences in developmental effects. We examined associations between maternal urinary concentrations of BPA and birth size. METHODS: In this cohort study of 893 mother–child pairs from the Odense Child Cohort, pregnant women provided spot urine samples at gestational week 28, which were analyzed for BPA by isotope diluted LC-MS/MS. Genetically adjusted urinary BPA concentrations were categorized into quartiles. Mother–child characteristics were obtained from hospital records and questionnaires. Linear regression models were used to estimate the association between BPA and offspring birth weight, length, head, and abdominal circumference] were performed for the full cohort and stratified by offspring sex. RESULTS: BPA was detected above the limit of detection in 86% of the urine samples, with a median concentration of 1.1 µg/L. The highest quartile of maternal BPA concentrations was associated with a 0.16 SD (95% CI: 0.01, 0.31) lower birth weight SDS in boys compared to the lowest quartile. No association was observed among girls. Maternal BPA was not associated with birth length, head, or abdominal circumference. In sex-stratified analyses, statistically significant decreases in birth weight were observed among offspring in the highest quartile of maternal urinary BPA concentrations (Q3: -116 g, 95% CI: -225, -5; p = 0.04) compared to mothers offspring of the lowest quartile and a possible dose–response association was suggested (p-trend = 0.08). No statistically significant associations were observed for birth weight amongst female offspring. CONCLUSIONS: Our findings suggest a negative association between maternal urinary BPA exposure and birth weight, driven by a lower birth weight in male offspring. Further research is required to explore the underlying mechanisms of BPA's possible sex-specific associations.	Environ Health. 2025 Apr 1;24(1):15.	10.1186/s12940-025-01169-4	40170055	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0770	S. Baykal and A. Nalbantoğlu	2023	An Examination of the Relationship Between Exposure to Bisphenol A and Attention-Deficit/Hyperactivity Disorder in Children and Adolescents	OBJECTIVES: Exposure to environmental toxic agents in the prenatal and/or postnatal periods may play in the acquired development of attention-deficit/hyperactivity disorder (ADHD) in groups with genetic risks. Bisphenol A (BPA) is a widely used industrial chemical with endocrinedisruptive effects. This study examined the relationship between exposure to BPA and clinical ADHD. METHODS: This cross-sectional, case-controlled clinical study compared 33 drug-naive children and adolescents with ADHD and 30 healthy controls in terms of serum BPA levels. Psychiatric comorbidities in the ADHD group were determined using the "Schedule for Affective Disorders and Schizophrenia for school-aged children, lifetime version." The Child Behavior Checklist (CBCL) tests was administered to all participants. RESULTS: Serum BPA levels were significantly higher in the ADHD group than in the healthy control group. In addition, significant, weak, positive correlations were found between BPA levels and CBCL attention and CBCL total problem scores. CONCLUSIONS: Our results show that BPA exposure may be a potential toxic agent with a potential role in the etiology of ADHD and particularly attention deficiency. Preventive interventions can be developed if this can be confirmed with longitudinal studies and repeated measurements.	Clin Neuropharmacol Vol.46 Issue 6 Pages 214-219	10.1097/wnf.0000000000000574	37962308	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0771	B. Barajas, Á. Meléndez-Ortega, L. López-Carrillo and M. E. Cebrián	2025	Urinary concentrations of total and free bisphenol A and daily intake estimation in northern Mexican women	Bisphenol A (BPA) is a component of polycarbonates used to manufacture plastic reusable bottles and miscellaneous containers; it is a constituent of epoxy resins used for the internal coating of beverage cans. Humans are mainly exposed by ingesting contaminated food and beverages. Experimental and human studies reported diverse health problems associated with BPA. Our objectives were to measure free (FBPA) and total (TBPA) urinary levels, to estimate daily BPA intake, and to investigate sources of exposure in northern Mexican women. This study is a secondary cross-sectional analysis. In controls (n = 281) participating in a population-based case-control study, TBPA and FBPA were measured in first-morning urine samples by ultra-performance liquid chromatography–tandem mass spectrometry. BPA was detected in 100% of samples conducted in July 2009. ESHYDRO/IMSS. Urinary BPA levels were quantified using either external calibration—applied to high-performance liquid chromatography instruments—or isotope dilution (IDMS) for gas chromatography–mass spectrometry. BPA ELECTRONIC AND MEASUREMENTS. Mainstay from all causes, cardiovascular disease, and cancer. RESULTS: This cohort study included 1882 adults aged 20 years or older who participated in the US National Health and Nutrition Examination Survey (NHANES) 2003-2004 and 2005-2006 and had complete data on BPA and mortality. BPA was detected in 93.3% of participants' urine samples. Higher urinary BPA levels were associated with higher risk for death. After adjustment for age, sex, race/ethnicity, socioeconomic status, drinker and lifestyle factors, and urinary creatinine levels, a 1-unit increase in log-transformed BPA was associated with a 1.09 (95% CI, 1.01-1.19) for all-cause mortality; 1.09 (95% CI, 0.97-1.21) for cardiovascular disease mortality, and 1.08 (95% CI, 0.92-1.26) for cancer mortality. CONCLUSIONS AND RELEVANCE: In this nationally representative cohort of US adults, higher BPA exposure was significantly associated with an increased risk of all-cause mortality. Further studies are needed to replicate these findings in other populations and determine the underlying mechanisms.	Environ Monit Assess Vol.197 Issue 6 Pages 675	10.1007/s10661-025-14074-7	40418384	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0772	W. Bao, B. Liu, S. Rong, S. Y. Dai, L. Trasande and H. J. Lehmler	2020	Association Between Bisphenol A Exposure and Risk of All-Cause and Cause-Specific Mortality in US Adults	IMPORTANCE: Bisphenol A (BPA) is a major public health concern because of its high-volume industrial production, ubiquitous exposure to humans, and potential toxic effects on multiple organs and systems in humans. However, prospective studies reporting the association of BPA exposure with long-term health outcomes are sparse. OBJECTIVE: To examine the association of BPA exposure with all-cause mortality and cause-specific mortality among adults in the United States. DESIGN, SETTING, AND PARTICIPANTS: This nationally representative cohort study included 1882 adults aged 20 years or older who participated in the US National Health and Nutrition Examination Survey (NHANES) 2003-2004 and 2005-2006 and had complete data on BPA and mortality. BPA was detected in 93.3% of participants' urine samples. EXPOSURES: Urinary BPA levels were quantified using either external calibration—applied to high-performance liquid chromatography instruments—or isotope dilution (IDMS) for gas chromatography–mass spectrometry. MAIN OUTCOMES AND MEASURES: Mortality from all causes, cardiovascular disease, and cancer. RESULTS: This cohort study included 1882 adults aged 20 years or older (weighted mean [SE] age, 43.6 [0.5] years; 2022 [51.2%] women; 1328 [70.6%] non-Hispanic White participants). The geometric mean (SE) urinary BPA level was 2.1 (0.1) ng/mL. After a median follow-up of 10.8 years, 178 participants died. Participants with higher urinary BPA levels were at higher risk for death. After adjustment for age, sex, race/ethnicity, socioeconomic status, drinker and lifestyle factors, and urinary creatinine levels, a 1-unit increase in log-transformed BPA was associated with a higher risk for all-cause mortality (1.09 [95% CI, 1.01-1.19] for all-cause mortality; 1.09 [95% CI, 0.97-1.21] for cardiovascular disease mortality, and 1.08 [95% CI, 0.92-1.26] for cancer mortality; CONCLUSIONS AND RELEVANCE: In this nationally representative cohort of US adults, higher BPA exposure was significantly associated with an increased risk of all-cause mortality. Further studies are needed to replicate these findings in other populations and determine the underlying mechanisms.	JAMA Netw Open. 2020 Aug 3;3(8):e2011620.	10.1001/jamanetworkopen.2020.11620	32804211	ヒト	その他(死亡率)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0773	B. D. Bagley, J. N. Smith and J. G. Teeguarden	2021	Risk assessment of predicted serum concentrations of bisphenol A in children and adults following treatment with dental composite restoratives, dental sealants, or orthodontic adhesives using physiologically based pharmacokinetic modeling	Bisphenol A (BPA) is a chemical used to manufacture bisphenol A glycidyl methacrylate (BisGMA). BisGMA has been used for decades in dental composite restoratives, sealants, and adhesives. Based on published studies, exposure to low concentrations of BPA are possible from dental and orthodontic devices. The current BPA concentrations arising from such devices are not known and existing PBPK model in children and adult females lacked in 1) published extraction data for cured and uncured 3M ESPE Filtek Supreme Ultra/Tetric, 3M ESPE Filtek Bulk Fill Restorative, and 3M ESPE Clinpro Sealant and 2) published 28% conversion of BisGMA to BPA. Physiologically based pharmacokinetic (PBPK) models were developed for children and adult females exposed to BPA from dental composite restoratives, dental sealants, or orthodontic devices to two median (50 kg treatment) and medium serum BPA concentrations were less than 1 nM (0.46). Even the maximum predicted exposure (<4% steady-state (SS) % of treatment) yields a margin of exposure of 7.5 relative to the FDA's TDI (5 µg/kg/day) and is only 2.8% of the daily BPA exposure for the US population in a 50 kg woman (11,000 ng/day). Therefore, the exposure to BPA arising from the 3M ESPE dental and orthodontic devices evaluated in this study is negligible relative to daily BPA exposure in the general population and these potential BPA sources do not contribute a risk to patients.	Regul Toxicol Pharmacol Vol.120 Pages 104839	10.1016/j.yrtph.2020.104839	33301868	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0774	N. Aytac Bektas, N. N. Yenigul, K. Paksoy, B. Dincgez, E. Yuce Bilgin, Y. Usluoglugil and E. Ucturk yurt	2024	Does Bisphenol-A play a role in the development of nasural tube defects?	OBJECTIVE: In this study, we aimed to evaluate BPA levels in the maternal serum and amniotic fluid of patients diagnosed with NTD. In addition, we wanted to investigate the relationship between neurodevelopmental defects, such as neural tube defects (NTD) and BPA levels. STUDY DESIGN: This prospective observational study was carried out at Bursa Yüksek Ihtisas Training and Research Hospital between April 01, 2021, and April 30, 2022. The study consisted of 50 patients between the ages of 18-45 who had an amniocentesis at 15-20 weeks of gestation. The patients were divided into two groups according to the indications of amniocentesis. Group 1 (n = 25) consisted of patients who had an amniocentesis for NTD, and Group 2 (n = 25) consisted of patients who had an amniocentesis for a non-NTD pre-diagnosis of NTD (if patients). The first 5 cc fluids and maternal serum samples taken during the amniocentesis procedure of all patients were delivered to the biochemistry laboratory. The BPA values between groups were compared. RESULTS: A statistically significant difference was found between the two groups in terms of amniotic fluid BPA levels (36.68 (19.60-60.30) and 38.87 (24.62-75.87)) and maternal blood BPA levels (22.51 (12.80-230) and 47.81 (13.04-219.30)). In cases with NTD, amniotic fluid BPA levels and maternal blood BPA levels were significantly higher than the control group. When ROC values were compared, the AFP numerical values are higher than the maternal blood BPA levels. CONCLUSION: Plastics, which is indispensable for modern life, may negatively affect fetal development in intrauterine life. The data in this study note that high maternal blood BPA may be associated with NTD.	J Perinatol Vol.44 Issue 7 Pages 1029-1034	10.1038/s41372-024-01925-3	38499756	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0775	G. Ayar, S. S. Yalçın, A. Yıldız, S. Emekci, A. Balcı and P. Ekekoğlu	2022	Associations between pediatric intensive care procedures and urinary free-BPA levels	MACHADINUNG: Bisphenol A (BPA) is found in many medical materials used in the paediatric intensive care unit (PICU). Our aim was to evaluate how the urinary free-BPA(BPA) and total-BPA(tBPA) levels were associated with the use of medical devices in the PICU in a prospective study. METHODS: The procedures applied to the patient were recorded during the follow-up period. Three urine samples were taken on the first day of hospitalization, the second day, and after 30 days or on the patients were discharged. Urinary tBPA and free-BPA levels were determined using high-pressure liquid chromatography. Generalized estimating equations with repetitive measures were used to determine the associations between PICU procedures and BPA levels. RESULTS: A total of 131 urine samples of 50 children were studied. Mean urinary levels were 1842.7 µg/g creatinine for tBPA and 1.5 µg/g creatinine for free-BPA. The urinary tBPA concentrations were significantly higher than the urinary free-BPA concentrations (median [IQR]: 1842.7 [1010.1-3744.6] versus 1.5 [0.8-2.8] µg/g creatinine, p < 0.001). Urinary tBPA levels and maternal blood BPA levels were significantly higher than the control groups. When ROC values were compared, the tBPA numerical values are higher than the maternal blood BPA levels. CONCLUSIONS: Plastics, which is indispensable for modern life, may negatively affect fetal development in intrauterine life. The data in this study note that high maternal blood BPA may be associated with NTD.	Environ Sci Pollut Res Int Vol.29 Issue 9 Pages 13555-13563	10.1007/s11356-021-16677-2	34595711	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0776	G. Ayar, S. S. Yalçın, S. Emekci, A. Yılz, A. Balcı, B. Kocer-Gumusel and P. Ekekoğlu	2021	The association between urinary BPA levels and medical equipment among pediatric intensive care patients	We aim to evaluate urinary total BPA (tBPA) levels and association with medical devices used on patients in pediatric intensive care units. This cross-sectional descriptive study included 117 critically ill children. Urinary tBPA levels were determined using high-performance liquid chromatography. General estimating equations with repeated measures analysed the effect of intervention on urinary tBPA levels. A total of 783 urine samples taken from 117 child intensive care patients were studied. When age, sex, and body mass index for age z-scores were controlled, cases having endotracheal intubation showed higher urinary tBPA levels (p = 0.001) and hemodialysed patients had considerably higher urinary tBPA levels (p = 0.002). When confounding factors were controlled, cases using both multiple iv treatment and more than four medical devices showed higher urinary tBPA levels than their counterparts (p = 0.007 and p = 0.028, respectively). The use of certain medical devices and interventions could increase BPA exposure in pediatric intensive care patients.	Environ Toxicol Pharmacol Vol.83 Pages 103585	10.1016/j.etap.2021.103585	33460802	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0777	S. Arya, A. K. Dwivedi, L. L. Alvarado and S. Kuzenko-Plevski	2020	Exposure of U.S. population to endocrine disruptive chemicals (Parabens, Benzophenone-3, Bisphenol-A and Triclosan) and their associations with female infertility	Ubiquitous exposure to endocrine disruptive chemicals (EDC) among women of reproductive age is alarming. Exposure to EDCs, could be contributing to infertility. We determined the association between common EDCs, and infertility among women in the U.S. A total of 1,455 women (ages 18-44 years) from National Health and Nutrition Examination Survey (NHANES) 2013-2014 with complete data on infertility and urinary EDCs of age-women was conducted. Multiple regression sociodemographic variables, and urinary concentrations of parabens (methyl paraben [MP], ethyl paraben [EP], propyl paraben [PP], and butyl paraben [BP]), Benzophenone-3 (BP-3), Bisphenol-A (BPA), and triclosan (TCC) were obtained from the NHANES databases. Clustering among EDCs, were obtained using variable cluster analysis. Relative risk regression models were used to estimate associations of individual and combined EDCs with self-reported infertility after applying appropriate survey weights to account for the complex survey design as well as to compensate for the four-year cycle. Results were summarized using prevalence ratio (PR) with 95% confidence interval (CI). Of total 786 individuals included in the study, 14% (95%CI: 12%-18%) had infertility. MP and PP were detected in 99% of urine samples. BP-3, BPA, and TCC were detected in 96%, 93%, and 83% of urine samples, respectively. Women with infertility had higher urinary MP (PR: 1.07; p = 0.0001), PP (PR: 1.06; p = 0.0001), BP (PR: 1.01; p = 0.029) even after adjusting for potential confounders. Our results suggested that MP and mixtures of hexadecimals, TCC, and BPA were associated with infertility among the U.S. women. However, because of the limitations inherent to the cross-sectional study design, prospective cohort studies are warranted to confirm these findings.	Environ Pollut Vol.265 Issue Pt A Pages 114763	10.1016/j.envpol.2020.114763	32806428	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通格性評価（動物）1：該当、0：該当しない　通格性評価（疫学）1：該当、0：該当しない　通格性評価（in vitro）1：該当、0：該当しない　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0778	F. Artacho-Cordón, S. Rios-Arrabal, J. León, H. Frederiksen, J. M. Sáenz, P. Martín-Olmedo, M. F. Fernández, N. Olea and I. P. Arrebola	2019	Adipose tissue concentrations of non-persistent environmental phenols and local redox balance in adults from Southern Spain	The aim was to evaluate the associations of environmental phenol and paraben concentrations with the oxidative microenvironment in adipose tissue. This study was conducted in a subsample (n = 162) of the Andalusian Center (Southern Spain). Concentrations of 4 phenols and 7 parabens, and levels of oxidative stress biomarkers were quantified in adipose tissue. Associations were estimated using multivariable linear regression models. Concentrations of benzylparaben (BzP) were associated with lower concentrations of glutathione disulfide (GSSG) (beta (β) = -0.35; p = 0.030). Concentrations of 2 phenols, 4 parabens, and BzP were associated with lower reduced glutathione (GSH) (beta (β) = -0.66, -0.31, -0.31, -0.32, -0.32, -0.32, and -0.31; p = 0.030). Concentrations of bisphenol A (BPA) and methylparaben (MeP) were associated to lower glutathione reductase (GR) activity (beta (β) = -0.66, and β = -0.71, respectively), and BPA was borderline associated to increased levels of oxidized glutathione (GSSG) (beta (β) = 0.73; p-value = 0.062). MeP was inversely associated to both homoisoprostane (2-iso)- (β and superoxide dismutase (SOD) activity, as well as to the levels of thiobarbituric acid reactive substances (TBARS) (β: 0.76 ; and β = 0.76). Our results suggest that some specific non-persistent pollutants may be associated with a disruption of the activity of relevant antioxidant enzymes, in addition to the depletion of the glutathione stock. They might act as a tissue-specific source of free radicals, contributing to the oxidative microenvironment in the adipose tissue.	Environ Int Vol.133 Issue Pt A Pages 105118	10.1016/j.envint.2019.105118	31610369	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0779	J. Ao, W. Zhu, W. Jiang, X. Zeng, W. Qiu, S. Yin, W. Wang and J. Zhang	2024	The mixture of non-persistent endocrine-disrupting chemicals in relation to endometriosis	Non-persistent endocrine-disrupting chemicals (EDCs) are of significant concern due to their reproductive toxicity. Previous research reported a relationship between a single type of EDCs and endometriosis. Yet, evidence regarding mixed exposure of multiple categories of EDCs is scarce. Between 2010 and 2018, our hospital-based case-control study recruited 258 endometriosis cases and 258 age-matched controls in China. Seventeen non-persistent EDCs (phthalates and bisphenols) were measured in urine. The association of single EDC with endometriosis was estimated using logistic regression, while the association of EDC mixtures was assessed using weighted quantile sum regression (WQS) and Bayesian kernel machine regression (BKMR). Single-pollutant analysis showed that urinary mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) was observed in both single- and mixture models, where phthalates and bisphenols were associated with increased risk of endometriosis. Inverse effect, adjusted odds ratios (aOR): 1.61, 1.23-2.10) and the major contributor were bisphenol A (BPA) and the metabolite of di(2-ethylhexyl) phthalate (DEHP). Interaction analysis showed that bisphenols exhibited significant synergistic interactions with phthalates. Our results suggest that non-persistent EDCs are associated with endometriosis, but the underlying mechanisms remain to be elucidated. Our finding may have important public health implications in preventing endometriosis.	Ecotoxicol Environ Saf. 2024 Nov 1;286:117129.	10.1016/j.ecoenv.2024.117129	39388968	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0780	J. Ao, Y. Wang, W. Tang, R. Aimuzi, K. Luo, Y. Tian, Q. Zhang and J. Zhang	2022	Patterns of environmental exposure to phenols in couples who plan to become pregnant	Phenols are widely used in consumer products and known for their reproductive toxicities. Little is known regarding the environmental exposure to phenols in couples prior to conception, a key period affecting fertility. We measured the urinary concentrations of six parabens and seven bisphenols in 982 pre-conceptive couples in China. We investigated the occurrence, distribution, source and health risk of phenols, in bisexuals and cross-separately, and the correlation and difference in phenol concentrations between couples. Similar distribution profiles of urinary phenols were observed between females and males. Methyl-4-hydroxybenzoate (MeP) and bisphenol A (BPA) were predominant parabens and bisphenols, with detection frequencies of 99.8% and 97.2%, median concentrations of 32.5 and 1.10 μg/L, respectively, in females. The correlation between bisphenols in males and females were moderate (0.34-0.668), while the correlation between parabens was poor to moderate (0.209-0.561). Urinary BPA concentrations were higher than other phenols in females than male ($P < 0.05$). Urinary phenols in couples were associated with family income, type of drinking water and frequency of household cleaning. Household factors accounted for >13.3% of variance in phenol level between couples, suggesting that individual variations may be the major factor. Risk assessment showed that exposure to phenols posed a low hazard to 7.73% of the couples in our population. Our findings provide important evidence of environmental exposure to phenols in couples of child-bearing age.	Sci Total Environ Vol.821 Pages 153520	10.1016/j.scitotenv.2022.153520	35101495	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0781	J. Ao, X. Hui, J. Zhang, Y. Miao, G. Li, J. Yu, Y. Shi, F. Jin, S. Bao and J. Zhang	2022	Environmental exposure to bisphenol analogues and unexplained recurrent miscarriage: A case-control study	The use of bisphenol A (BPA) has been substantially limited since 2010 due to its toxicity to human health. A group of bisphenol analogues that are structurally similar to BPA have been developed as the alternatives and used widely. The reproductive toxicity of these emerging chemicals has caused substantial concerns in recent years. Whether bisphenol analogues affect miscarriage is unclear, especially unexplained recurrent miscarriage (URM). remains to be explored. We conducted a hospital-based, case-control study with 1180 URM cases and 571 controls in China from 2013 to 2016. Concentrations of six bisphenol analogues (BPA, BPAF, BPAP, BPB, BPF and BPS) were measured in the urine samples collected at median intervals of 7.0 months after the last menstrual period (range: 3.0, 14.7 months). Multivariate logistic regression models were used to estimate the associations of bisphenol analogues (BPA/BPS and quartile or nonquartile 1[a grams] were used to assess the relationship of bisphenol analogues with URM risk. We observed significantly higher levels of all urinary bisphenols in the cases than the controls (all $P < 0.001$). Urinary bisphenol concentrations were positively associated with URM risk in a dose-dependent manner. Women in the highest quartile of BPA, BPAF, BPAP, BPB, BPF and BPS quartiles with URM. The mixed exposure of six bisphenol analogues was positively associated with the risk of URM (adjusted odds ratio (aOR) = 1.25, 1.11-1.42), which was driven by BPAP (46.1%), BPAF (25.1%) and BPS (14.8%). After age stratification, the risks tended to be higher in women aged 30 years or older, compared to women < 30 years. Our large case-control study indicates that environmental exposure to bisphenol analogues is associated with an increased risk of URM. Older women may be more vulnerable to the insult.	Environ Res. 2022 Mar;204(Pt C):112293.	10.1016/j.envres.2021.112293	34728239	ヒト	生殖発生	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0782	S. J. An, E. J. Yang, S. Oh, K. J. Park, T. Kim, Y. P. Hong and Y. J. Yang	2021	The association between urinary bisphenol A levels and nonalcoholic fatty liver disease in Korean adults: Korean National Environmental Health Survey (KoNEHS) 2015-2017	BACKGROUND: Nonalcoholic fatty liver disease (NAFLD) is becoming a global health problem. Bisphenol A (BPA), one of most widely used environmental chemicals, is suspected to be a contributor to the development of NAFLD. However, the association between BPA exposure and NAFLD is unclear. METHODS: In this cross-sectional study, we used data from 1,620 adults aged ≥ 19 years who participated in the Korean National Environmental Health Survey VI (2015-2017). BPA levels were measured in urine samples. NAFLD was defined using hepatic steatosis index and the absence of hepatitis. Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for NAFLD according to urinary BPA concentrations. RESULTS: There was a significant linear relationship between the elevated urinary BPA concentrations and risk of NAFLD. In a univariate analysis, odds ratio (OR) of the highest quartile of urinary BPA level was 1.47 (95% confidence interval (CI): 1.11-1.96) compared to the lowest quartile. After adjusted OR in countries, the ORs for NAFLD in the third and fourth quartiles were 1.32 (95% CI: 1.01-1.72) and 1.32 (95% CI: 1.00-1.75), respectively. CONCLUSIONS: Urinary BPA levels are positively associated with the risk of NAFLD in adults. Further experimental studies are needed to understand the molecular mechanisms of BPA on NAFLD prevalence.	Environ Health Prev Med Vol.26 Issue 1 Pages 91	10.1186/s12199-021-01010-7	34521354	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0783	M. M. Amin, Z. Ghassemi, M. Khoshhali, E. Tahvili, B. Dehdashti, A. Fakhrizadeh, N. Rafiei and R. Kelishadi	2021	Association of maternal exposure to bisphenol A with her β -hCG level and neonatal anthropometric measures	Bisphenol A (BPA) is one of the organic compounds that might interfere with estrogenic receptors, which could make difficulties in pregnancy hormones and fetal growth. Human chorionic gonadotropin (β -hCG) is one of the important pregnancy hormones that might be affected by environmental pollutants. The aim of this study is to investigate the probable impacts of maternal exposure to BPA on anthropometric measures of newborns and its association with maternal β -hCG level. METHODS: In this study, 200 pregnant women were recruited from Isfahan Birth Cohort Study (IBCS) in 2014. Urine samples of BPA and β -hCG were taken from them and newborns information were collected from participants of a birth cohort. BPA concentration was measured using gas chromatography-mass spectrometry (GC-MS). Second-trimester urine samples were collected and used for β -hCG analysis. Anthropometric measurements of neonates was conducted at the time of birth. BPA and β -hCG level were grouped by quartiles, and their associations with birth weight, height, and head circumference were tested using multiple linear regression model. The adjustment was done for urine creatinine, gender, and gestational age, as well as maternal age, body mass index, and education level. Data of 200 pairs of mothers and infants were available for the present study. The mean (SD) age of mothers was 29.26 (5.75) years; 50.5% of newborns were boys. Geometric mean of urinary BPA and β -hCG concentrations were 0.36 ng/g cree. Considered and 1.36 mIU/ml, respectively. The mean (SD) birth weight, height, and head circumference of newborns were 3.29 (0.46) kg, 49.61 (2.03) cm, and 34.23 (1.46) cm, respectively. No significant association existed between unadjusted and adjusted tertiles of BPA and β -hCG with abovementioned birth outcomes. It seems that the non-significant association found in this study is because of low levels of urinary BPA levels. Due to other studies, the adverse effects on infants might be related to high concentration of BPA passed from placenta. Future longitudinal studies with large sample size are necessary to document the adverse health effects of maternal exposure to endocrine disruptor chemicals, including BPA.	Environ Sci Pollut Res Int Vol.28 Issue 44 Pages 62809-62815	10.1007/s11356-021-15094-9	34215981	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0784	B. Alvarez-González, A. F. Hernández, A. Zafra-Gómez, L. Chico-Rebechiba, S. Cuenca-López, F. Vázquez-Alonso, L. J. Martínez-González and M. J. Alvarez-Cubero	2024	Exposure to environmental pollutants and genetic variants related to oxidative stress and xenobiotic metabolism-Association with prostate cancer	This study assessed whether genetic variants coding for certain enzymes involved in xenobiotic detoxification, antioxidant defenses and DNA repair, along with exposure to environmental chemicals, were associated with prostate cancer (PCa) risk. METHODS: In this case-control study, 55 newly diagnosed PCa patients and 55 healthy controls were recruited. Genotyping assays on their normal peripheral blood samples, using an ITAQ Sweta screening panel from Agilent. Genetic variants in CYP1A1, GSTP1, GSS1, CAT, GPX1, MEC1 were determined and data for chemical exposure was obtained through a structured questionnaire used by Granada Living in a subsample of cases and controls. High-serum PSA levels were associated with a greater risk of PCa, while physical exercise appears to exert a protective effect against its development. In addition, elevated urinary levels of certain organic pollutants, such as benzo[a]pyrene (BaP), bisphenol A (BPA), and ethyl paraben (EPB), were associated with an increased risk of PCa.	Environ Toxicol Pharmacol Vol.108 Pages 104455	10.1016/j.etap.2024.104455	38657881	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0785	P. Altun Yildirim, E. Nacitarhan, Z. Haytoglu, I. Turan, B. Kilincli, A. A. Aydin, E. Mengen and N. Dogludas	2025	Evaluation of the Relationship Between Thyroid Hormone Levels and Bisphenol A in Children Aged 6-14 Years	BACKGROUND: The incidence of hypothyroidism in childhood is increasing. This study aimed to investigate the potential role of exposure to bisphenol A, an environmental endocrine disruptor, and its substitutes in the development of hypothyroidism. To this end, thyroid hormone levels and urinary bisphenol concentrations were compared in newly diagnosed hypothyroid children and a healthy control group. METHODS: In this case-control study, 51 newly diagnosed hypothyroid children aged 6-14 years were matched with 51 healthy controls. Free thyroxine (fT4) and thyroid-stimulating hormone (TSH) hormone levels were measured from fasting blood samples. Urinary bisphenol A, S, and F concentrations were determined and data for chemical exposure was obtained through a structured questionnaire used by Granada Living in a subsample of cases and controls. High-serum PSA levels were associated with a greater risk of PCa, while physical exercise appears to exert a protective effect against its development. In addition, elevated urinary levels of certain organic pollutants, such as benzo[a]pyrene (BaP), bisphenol A (BPA), and ethyl paraben (EPB), were associated with an increased risk of PCa. RESULTS: The mean fT4 level was found to be significantly lower in the hypothyroid group than in the control group (1.1 ± 0.2 ng/dL vs. 1.3 ± 0.1 ng/dL, $p < 0.001$). Urinary BPA levels were also significantly higher in the hypothyroid group (2.4 ± 1.6 µg/g creatinine vs. 1.7 ± 1.3 µg/g creatinine, $p = 0.013$). Receiver operating characteristic (ROC) analysis revealed that urinary BPA concentration was a significant predictor of hypothyroidism (AUC = 0.66, 95% CI: 0.54-0.78, $p = 0.013$). The optimal cut-off value for urinary BPA was determined as 1.3 µg/g creatinine, with a sensitivity of 72.5% and a specificity of 56.9%. Logistic regression analysis indicated that each 1 µg/g creatinine increase in urinary BPA was associated with a 1.4-fold increased risk of hypothyroidism (OR = 1.4, 95% CI: 1.1-1.8, $p = 0.006$). Urinary bisphenol S and F levels were not significantly different between the groups. CONCLUSIONS: Urinary BPA levels are positively associated with the risk of hypothyroidism in children. Further experimental studies are needed to understand the molecular mechanisms of BPA on thyroid function.	Clin Endocrinol (Oxf). 2025 Jul;103(1):97-105.	10.1111/cen.15221	40025791	ヒト	甲状腺	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0786	K. Almstrup, H. Fredriksen, A. M. Andersson and A. Juul	2020	Levels of endocrine-disrupting chemicals are associated with changes in the peri-pubertal epigenome	Puberty marks a transition period, which leads to the attainment of adult sexual maturity. Timing of puberty is a strongly heritable trait. However, large genetic association studies can only explain a fraction of the observed secular trends in pubertal timing. Endocrine-disrupting chemicals (EDCs) are suspected to contribute to the observed changes in pubertal timing. We investigated the association between urinary concentrations of 13 EDCs, including bisphenol A, benzophenone-3, 2,4-dichlorophenol, 11 alkylphenols and 11 metabolites from 6 phthalates in longitudinal urine samples obtained biannually from peri-pubertal children included in the COPENHAGEN puberty cohort. EDC levels were associated with blood DNA methylation profiles from 51 boys and 50 girls measured both pre- and post-puberty. We found little evidence of single methylation sites that on their own showed association with urinary secretion levels of EDCs, detected either the same day or measured up to the yearly interval of duration of peri-pubertal EDC levels. In contrast, methylation of promoter regions was found to be associated with time or mean EDCs, overlap with known gene-chemical interactions, and form a core network with genes known to be important for puberty. Furthermore, children with the highest yearly mean of dichlorinated urinary phthalate metabolites levels were associated with higher promoter methylation of the thyroid hormone receptor interactor 6 gene (TRIP6), which again was reversed by home cleaning TRIP6 serum levels. In general, the mean TRIP6 promoter methylation was elevated by circulating TRIP6 protein levels. Our results provide a potential molecular mode of action of how exposure to environmental chemicals may modify pubertal development.	Endocr Connect. 2020 Aug;9(8):845-857.	10.1530/ec-20-0286	32755991	ヒト	遺伝毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0787	S. Alizadeh-Fanalou, S. Mehdipour, S. Rahimzadeh, A. Rad, F. Mohammadi, K. Gholivan, S. Arzi, S. H. Mousavi and M. Karami	2024	Evaluation of novel biomarkers for early diagnosis of bisphenol A-induced coronary artery disease	INTRODUCTION: Bisphenol A (BPA), a ubiquitous synthetic monomer primarily used in the manufacture of polycarbonate plastic and epoxy resins and as a non-polymer additive to other plastics, can leach into the food and water supply and has been linked to cardiovascular disease (CVD). This study aimed to analyze BPA levels in patients with varying markers of coronary artery stenosis and evaluate the prognostic value of new biomarkers. cluster of differentiation 34 (CD34) and heart-type fatty acid-binding protein (H-FABP), respectively. Logistic and receiver-operator characteristic (ROC) curve analyses were used to assess the diagnostic value of BPA, CD34, and H-FABP. RESULTS: Eighty-nine patients with CAD and 30 healthy controls were enrolled in this study. Patients with CAD were divided into three groups based on the severity of coronary artery stenosis: mild, moderate, and severe. Compared with the healthy controls, the CAD patients had significantly higher levels of BPA, CD34, and H-FABP. Logistic regression analysis revealed that BPA, CD34, and H-FABP were significantly associated with CAD. Furthermore, ROC curve analysis revealed that BPA, CD34, and H-FABP had higher accuracy than troponin I and CK-MB in diagnosing CAD. Moreover, BPA, CD34, and H-FABP were significantly associated with the severity of coronary artery stenosis. Logistic regression analysis revealed that BPA, CD34, and H-FABP had higher accuracy than troponin I and CK-MB in diagnosing severe coronary artery stenosis. Logistic, scientific significant alterations were detected in age, sex, BMI, hypertension, diabetes, dyslipidemia, and smoking. BPA serum concentration significantly increased compared to normal subjects. CONCLUSIONS: Our study revealed that serum biomarkers were valuable for prognosticating myocardial injury. Among these, CD34 and H-FABP were more accurate. BPA concentration correlated with myocardial necrosis, underlying diseases, and occlusion stage, suggesting BPA's harmful effects.	Heliyon Vol.10 Issue 1 Pages e23768	10.1016/j.heliyon.2023.e23768	38234885	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0788	H. T. Alhomaidan, N. Rasheed, S. Almatrafi, F. H. Al-Rashidi and Z. Rasheed	2019	Bisphenol A modified DNA: A possible immunogenic stimulus for anti-DNA autoantibodies in systemic lupus erythematosus	Anti-DNA antibodies are now considered as a universal diagnostic feature for the patients with systemic lupus erythematosus (SLE) but the mechanism(s) involved in the generation of these autoantibodies remains to be investigated. Bisphenol A (BPA) is a synthetic phenol extensively used in the manufacturing of polycarbonated plastics. Upon mixing in the diet, it causes several health hazards. This study was undertaken to investigate the contribution of BPA toward DNA damage in SLE patients. Human DNA was modified by BPA in vitro and the binding characteristics of SLE circulating immunoglobulin G (IgG) with BPA damaged DNA (BPA-DNA) were screened and compared with the IgGs from normal healthy humans. Only IgG1 immunogenicity of BPA-DNA was determined by immunoblot in rabbits. DNA from SLE patients (SLE-DNA) or healthy humans (H-DNA) was also modified by BPA in vitro and the binding of IgG1 with BPA-SLE-DNA and BPA-H-DNA was compared by indirect enzyme linked immunosorbent assay. Circulating SLE IgGs showed strong recognition of BPA-DNA. BPA-DNA induced high titre antibodies in rabbits. Rabbit anti-BPA-DNA IgG1 showed strong cross-reaction with isolated DNA from SLE patients. In short, we concluded that the structural alterations in DNA by BPA, generate neo-epitopes that may be a factor responsible for the induction of anti-DNA autoantibodies in SLE.	Autoimmunity Vol.52 Issue 7-8 Pages 272-280	10.1080/08916934.2019.1683545	31656085	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0789	J. D. Alampi, B. P. Lanphear, J. M. Braun, A. Chen, T. K. Takaro, G. Muckle, T. E. Arbuckle and L. C. McGarvey	2021	Association Between Gestational Exposure to Toxicants and Autistic Behaviors Using Bayesian Quantile Regression	Autism spectrum disorder, which is characterized by impaired social communication and stereotypic behaviors, affects 1% of children. Although prenatal exposure to toxicants has been associated with autistic behaviors, previous studies have focused on single chemicals. We used Bayesian quantile regression to estimate associations between prenatal exposure to a mixture of toxicants and autistic behaviors across the distribution of behaviors. We used data from the Maternal Adrenal Response to Environmental Chemicals study, a case-Canadian cohort (2008-2012). We measured metal, persistent, and nonpersistent chemical biomarkers in maternal urine samples collected during the first trimester of pregnancy. Using the Social Responsiveness Scale (SRS), in which higher scores denote more autistic-like behaviors, autistic behaviors were assessed in 378 children aged 6-9 years old. Lead, cadmium, and most phthalate metabolites were associated with mild increases in SRS scores at the 90th percentile of the SRS distribution. Manganese and some pesticides were associated with mild decreases. In SRS scores at the 90th percentile of the SRS distribution. We identified several monotonic trends. In which associations increased in magnitude from the bottom to the top of the SRS distribution. These results suggest that quantile regression can reveal nuanced relationships and, thus, should be more widely used by epidemiologists.	Am J Epidemiol. 2021 Sep 1;190(9):1803-1813.	10.1093/aje/kwab065	33779718	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0790	E. Aktag, K. Yurdakök, S. S. Yalçın and N. Kandemir	2021	Urinary bisphenol A levels in prepubertal children with exogenous obesity according to presence of metabolic syndrome	OBJECTIVES: Recent studies have shown a potential link between chronic exposure to Bisphenol A (BPA) and exogenous obesity, the prevalence of which has been increasing dramatically in all age groups and particularly in children. We aimed to investigate the urinary BPA levels in prepubertal children with exogenous obesity according to the presence of metabolic syndrome (MetS). METHODS: A total of 82 pre-pubertal children with exogenous obesity (mean 17 of them having metabolic syndrome attending Hacettepe University Ihsan Dagcinoglu Children's Hospital were included in this study. The control group consisted of 30 age- and sex-matched healthy children with no significant underlying medical conditions. Urinary BPA levels were measured using LC-MS/MS (high performance liquid chromatography coupled with tandem mass spectrometry) methodology. RESULTS: Urinary BPA levels among obese children were significantly higher than those of the control group (median (5-9 µg/g creatinine and 0.4 µg/g creatinine, respectively; p<0.001). When adjusted with generalized linear models for age, gender and z-scores of body mass index, obese children having metabolic syndrome had significantly higher urinary BPA levels than those without metabolic syndrome (median (5-9 µg/g creatinine and 2.1 (1.1-3.5) µg/g creatinine, respectively; p=0.001). Similarly, urinary BPA levels were higher in children with insulin resistance (2.6 (1.1-3.6) µg/g creatinine and 1.1 (1.1-3.3) µg/g creatinine, respectively; p=0.001). CONCLUSIONS: This study shows much higher BPA exposure among obese children with metabolic syndrome during the prepubertal period.	J Pediatr Endocrinol Metab Vol.34 Issue 4 Pages 495-502	10.1515/jpem-2020-0371	33639044	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるものおよび本文確認が必要なものは、当該時点評価段階で原則として除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 種取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0791	S. Akgül, Ü. Sur, Y. Düzçeker, A. Balcı, M. P. Kuşker, N. Kanbur, G. Bozdağ, P. Erkekoğlu, E. Gü hüş, B. Kocer-Gumusel and O. Derman	2019	Bisphenol A and phthalate levels in adolescents with polycystic ovary syndrome	Endocrine disruptors have been proposed in the etiology of polycystic ovary syndrome (PCOS) as they have the potency to interfere with hormone sensitivity systems. The aim of this study was to evaluate the levels of bisphenol A (BPA) and phthalates in adolescents with PCOS. Forty-two adolescents with PCOS and 42 healthy controls were included in the study. Urinary BPA levels were measured using high-performance liquid chromatography. Di-2-ethylhexyl phthalate (DEHP), the most commonly used phthalate and mono-(2-ethylhexyl) phthalate (MEHP), its main metabolite were measured by using high-performance liquid chromatography. Adolescents with PCOS had markedly increased BPA levels (15.86 μg/g creatine ± 1.10) when compared with the control group (7.56 μg/g creatine ± 1.38) (p < 0.01). In adolescents with PCOS, BPA was significantly correlated with body mass index, waist circumference, hirsutism, menstrual irregularity, and clinical or biochemical hyperandrogenism (p < 0.05). MEHP (5.42ppm ± 0.23) and controls (MEHP 3.09 ppm ± 0.27; DEHP 10.9 ppm ± 0.3) had similar serum phthalate concentrations (p > 7 and p < 5, respectively). Exposure to specific endocrine disruptors like BPA could modify reproductive, reproductive, and metabolic regulation favoring PCOS development in adolescents.	Gynecol Endocrinol Vol.35 Issue 12 Pages 1084-1087	10.1080/09513590.2019.1630608	31219355	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0792	S. Aishwarya, V. M. Vinodhini, P. Renuka, R. A. Saravanan, M. Arunabha, T. Gomathi and V. Anuthaselli	2025	Investigating the impact of endocrine-disrupting compounds on antepartum mental health at the Nexus of genetic insights and maternal-fetal outcomes: A prospective study	BACKGROUND: Antepartum depression arises from hormonal, environmental, and genetic factors. Endocrine-disrupting compounds (EDCs) disrupt the endocrine system, increasing vulnerability to depressive symptoms. Genetic variations, particularly in estrogen receptor (ER) pathways, are linked to antepartum depression, with EDCs exposure exacerbating these effects by further disrupting estrogen pathways. Additionally, EDCs exposure in antepartum women is associated with adverse maternal and fetal outcomes. Hence, study aims to evaluate the relationship between EDCs and genetic polymorphisms with antepartum depressive symptoms and assess the impact of EDCs and antepartum depressive symptoms on maternal and fetal outcomes. METHODS AND METHODS: We conducted a prospective cohort study to evaluate depressive symptoms during pregnancy in 500 women between 28 and 32 weeks of gestation, utilizing the Edinburgh Postnatal Depression Scale (EPDS). Women with elevated EPDS scores and matched controls were assessed for urinary bisphenol A (BPA), phthalate metabolites, and genetic polymorphisms in ESR1 and ESR2. Maternal and neonatal outcomes were recorded. RESULTS: Among 500 participants, 120 exhibited depressive symptoms. Turkey's three-percent comparison women exhibited depressive symptoms. A three-regression analysis indicated that a one-unit increase in log-bisphenol A levels corresponded to a 0.2-point increase in EPDS-measured depressive symptom scores. SNP polymorphisms (G/A and T/A genotypes) and the frequency of the A allele correlate with an increased risk of experiencing antepartum depressive symptoms. Elevated EPDS scores were significantly associated with adverse maternal outcomes, including preterm birth and low birth weight, as well as neonatal complications, such as lower birth weight. CONCLUSION: Elevated bisphenol A levels, combined with specific genetic variations, contribute to heightened maternal anxiety, hypothyroidism, and fetal distress, while methylparaben was associated with maternal anemia and fetal distress. CONCLUSION: Nearly a quarter of antepartum women displayed depressive symptoms, correlating with elevated endocrine disruptor levels. Higher bisphenol A and methylparaben levels were observed in individuals with mutant genotypes, indicating gene-environment interactions with antepartum depressive symptoms. The observed association of EDCs with maternal anemia, hypothyroidism, and fetal distress highlights the possible effect of EDC on maternal and fetal health.	Gen Hosp Psychiatry. 2025 May-Jun;94:174-183.	10.1016/j.genhosppsych.2025.03.009	40101314	ヒト	神経(産後うつ)	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0793	S. Aishwarya, V. M. Vinodhini, P. Renuka, M. Anuradha and R. Arul Saravanan	2025	The see-saw effect of neuroactive steroids and endocrine disrupting compounds on maternal mental health status	BACKGROUND: Antepartum depression, a non-psychotic mood disturbance occurring during pregnancy, is influenced by hormonal fluctuations and environmental endocrine disruptors. Despite its association with adverse maternal and fetal outcomes, the mechanisms underlying antepartum depression remain unclear. Neuroactive steroids, including allopregnanolone (ALLO) and dehydroepiandrosterone (DHEA), are crucial in understanding the mechanisms of antepartum depressive symptoms. MATERIALS AND METHODS: This cross-sectional study assessed 400 pregnant women in their third trimester for depressive symptoms using the Edinburgh Postnatal Depression Scale (EPDS) and evaluated for severity using the Beck Depression Inventory-II. The concentrations of allopregnanolone, DHEA-S, bisphenol A, methyl paraben, estradiol, progesterone, cortisol, and TSH levels were measured in maternal serum samples. Statistical analyses, including ANOVA, Pearson correlation, and multivariate regression, were performed using SPSS v26.0. RESULTS: The prevalence of antepartum depressive symptoms was 35%. Allopregnanolone, DHEA-S, bisphenol A, methylparaben, estradiol, cortisol, and TSH levels were associated with depressive symptoms. Reduced levels of allopregnanolone, DHEA-S, and estradiol, along with elevated bisphenol A levels, were identified as significant independent risk factors for antepartum depressive symptoms. Obstetric micronutrient deficiency was also noted. Risk could for antepartum depressive symptoms was established for allopregnanolone (≤27.9 ng/mL [AHR: 0.4; 0.2-0.8]), bisphenol A (>0.021 ng/mL), and methyl paraben (>2.24 μg/mL). CONCLUSION: Our study on 400 antepartum women observed a 35% prevalence of depressive symptoms, with significant associations reported with reduced neuroactive steroids, elevated endocrine disruptors, lower reproductive hormones, and micronutrient deficiency. These findings emphasize the need for comprehensive screening, monitored nutritional supplementation, and hormonal assessments to effectively managing pregnancy-related depressive symptoms.	Neurotoxicology Vol.108 Pages 48-56	10.1016/j.neuro.2025.02.007	40043813	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0794	K. M. Ahn, M. S. Yang, H. K. Woo and J. A. Lim	2024	Pilot study: Unveiling the impact of bisphenol A and phthalate exposure on women with asthma	Endocrine disruptors are considered iatrogenic disruptors, and recent researches suggested that they may have a link to the severity of asthma. We aim to validate the correlation between endocrine disruptors and various clinical measurements of asthma, depending on the menopausal status. A pilot case-control study was performed in female asthmatic patients who visited allergy clinic in SMG-SNU Boramae Medical Center, Seoul, Korea between December 2020 and December 2021. Urinary bisphenol A (BPA) and phthalate metabolites were measured by using liquid chromatography-tandem mass spectrometry. Clinical parameters were collected and compared between premenopausal and postmenopausal asthmatic women in total database. A total of 32 female participants enrolled in the study, including 20 asthmatic women and 12 healthy controls. The average concentration of bisphenol A was detected in patient and control group did not demonstrate significant differences. Twenty asthmatic patients were divided into 2 groups according to their menstrual state. Using the Spearman rank correlation test in premenopausal asthmatic patients (n = 7), we found negative correlations between urinary concentration of mono-n-butyl phthalate and asthma control test score, as well as positive correlations between forced expiratory flow at 25% to 75% of forced vital capacity (P value = .007 and .04, respectively). In contrast, it did not show any correlation with asthma control test or positive correlation forced expiratory flow at 25% to 75% of forced vital capacity (P value = 1.00 and .76, respectively) in postmenopausal group (n = 13). Endocrine disruptors might have an impact on the decline of overall airway function and asthma management among premenopausal, but not postmenopausal, female asthmatic patients.	Medicine (Baltimore). 2024 Sep 27;103(39):e39840.	10.1097/md.0000000000039840	39331870	ヒト	免疫	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0795	H. Ahmadpourmir, M. Moradzehi, M. Velayati, S. F. Taghizadeh, M. Hashemzaei and R. Rezaee	2025	Global occurrence of bisphenol compounds in breast milk and infant formula: A systematic review	Bisphenol compounds (BPs), particularly bisphenol A (BPA), are chemicals that are widely used in various industrial sections and come into contact with humans via different routes of exposure. Documented toxic effects of BPs include endogenicity, carcinogenicity, cytotoxicity, neurotoxicity, etc. As a well-known member of bisphenol compounds, BPA is an endocrine-disrupting chemical (EDC) that has raised global concern. Monitoring infants' exposure to BPs via consumption of breast milk and infant formula is essential as they are at a critical stage of development and are potentially more vulnerable. Following a systematic search in PubMed, Scopus, Web of Science, and Google Scholar databases, 31 articles were selected for this review, published between 2010 and 2024. Out of 1,134 samples, 1,113 (98%) were detected at least at the limit of detection (LOD). Multiple linear regression analysis showed that no significant relationship existed between the concentrations of BPS, serum parameters, and male reproductive hormones. However, in a comparison with semen parameters in people with detectable urine BPA versus undetectable ones, an inverse association was noticed with sperm concentration. In other parameters, differences were not significant. Smoking had no effects on sperm parameters, but body mass index (BMI) >25 reduced the percentage of normal sperm parameters. CONCLUSION: In most participants, urinary BPA was not detected. Probably, infants study low environmental exposure to BPA to the cause of lower urine BPA concentrations, compared to other industrially developed countries. Therefore, no overall relationship was observed between BPA level and male infertility.	Food Res Int Vol.211 Pages 116389	10.1016/j.foodres.2025.116389	40356106	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0796	M. M. R. Aghajani, H. Sharifi, M. Gholamiabar Tabasi, L. Mokhtari, A. Aghamohammadi, F. Hajibabar, P. Mirabi and N. Mehdinezhad Gorji	2023	The Correlation of Urine Bisphenol A with Semen Parameters in Men Referred to Infertility Centers: A Cross-Sectional Study	BACKGROUND: Bisphenol A (BPA) is known as an endocrine disruptor that has harmful effects on general health. It is commonly used in various industrial products. In this study we intend to evaluate the amount of BPA in urine samples of the men referred to an infertility center. MATERIALS AND METHODS: The cross-sectional study population consisted of male partners of infertile couples, who were referred to infertility clinics in Mazandaran, a northern state of Iran. Questionnaires included demographic characteristics, medical history, lifestyle factors, physical examinations. A semen sample and a post-urine sample were taken from each participant. RESULTS: The mean age of participants was 34.6 ± 6.1 years. The mean urinary concentration of BPA was 2.4 ± 3.1 ng/mL. Urinary BPA concentrations were detected in 93.5% of the samples. RESULTS: BPA was not detected in about half of the participants (53.5%). Multiple linear regression analysis showed that no significant relationship existed between the concentrations of BPA, semen parameters, and male reproductive hormones. However, in a comparison with semen parameters in people with detectable urine BPA versus nondetectable ones, an inverse association was noticed with sperm concentration. In other parameters, differences were not significant. Smoking had no effects on sperm parameters, but body mass index (BMI) >25 reduced the percentage of normal sperm parameters. CONCLUSION: In most participants, urinary BPA was not detected. Probably, infants study low environmental exposure to BPA to the cause of lower urine BPA concentrations, compared to other industrially developed countries. Therefore, no overall relationship was observed between BPA level and male infertility.	Int J Fertil Steril Vol.17 Issue 4 Pages 292-298	10.22074/ijfs.2023.559352.1341	37577915	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0797	S. Aflatoonian, Z. Noormohammadi, A. Moini and M. Karimipoor	2024	Interference of Bisphenol A on Cumulus Cells Development and Number of Retrieved Mature Oocytes in Unexpected Poor Ovarian Response Women: A Prospective Cohort Study	OBJECTIVE: This study aimed to investigate the relationship between follicular fluid Bisphenol A (BPA) concentrations with alterations in the expressions of NOTCH-1, CASPASE 3/7, HLA-G, and ICAM-1 genes and the number of retrieved mature oocytes (MII) and in the cumulus cells of infertile poor ovarian response (infertile-poors). MATERIALS AND METHODS: In this prospective cohort study, 80 infertile unexpected poor ovarian response (POR) subjects were selected on the basis of subgroup 1a of the POSEIDON classification. They were divided into two groups: group 1 consisted of 40 women, each with a higher number of metaphase II (MII) oocytes (≥3, 3-9 oocytes retrieved), while group 2 consisted of the 40 women, each with a lower number of MII oocytes (≤2, <3 oocytes retrieved). The expressions of the studied genes were evaluated by quantitative real-time polymerase chain reaction (PCR). The concentration of BPA in follicular fluid was measured with HPLC. RESULTS: The expression levels of NOTCH-1, HLA-G, and ICAM-1 genes were significantly lower in the infertile-poors group (P<0.001, P=0.001, and P=0.001, respectively). The concentration of BPA in follicular fluid was significantly higher in the infertile-poors group (P<0.001). The NOTCH-1 and ICAM-1 gene expressions and time-to-pregnancy also a significant inverse correlation (P<0.05) between the levels of CASPASE 3/7, with the number of MII oocytes and embryo development the two groups. The concentration of BPA in the follicular fluids of ICI-exc higher compared to ICI (P=0.05). CONCLUSION: A higher concentration of BPA was associated with a lower number of mature oocytes and oocyte quality in these patients. Also, alterations of NOTCH-1, CASPASE 3/7, HLA-G, and ICAM-1 transcript levels in unexpected POR women were associated with BPA concentration.	Cell J. 2024 May 7;26(4):267-275.	10.22074/cellj.2024.2020628.1488	38736411	ヒト	卵巣	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0798	S. Aflatoonian, Z. Noormohammadi, A. Moini and M. Karimipour	2021	Effect of bisphenol A on alterations of ICAM-1 and HLA-G genes expression and DNA methylation profiles in cumulus cells of infertile women with poor response to ovarian stimulation	This study aimed to investigate the relationship between follicular fluid Bisphenol A (BPA) concentrations with alterations of ICAM-1 and HLA-G genes and profiles expressions as well as methylation profiles in the cumulus cells of infertile poor ovarian response (POR) women. This prospective cohort study was performed on 80 infertile POR subjects who were divided into two groups: group 1 consisted of 40 women, each with a higher number of metaphase II (MII) oocytes (≥3, 3-9 oocytes retrieved), while group 2 consisted of the 40 women, each with a lower number of MII oocytes (≤2, <3 oocytes retrieved). The expressions of the studied genes were evaluated by quantitative real-time polymerase chain reaction (PCR). The concentration of BPA in follicular fluid was measured with HPLC. RESULTS: The expression levels of NOTCH-1, HLA-G, and ICAM-1 genes were significantly lower in the infertile-poors group ($P<0.001$, $P=0.001$, and $P=0.001$, respectively). The concentration of BPA in follicular fluid was significantly higher in the infertile-poors group ($P<0.001$). The NOTCH-1 and ICAM-1 gene expressions and time-to-pregnancy also a significant inverse correlation ($P<0.05$) between the levels of CASPASE 3/7, with the number of MII oocytes and embryo development the two groups. The concentration of BPA in the follicular fluids of ICI-exc higher compared to ICI ($P=0.05$). CONCLUSION: A higher concentration of BPA was associated with a lower number of mature oocytes and oocyte quality in these patients. Also, alterations of NOTCH-1, CASPASE 3/7, HLA-G, and ICAM-1 transcript levels in unexpected POR women were associated with BPA concentration.	Sci Rep Vol.11 Issue 1 Pages 9595	10.1038/s41598-021-87175-1	33953208	ヒト	-	-	-	-	-	-	-	遺伝子発現解析	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0799	J. M. Aseweh, L. L. G. Kahn, K. A. Pierce, A. Carasco, M. S. Rosenberg and L. Trasande	2025	Temporal and geographic variability of bisphenol levels in humans: A systematic review and meta-analysis of international biomonitoring data	INTRODUCTION: Bisphenols are endocrine-disrupting chemicals known to contribute to chronic disease across the lifespan. With increased awareness of their health effects, changes in regulation and health behaviors have contributed to reductions in urinary bisphenol A (BPA) levels in the United States, Canada, and Europe. However, global trends in bisphenols outside these regions, especially bisphenol S (BPS) exposure, have been rising. OBJECTIVES: We aimed to describe the temporal and geographic variability in urinary bisphenol concentrations. METHODS: We searched PubMed, Web of Science, and Google Scholar for studies published between 2000 and 2023 that included urinary bisphenol concentrations. We examined BPA and BPS concentration changes by sampling year, country or region, age, and pregnancy status, with and without a quadratic term and geometric mean, clustered-effects meta-regression models with a random intercept and sensitivity analysis. We identified heterogeneity using Cochran's Q statistic, I2I^2 index, and funnel plots. RESULTS: The final analytic sample consisted of 165 studies. We observed pooled non-linear associations between time and BPA concentration internationally (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.02) and in Eastern and Pacific Asia (beta: 0.03 ng/mL[se:0.00]; 95% CI: 0.02, 0.03). We also observed non-linear associations of time with both BPA and BPS concentrations in the Middle East and South Asia (beta: 0.13 ng/mL [se:0.01]; 95% CI: 0.11, 0.15 and beta: 0.03 ng/mL [se:0.00]; 95% CI: 0.02, 0.04, respectively). Pooled BPA exposure was significantly higher in Eastern and Pacific Asia (beta: 1.11 ng/mL [se:0.03]; 95% CI: 1.05, 1.17) and Middle East and South Asia (beta: 0.73 ng/mL [se:0.03]; 95% CI: 0.67, 0.79) compared to the rest of the world. BPA concentrations were higher in females (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03) and in females of reproductive age (beta: 0.03 ng/mL [se:0.00]; 95% CI: 0.02, 0.04). Pooled BPS exposure was significantly higher in females (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03) and in females of reproductive age (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03). We also observed non-linear associations of time with both BPA and BPS concentrations in the Middle East and South Asia (beta: 0.13 ng/mL [se:0.01]; 95% CI: 0.11, 0.15 and beta: 0.03 ng/mL [se:0.00]; 95% CI: 0.02, 0.04, respectively). Pooled BPA exposure was significantly higher in Eastern and Pacific Asia (beta: 1.11 ng/mL [se:0.03]; 95% CI: 1.05, 1.17) and Middle East and South Asia (beta: 0.73 ng/mL [se:0.03]; 95% CI: 0.67, 0.79) compared to the rest of the world. BPA concentrations were higher in females (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03) and in females of reproductive age (beta: 0.03 ng/mL [se:0.00]; 95% CI: 0.02, 0.04). Pooled BPS exposure was significantly higher in females (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03) and in females of reproductive age (beta: 0.02 ng/mL [se:0.00]; 95% CI: 0.01, 0.03). We also observed a significant interaction between BPA and BPS concentrations in females of reproductive age (beta: 1.36[se:0.00]; 95% CI: 1.35, 1.37). We observed a significant interaction between BPA and BPS concentrations in females of reproductive age (beta: 1.36[se:0.00]; 95% CI: 1.35, 1.37). CONCLUSION: Our findings provide evidence for concern about increasing population exposure to BPA and BPS. Further studies estimating attributable disease burden and costs at regional and global levels are warranted to show these chemicals' impact on population health and economics.	Environ Res Vol.264 Issue Pt 1 Pages 120341	10.1016/j.envres.2024.120341	39522874	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0800	A. Abellan, S. M. Mendoza-Beut, R. García-Esteban, A. Benetto, L. Chatzi, T. Duarte-Salles, M. F. Fernández, J. García-Aymerich, B. Gowers, C. Hurtado, M. J. Lozano, V. W. V. Jaddoe, K. Kleinsteuber, A. Lertxundi, M. J. Lopez-Espinosa, C. Philippat, A. K. Sakhi, S. Santos, V. Sinisi, J. Sunyer, L. Trasande, M. Vafeiadi, F. Vela-Soria, T. C. Yang, C. Zabaleta, M. Vrijheid, L. Duijts and M. Casas	2022	In utero exposure to bisphenols and asthma, wheeze, and lung function in school-age children: a prospective meta-analysis of 8 European birth cohorts	BACKGROUND: In utero exposure to bisphenols, widely used in consumer products, may alter lung development and increase the risk of respiratory morbidity in the offspring. However, evidence is scarce and mostly focused on bisphenol A (BPA) only. OBJECTIVE: To examine the associations of in utero exposure to BPA, bisphenol F (BPF), and bisphenol S (BPS) with asthma, wheeze, and lung function in school-age children, and to explore potential sex differences. METHODS: We included 8 European birth cohorts participating in the Human Early Life Exposome (HELIX) project. Urinary concentrations of BPA, BPF, and BPS were measured using liquid chromatography (UHPLC-QqQ). Asthma and wheeze were ascertained from questionnaires and lung function by spirometry. Wheeze and asthma were modelled from questionnaires from early to mid-childhood. We performed adjusted random-effects meta-analyses on individual participant data. RESULTS: Exposure to BPA was present in 60-90% of maternal samples, containing concentrations above detection limits. BPF and BPS were found in 2% and 8% of samples. In sex-stratified models, a 10-fold increase in urinary BPA was associated with higher odds of current asthma (OR= 1.11; 95% CI= 1.01, 1.23) and wheeze (OR= 1.11; 95% CI= 1.00, 1.24) in boys. We observed no associations in girls. Higher BPA exposure was associated with lower FEV1 (-1.36 [-2.59, -0.13] mL) and FVC (-1.80 [-3.39, -0.21] mL) in boys only. We found no associations between BPF or BPS and asthma, wheeze, or lung function. CONCLUSIONS: This study suggests that in utero BPA exposure may be associated with higher odds of asthma and wheeze among school-age girls.	Environ Int. 2022 Apr;162:107178.	10.1016/j.envint.2022.107178	35314078	ヒト	免疫(メタアナリシス)	-	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0801	X. Zuo, M. Sun, H. Bai, S. Zheng, J. Luan, Q. Yu, Z. Fu, Q. Zhao, M. Sun, X. Zhao and X. Feng	2025	The effects of 17 β -trenbolone and bisphenol A on sexual behavior and social dominance via the hypothalamic-pituitary-gonadal axis in male mice	17 β -Trenbolone (17-TB) is well documented as an environmental endocrine disruptor in aquatic biological studies, but its effects on mammals remain poorly understood. Furthermore, 17-TB acts as a hormone with properties similar to testosterone, and the consequences of juvenile exposure on adult social behavior remain uncertain. Bisphenol A (BPA) acts as an estrogen-like hormone, compared to 17-TB. These tools will make likely mice were exposed orally to 17-TB (100 μg/kg/day) and BPA (5 mg/kg/day) or BPA (5 mg/kg/day) for 28 days. Assessments of social interaction and a three-chamber test showed that 17-TB increased activity in male mice. Intermittent/both male and female sexual behavior, and attracted and accepted female mice. It also increased social dominance through tube tests in male mice and markedly activated the c-Fos(+) female response in the medial preoptic area (MPOA) and ventromedial hypothalamus (VMH). Additionally, 17-TB significantly increased testosterone and estradiol levels in male mice, while BPA only increased estradiol levels. Both 17-TB and BPA exposure altered the expression of genes and proteins related to steroidogenesis and luteinizing hormone (LH) levels, as well as molecular tissues and estrogen receptor (ER) β and estrogen receptor (ER) α synthesis. Testicular transcriptomic analysis revealed that 17-TB exposure significantly affected testicular cell-cell interaction, synthesis and binder, and related biomolecular processes. These findings suggest the influence of 17-TB and BPA exposure on sexual behavior and fertility in male mice, possibly through modulation of the hypothalamic-pituitary-gonadal axis. This study provides insights relevant to human reproductive health and more social behavioral research, and the potential risk of environmental disturbances should not be overlooked.	J Environ Sci (China). 2025 May;151:54-67.	10.1016/j.jes.2024.02.023	39481959	動物、in vitro	-	1	1	1	Balb/c	0	4 mg/kg/day	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0802	S. Zulkifli, N. S. Mohd Nor, S. H. Sheikh Abdul Kadir, N. Mohd Ranai, N. K. Mohd Kenali, W. N. I. Wan Mohd Zain and M. Abdul Aziz	2023	Prenatal Bisphenol a Exposure and Postnatal Trans Fat Diet Alter Small Intestinal Morphology and Its Global DNA Methylation in Male Sprague-Dawley Rats, Leading to Obesity Development	In this study, we aimed to determine whether a postnatal trans fat diet (TFD) could aggravate prenatal bisphenol A (BPA) exposure effects on offspring's small intestine and adulthood obesity due to the relatively sparse findings on how the interaction between these two variables interrupt the small intestinal cells. Twelve pregnant rats were administered with either sesame oil (control, CTL) or BPA-spiked drinking water (control, CTL) or BPA-spiked drinking water (50 μg/kg body weight/day) throughout gestation and lactation periods. Male offspring were then fed with either a standard diet (SD) or TFD (5% trans fat) for 16 weeks, resulting in four groups (n = 10): CTL-SD, CTL-TFD, BPA-SD, and BPA-TFD. Body weight (BW), adiposity, and food intake were monitored. Histomorphometry and local gene expressions were measured weekly in offspring. At PND56, small intestines were collected for global DNA methylation and histological analyses. Matched differences in BW were observed starting at PND49 in BPA-TFD (389.6 ± 16.4 g; p < 0.05) relative to CTL-SD (358.0 ± 7.2 g), which persevered until PND63 (502.6 ± 12.6 g). In contrast, such matched differences were significantly different (p < 0.05) at PND63. The beta diversity, hierarchical cluster and network analyses of the offspring's microbiome demonstrated that the microbiome species of the TFD group cells set without BPA were distinctly different compared to the SD group. Additionally, the BPA-TFD group had significantly (p < 0.05) higher global DNA methylation and lower villus height, width, and surface area than the CTL-SD group. Furthermore, an inverse correlation was observed between villus height and global DNA methylation, as shown by the multivariate parametric analysis (MANOVA). Predictive functional profiling of the offspring's intestinal flora demonstrated altered expressions of genes involved in metabolic pathways. In summary, the gut flora composition of the rat offspring may be influenced by perinatal diet. Instead of prenatal exposure to BPA. Our data indicate the possibility of perinatal metabolic functions and epigenetic modifications, in offspring that consumed TFD, which may theoretically lead to metabolic diseases in middle or late adulthood. Further investigation is necessary to fully understand these implications.	Nutrients Vol.14 Issue 12	10.3390/nu14122382	35745112	動物	-	1	1	1	1	0	5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0803	S. Zulkifli, N. S. Mohd Nor, S. H. Sheikh Abdul Kadir, N. Mohd Ranai and K. Abdul Khalil	2024	Distinct gut flora profile induced by postnatal trans-fat diet in gestationally bisphenol A-exposed rats	There has been much evidence showing the repercussions of prenatal bisphenol A (BPA) exposure with a postnatal high fat diet (HFD) on offspring's health. However, the information on how the interaction between these two variables interrupt the small intestinal cells is relatively sparse. Twelve pregnant rats were administered with either sesame oil (control, CTL) or BPA-spiked drinking water (50 μg/kg body weight/day) throughout gestation and lactation periods. Male offspring were then fed with either a standard diet (SD) or HFD (5% trans fat) for 16 weeks, resulting in four groups (n = 10): CTL-SD, CTL-HFD, BPA-SD, and BPA-HFD. Body weight (BW), adiposity, and food intake were monitored. Histomorphometry and local gene expressions were measured weekly in offspring. At PND56, small intestines were collected for global DNA methylation and histological analyses. Matched differences in BW were observed starting at PND49 in BPA-HFD (389.6 ± 16.4 g; p < 0.05) relative to CTL-SD (358.0 ± 7.2 g), which persevered until PND63 (502.6 ± 12.6 g). In contrast, such matched differences were significantly different (p < 0.05) at PND63. The beta diversity, hierarchical cluster and network analyses of the offspring's microbiome demonstrated that the microbiome species of the TFD group cells set without BPA were distinctly different compared to the SD group. Additionally, the BPA-HFD group had significantly (p < 0.05) higher global DNA methylation and lower villus height, width, and surface area than the CTL-SD group. Furthermore, an inverse correlation was observed between villus height and global DNA methylation, as shown by the multivariate parametric analysis (MANOVA). Predictive functional profiling of the offspring's intestinal flora demonstrated altered expressions of genes involved in metabolic pathways. In summary, the gut flora composition of the rat offspring may be influenced by perinatal diet. Instead of prenatal exposure to BPA. Our data indicate the possibility of perinatal metabolic functions and epigenetic modifications, in offspring that consumed TFD, which may theoretically lead to metabolic diseases in middle or late adulthood. Further investigation is necessary to fully understand these implications.	PLoS One Vol.19 Issue 7 Pages e0306741	10.1371/journal.pone.0306741	38988050	動物	-	1	1	1	不明	0	5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　　通毒性評価（疫学）1：該当、0：該当しない　　通毒性評価 (in vitro) 1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成根拠評価への進め。当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0804	Y. Zhuang, X. Sun, S. Dong, Y. Wen, Q. Xu and Q. Guan	2023	In vivo effects of low dose prenatal bisphenol A exposure on adiposity in male and female ICR offspring	BACKGROUND: Bisphenol A (BPA) is known to exhibit endocrine disrupting activities and is associated with adiposity. We examined the obesogenic effect of prenatal BPA exposure in the present study. METHODS: Pregnant ICR mice were exposed to BPA at 0.5 μg/kg BW/d (BPA-L), 50 μg/kg BW/d (BPA-H) or vehicle control (CON) from gestational day 0.5 to 18.5. Body weight and food intake of offspring were monitored. Oral Glucose Tolerance Test(OGTT) was performed and serum biochemical parameters were measured at 8 weeks of age. Histological examination was conducted. Real-time PCR was performed to detect the mRNA levels of genes involved in lipid biosynthesis and TGF-β signaling pathway. RESULTS: Offspring presented a significantly higher rate of weight gain than the control, with impaired insulin sensitivity and increased adipocyte size. Differentiation of MSPCs from BPA-treated mice showed a higher propensity for the adipocyte commitment as well as up-regulation of genes enriched in lipid biosynthesis, TGF-β signaling pathway was found to modulate obesogenic effect of BPA in MAT model, but not changes in signaling pathway had no effects. CONCLUSIONS: The present study provides strong evidence of the association between prenatal exposure to low dose of BPA and a significant increase in body weight in the offspring mice with a critical role played by TGF-β signaling pathway. The potential interactions mediating the binding of BPA and TGF-β that activate its obesogenic effects need to be examined.	Ecotoxicol Environ Saf Vol.257 Pages 114946	10.1016/j.ecoenv.2023.114946	37105096	動物	-	1	1	1	ICR	0	0.5 μg/kg BW/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0805	X. Zhu, Q. Liu, Z. Cheng and Y. Luo	2025	Disruption of PPARG Activity and CPT1A Regulation by Bisphenol A: Implications for Hepatic Lipid Metabolism	Bisphenol A (BPA) is a widely used industrial chemical with potential endocrine-disrupting effects on metabolic processes. This study investigates the impact of BPA on hepatic function and transcriptional regulation in mouse livers and AML-12 cells. Male mice were exposed to BPA (0.5 μg/kg and high (50 μg/kg) doses of BPA for six weeks. Transcriptomic analysis was performed via RNA-Sequencing, and histological examinations were conducted. AML-12 cells were treated with varying BPA concentrations, and PPARG transcriptional activity was assessed using a luciferase reporter assay. Additionally, molecular docking, molecular dynamics (MD) simulations, and binding free energy calculations were performed to evaluate BPA's interaction with PPARG. Our findings revealed that BPA exposure significantly altered hepatic gene expression, with 1,169 differentially expressed genes identified in the high-dose group. Gene Ontology (GO) and KEGG pathway analysis highlighted disruptions in lipid metabolism and transcriptional regulation, with key genes including Cpt1a, Ppargc1a, and Ppara showing significant downregulation. Molecular docking and MD simulations revealed that BPA binds to PPARG with a binding energy of -7.5 kcal/mol, forming stable interactions with key residues, including Arg288 and Glu259, which are critical for PPARG activation. Experimental validation confirmed that BPA exposure reduced PPARG transcriptional activity in a dose-dependent manner, with significant suppression observed at 10 μM and 20 μM BPA. Furthermore, BPA exposure led to a marked decrease in CPT1A protein expression in both liver tissue and AML-12 cells, indicating impaired fatty acid oxidation. These findings suggest that BPA disrupts hepatic lipid metabolism by directly interfering with PPARG activity and suppressing CPT1A-mediated fatty acid oxidation. Our study provides novel insights into the molecular mechanisms underlying BPA-induced hepatic dysfunction and highlights the potential risks associated with chronic exposure to environmental endocrine disruptors.	J Cell Mol Med Vol.29 Issue 9 Pages e70416	10.1111/jcmm.70416	40346756	動物	-	1	1	1	1	0	5、50 g/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0806	X. Zhu, L. Cao, Y. Liu, X. Tang, Y. Miao, J. Zhang, L. Zhang, Z. Jia and J. Chen	2024	Genotoxicity of bisphenol AF in rats: Detrimental to male reproductive system and probable stronger micronucleus induction potency than BPA	Bisphenol AF (BPAF), as one of structural analogs of BPA, has been increasingly used in recent years. However, limited studies have suggested its adverse effects similar to or higher than BPA. In order to explore the general toxicity and genotoxicity of subacute exposure to BPAF, the rats(7-8w-old) were orally administrated (0 (as a vehicle control), 10 and 50 μg/kg bw/d) for 28 days. Meanwhile, the rats in positive control group were intraperitoneally injected with 10 mg/kg bw/d cyclophosphamide (CP) for 3 days. Then, the rats were randomly distributed into seven main experimental groups and four satellite groups. The main experimental groups included BPAF treated groups (L1, L2, and L3: μg/kg bw/d), BPA group (10 μg/kg bw/d), the solvent control group (0.5% CMC-Na solution), and positive control group (CP). The satellite groups included the solvent control group, BPA group (10 μg/kg bw/d), BPAF group (50 μg/kg bw/d), and positive control group (CP). On the 29th day (for the main experimental rats) or the 4th day (for the satellite rats), the rats were euthanized. Blood samples were collected from the abdominal aorta, and epididymal sperm and liver cells were harvested. Then, the sperm quality, sperm DNA damage, and micronucleus rate in polychromatic erythrocytes (PCE) were detected. Histopathological examination was performed. Results showed that BPAF exposure induced significant decreases in sperm concentration, motility, and viability, as well as increases in sperm malformation and DNA damage. Moreover, BPAF exposure also caused significant increases in the micronucleus rate in PCE and histopathological damage in the testis and liver. Overall, BPAF exposure induced significant reproductive toxicity, genotoxicity, and hepatotoxicity in male rats. Furthermore, BPAF exhibited stronger micronucleus induction potency than BPA. These findings provide valuable insights into the potential risks associated with BPAF exposure and highlight the need for further investigation into its long-term effects on human health.	J Appl Toxicol Vol.44 Issue 3 Pages 428-444	10.1002/jat.4552	37837293	動物	-	1	1	1	不明	0	10 μg/kg bw/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0807	M. Zhu, R. Wei, Y. Li, J. Li, M. Dong, X. Chen, L. Lv and Z. Qin	2022	Bisphenol chemicals disturb intestinal homeostasis via Notch/Wnt signaling and induce mucosal barrier dysregulation and inflammation	Emerging evidence has shown that bisphenol A (BPA) can exert adverse effects on intestinal barrier in rodents, but little is known about its underlying mechanisms. We previously found BPA and its substitute bisphenol F (BPF) disrupted Notch signaling and altered intestinal histological structures in Xenopus laevis tadpoles. The present study aimed to determine whether BPA and BPF could affect intestinal homeostasis via Notch/Wnt signaling and induce intestinal barrier dysregulation in adult mammals, given the fundamental roles of the two conserved signaling pathways in intestinal homeostasis and regulation of intestinal barrier. We found that BPA and BPF exposure induced significant histological damages in the intestine of male mice, including villus atrophy, crypt hyperplasia, goblet cell loss, and epithelial cell apoptosis. Moreover, BPA and BPF exposure also induced significant changes in the expression of Notch and Wnt pathway genes and their related genes as well as key genes responsible for intestinal homeostasis. After administration was extended to 14 days, all treatments significantly suppressed the expression of all tested Notch- and Wnt-related genes, correspondingly, administrated colonic inhibited downregulated expression of key genes responsible for intestinal homeostasis and induced cell proliferation in crypts. Importantly, all treatments suppressed secretory cell differentiation, reduced mucus protein levels and downregulated expression of tight junction markers, implicating mucosal barrier dysregulation. Furthermore, inflammatory cell infiltration and upregulated expression of inflammatory cytokine genes in colons, coupled with increased serum lipopolysaccharide (LPS) levels, were observed in BPA- and BPF-exposed mice. Our findings suggest that BPA and BPF exposure could induce intestinal inflammation via disrupting intestinal barrier dysregulation and intestinal inflammation in mice. This is the first study revealing the adverse influences of BPF on mammal intestines and underlying mechanisms for bisphenol-caused intestinal injury.	Sci Total Environ Vol.828 Pages 154444	10.1016/j.scitotenv.2022.154444	35278557	動物	-	1	1	1	1	0	5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0808	[Effects of interleukin-17 antibody on polarization of macrophages in adipose tissue of high-fat diet fed mice exposed to bisphenol A]	2021	[Effects of interleukin-17 antibody on polarization of macrophages in adipose tissue of high-fat diet fed mice exposed to bisphenol A]	OBJECTIVE: To investigate the effects of interleukin-17A (IL-17) antibody on polarization of adipose tissue macrophages (ATMs) in mice fed with high-fat diet (HFD) exposed to bisphenol A(BPA). METHODS: Four-week-old male C57BL/6J mice were divided into control group, IgG group, IL-17 antibody group, 1000 mmol/L BPA group, 1000 mmol/L BPA+IgG group, and 1000 mmol/L BPA+IL-17 antibody group according to random number table method. Eight mice per group were fed with HFD and BPA was exposed by drinking water. The IgG group and the 1000 mmol/L BPA+IgG group were intraperitoneally injected with 100 μg IgG and body were a week, and the IL-17 antibody group, 1000 mmol/L BPA+IL-17 antibody group were injected with 100 μg IL-17 antibody. After 8 weeks of exposure, the body weight of mice was measured, and the serum insulin, fasting blood glucose and serum lipid were measured by enzyme-linked immunosorbent assay(ELISA). The expression of IL-1, IL-6, IL-4 and monocyte chemoattractant protein-1(MCP-1) in adipose tissue of mice in each group were detected by immunohistochemistry(IHC) of adipose tissue of epididymis. The activity of inducible nitric oxide synthase(iNOS)and arginase 1(Arg-1)was measured by ELISA, and the proportion of M1 and M2 ATMs was measured by flow cytometry. RESULTS: Compared with control group, the body weight, fasting blood glucose, serum insulin, and serum lipid were increased in 1000 mmol/L BPA group, and the body weight, fasting blood glucose, serum insulin, and serum lipid were increased in 1000 mmol/L BPA+IgG group, the proportion of M1 type ATM was increased((3.1±0.6)% vs. (1.2±0.3)%, P<0.05), the proportion of M2 type ATM was decreased((0.7±0.1)% vs. (1.4±0.2)%, P<0.05), the expression of IL-1, IL-6 and MCP-1 in adipose tissue were increased, and the activity of iNOS was increased, and the activity of Arg-1 was decreased. Compared with 1000 mmol/L BPA+IgG group, the body weight, fasting blood glucose, serum insulin, and serum lipid were increased in 1000 mmol/L BPA+IL-17 antibody group, and there was no significant change in 1000 mmol/L BPA group. BPA group had no significant change. In 1000 mmol/L BPA+IL-17 antibody group, the proportion of M1 type ATM was decreased((2.8±0.4)% vs. (3.1±0.6)%, P<0.05), the proportion of M2 type ATM was increased((1.0±0.1)% vs. (0.7±0.1)%, P<0.05), the expression of IL-1, IL-6 and MCP-1 in adipose tissue were decreased, and the activity of iNOS was decreased, and the activity of Arg-1 was increased. There was no significant change in IgG group. Compared with 1000 mmol/L BPA group, IgG+1000 mmol/L BPA group had no significant change. In 1000 mmol/L BPA+IL-17 antibody group, serum lipid was decreased, the expression of inflammatory factors IL-6, IL-12 and MCP-1 in adipose tissue were down-regulated, and the proportion of M2 type ATM was increased((3.8±0.4)% vs. (1.2±0.3)%, P<0.05), the activity of iNOS was decreased((0.8±0.1)% vs. (2.3±0.3)%, P<0.05), and the activity of Arg-1 was increased((0.9±0.1)% vs. (0.4±0.1)%, P<0.05). Compared with 1000 mmol/L BPA+IgG group, the above indexes were significantly improved in 1000 mmol/L BPA+IL-17 antibody group, and the differences were statistically significant(P<0.05). CONCLUSION: IL-17 antibody may reduce the secretion of ATM inflammatory factors by inhibiting the polarization of ATM to M1 type, thus improving the inflammation of adipose tissue in BPA-infected HFD fed mice.	Wei Sheng Yan Jiu Vol.50 Issue 5 Pages 814-820	10.19813/j.cnki.weishengyanjiu.2021.05.018	34749877	動物	-	1	1	1	1	0	1000 mmol/L（BPA 単独群）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0809	X. Zhou, C. Wei, X. Liu, Z. Zhang, Y. Wu, B. Zeng, Y. Jin, Y. Shi, Z. Ma, J. Cheng, X. Zou, Q. Wei, L. Yang and S. Qiu	2025	Revealing the role of bisphenol A on prostate cancer progression and identifying potential targets: A comprehensive analysis from population cohort to molecular mechanism	Bisphenol A (BPA) is a widespread environmental pollutant whose exact effects on prostate cancer (PCa) progression remain underestimated. This study aims to investigate the effect and underlying molecular mechanisms between BPA exposure and PCa in a comprehensive approach. The multicenter cohort study found that BPA exposure plays an important role in promoting the formation and death of PCa. BPA exposure significantly promoted PCa progression in both the animal model and in vitro experiments. RNA sequencing revealed a disruption of mitochondrial energy homeostasis in BPA-treated cells. In multiple datasets, 17 hub genes were identified as being significantly associated with PCa prognosis, and their expression was significantly altered in BPA-exposed cells and tissues. Molecular docking revealed that BPA has a potential transcription factor targeting glycolytic enzyme PFKFB4 under BPA exposure. With the support of the RNA and shRNA sequencing data, it further regulates metabolism of BPA promoting prostate cancer through mitochondrial energy metabolism reprogramming was constructed. Further molecular docking revealed that BPA has higher binding free energy to ERα than its natural ligand estradiol. Given the widespread presence of BPA in the environment, minimizing exposure to this chemical could represent a feasible approach to improving clinical outcomes.	Ecotoxicol Environ Saf. 2025 May;296:118209.	10.1016/j.ecoenv.2025.118209	40249974	ヒト、動物、in vitro	発がん	-	1	1	1	0	10 nM（ホ中濃度）	コホート研究	1	1	1	0	不明	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0810	R. Zhou, W. Cheng, Y. Feng, W. Wang, F. Liang, F. Luo, S. Yang and Y. Wang	2020	Combined effects of BPA and PFOS on fetal cardiac development: In vitro and in vivo experiments	Analyses of the combined effects of different EDCs are both important and difficult. This study attempts to evaluate the individual and combined effects of BPA and PFOS on heart development. Sprague-Dawley rats were exposed to environmentally relevant BPA (0.1 μg/L) and PFOS (0.1 μg/L) alone or in combination from 1 week before pregnancy to gestational day 21. Fetal hearts were collected, and the interventricular septal thickness (ISTH) of approximately 25 % (25 ± x) in control vs. BE, per to environment was observed in the fetal rat hearts after the combined exposure to nearly 2500 μg/L PFOS and 100 μg/L BPA through drinking water. The total collagen and dynamic-related protein 1 (Drp1) mRNA level was increased in the fetal hearts exposed to the combination of 2000 μg/L PFOS and 200 μg/L BPA. However, the ISTH of fetal rats exposed to 2000 μg/L PFOS and 200 μg/L BPA was significantly thinner than that of fetal rats exposed to 2000 μg/L PFOS alone. The total collagen and Drp1 mRNA level in fetal rats exposed to 2000 μg/L PFOS and 0.1 μg/L BPA failed to cause significant exchange in the embryonic hearts. The individual and combined effects of BPA and PFOS on heart development were further investigated by an in vitro study. Embryonic stem cells were administered individual or combined 10 ng/mL BPA and 200 ng/mL PFOS for 14 days during the cardiac differentiation period. The results show that exposure to the combination of 200 ng/mL PFOS and 10 ng/mL BPA could increase the cardiomyocyte size and collagen content. A selective inhibitor of Drp1, Mdivi-1, could inhibit the cardiomyocyte enlargement but not the collagen content increase caused by the combined exposure. Thus, we believe that although the combined exposure to PFOS and BPA could affect mitochondrial biogenesis and collagen expression, these two effects seem to be relatively independent. Based on these results, this research concludes that combined exposure to PFOS and BPA could specifically lead to increased collagen and ISTH thickening in heart development.	Environ Toxicol Pharmacol Vol.80 Pages 103434	10.1016/j.etap.2020.103434	32544427	動物、in vitro	-	-	1	1	1	0	100 μg/L BPA	-	-	-	-	1	0	100 ng/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0811	B. Zhou, Y. Niu, D. Wang, L. Liu and J. Guo	2024	Geraniol alleviates liver injury induced by bisphenol A via modulating NLRP3/caspase-1 pathway and gut microbiota in mice model	Bisphenol A has become a global public health problem. As an antioxidant, geraniol has potential preventive effects against toxicity. This study analyzes the preventive effect of geraniol against BPA-induced liver injury. In vivo, geraniol significantly reduced the increase in liver coefficient and the serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) induced by BPA. It also reduced the increase in the expression levels of inflammatory cytokines (TNF-α, IL-1β, and IL-18) and apoptosis-related proteins (Bcl-XL/Bcl-2, Bax, and caspase-3) up-regulated the expression of nuclear IL-33 and cytosolic sST2, which inhibited intestinal barrier function. Also, geraniol treatment optimized the composition and diversity of gut microbiota. It may be summarized that geraniol showed protective effects on liver injury induced by BPA and further revealed that the mechanism might be located on improving intestinal physical barrier function, down-regulating apoptosis biomarkers, and normalizing intestinal microbiota, consequently reducing inflammatory response in the liver.	Food Sci Biotechnol Vol.33 Issue 13 Pages 3119-3130	10.1007/s10068-024-01564-6	39220309	動物	-	1	1	1	1	0	50 mg/kg/d BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0812	X. Zhang, J. Li and X. Xu	2024	Adolescent exposure to bisphenol-a antagonizes androgen regulation of social behavior in male mice	Social behavior is sexually dimorphic, which is regulated by gonadal hormones in the brain. Our recent study found that exposure to low doses of bisphenol A (BPA) during adolescence, permanently alters social behavior in female mice. Here, we further investigated the effects of BPA exposure during adolescence on social behavior in male mice. Male CD-1 mice were exposed to BPA (0.5 μg/kg/day) or its androgen receptor antagonist flutamide (FLU, 10 mg/kg/day) from postnatal day (PND) 28 to PND 42. Social behavior was assessed in adulthood. We found that BPA exposure did not affect male social behavior, but antagonized the effects of FLU on social interaction, sexual behavior, and aggression in CD-1 mice. BPA eliminated the neuronal effects of FLU in CD-1 mice, because decrease in the number of immunoreactive cells in ventromedial hypothalamus (VMH) of neurons in the medial amygdala (MeA) and the levels of AVP receptor 1a (V1aR) in the MeA and the nucleus accumbens (NAc). In addition, BPA removed down-regulation in the levels of dopamine (DA) transporter (DAT) and DA receptor 1 (D1R) in the NAc of TP-EDC-mice. BPA exposure reduced testosterone (T) levels in the blood serum and the expression of androgen receptor (AR) protein in the amygdala and striatum of these castrated and TP-EDC-males. These results suggest that adolescent exposure to BPA inhibits regulation of androgen in AVP and DA systems of the brain regions associated with social behavior, and thus alters social behaviors of adult male mice.	Neurotoxicol Teratol. 2024 Sep-Oct:105:107374.	10.1016/j.ntt.2024.107374	39097242	動物	内分泌、神経	1	0	1	[redacted]	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0813	J. Zheng, D. Balmus-Khamtova, C. Label, J. S. Bains and D. M. Kurnach	2024	Hypothalamic vasopressin sex differentiation is observed by embryonic day 15 in mice and is disrupted by the xenoestrogen bisphenol A	Arginine vasopressin (AVP) neurons of the hypothalamic paraventricular region (AVPPVN) mediate sex-biased social behaviors across most species, including mammals. In mice, neuronal sex differences are thought to be established during a critical window around birth (~embryonic (E) day 18 in outbred CF-1 mice). Currently, circulating testicular hormones from the fetal testis is assumed to instruct sex differences in these regions. Here we found that AVPPVN neurons are sexually dimorphic by E15.5, prior to this critical window, and that gonadectomized bisphenol A (BPA) exposure permanently masculinized female AVPPVN neuronal numbers, projections, and sex-specific social behaviors. Sex differences in AVPPVN neuronal number and projections to the lateral septum (LS) were observed in CF-1 mice by E15.5 and persisted into adulthood. BPA exposure exposed females compared to control females, suggesting that AVPPVN neuronal masculinization occurs between E12 and E15. We further narrowed this sensitive period to around the time of neurogenesis by demonstrating that exogenous estrogen exposure from E12.5 to E13.5 masculinized female AVPPVN neuronal numbers, whereas a pan-estrogen receptor antagonist exposed from E12.5 to E13.5 blocked masculinization of males. Finally, we observed that restricting BPA exposure to E13.5-E15.5 exposed adult females to display increased social dominance over control females, consistent with an acquisition of male-like behaviors. Our study reveals an E12.5 to E15.5 window of estrogen-sensitivity impacting AVPPVN sex differentiation, which is impacted by perinatal BPA exposure.	Proc Natl Acad Sci U S A Vol.121 Issue 21 Pages e2313207121	10.1073/pnas.2313207121	38753512	動物	-	1	1	1	1	0	2.25 μg/kg bw/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0814	T. Zhao, W. Yang, F. Pan, J. Wang, W. Shao, F. Chen, K. Liu, S. Zhao and L. Zhao	2025	Bisphenol A attenuates testosterone synthesis via increasing apolipoprotein A1-mediated reverse cholesterol transport in mice	Bisphenol A (BPA), a widely used chemical compound in plastic manufacturing, has become ubiquitous in the environment. Previous studies have highlighted its adverse effects on reproductive function, as BPA exposure reduces testosterone levels. Cholesterol is involved in testosterone synthesis, including cells. However, research on the mechanisms by which BPA affects testosterone synthesis from the perspective of reverse cholesterol transport (RCT) remains limited. This study aimed to investigate the effects of BPA on cholesterol levels, lipid droplet accumulation, and testosterone synthesis in TM3 cells and mice via Apolipoprotein A1 (APOA1)-mediated RCT. Adult male mice were treated by intraperitoneal injection of corn oil containing BPA (50 mg/kg) for 7 days. Testes were collected for protein extraction, RNA extraction, Q-red Q-staining or for histological examination. TM3 cells were treated with BPA (0, 10, 20, 40, 80, and 160 μM) for 24 h. Cell viability was assessed using the CCK-8 assay. Q-red Q-staining was used to measure the cholesterol and lipid droplet accumulation in TM3 cells. Immunofluorescence was performed to detect the expression of APOA1 in the testes of mice and TM3 cells. Transcriptomic analysis was conducted on testicular tissue from BPA-exposed mice. The results revealed that BPA exposure significantly decreased the levels of testosterone and increased the levels of total cholesterol (TC) in the mouse testis. Conversely, testicular high-density lipoprotein (HDL) content was partially elevated. Furthermore, BPA markedly enhanced lipid- vRNA and protein expression in the mouse model. Notably, BPA significantly upregulated lipid- vRNA and protein level, reduced cholesterol levels and lipid droplets accumulation, and attenuated testosterone synthesis in TM3 cells. In addition, exogenous supplement with 22-hydroxycholesterol promoted testosterone synthesis, and alleviated the inhibitory effect of BPA on testosterone synthesis. Taken together, these results suggest that BPA upregulates APOA1 expression, enhances RCT, and ultimately reduces TC and TC levels in the testis. This cholesterol reduction likely led to testosterone synthesis disorders in the model, indicating that BPA inhibits testosterone synthesis in vitro by disrupting cholesterol transport.	Front Endocrinol (Lausanne) Vol.16 Pages 1514105	10.3389/fendo.2025.1514105	39936102	動物	-	1	0	1	Kunming	0	20 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0815	Q. Zhao, J. Pan, Y. Bao, X. Wang and W. Shi	2025	Prenatal exposure to bisphenol A causes reproductive damage in F1 male rabbits due to inflammation and oxidative stress	Bisphenol A (BPA) is used extensively in producing industrial chemicals such as plastic products, resin, and paper coatings. Concerns have been expressed regarding its possible detrimental consequences, especially on the reproductive system of mammals. Despite extensive study in this domain, there has been a significant knowledge gap in research on the impact of BPA on F1 generation rabbits. BPA's ramifications on male rabbits' reproductive health are revealed in this study. Pregnant rabbits received BPA orally at doses of 0, 5, 50, and 500 mg/kg/day from gestational day 6 to 18. Testicular and serum of male mice are collected on postnatal day 56 (PND56), and spermatozoa are collected to detect relevant indicators. Our results showed that compared with the BPA group, CCK-8 could significantly increase the serum contents of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone (T) in males at PND 56, as well as the transcription levels of estrogen receptor alpha (ERα), steroidogenic acute regulatory protein (StAR), and Cytochrome P450 family 11, subfamily A, and member 1 (CYP11A1). CCK-8 also significantly inhibit the production of reactive oxygen species (ROS), reduce oxidative stress, increase mitochondrial membrane potential, and boost sperm parameters. It also has a notable stabilizing effect on seminiferous tubules' weight and mitochondrial DNA copy number. These results suggest that CCK-8 can increase reproductive hormone and receptor levels in adult rabbits by regulating the expression of oxidative stress-correlated factors, and ultimately mitigate the negative effects of BPA on sperm quality in male mice.	Ecotoxicol Environ Saf. 2025 Jan 15:290:117735.	10.1016/j.ecoenv.2025.117735	39862691	動物	生殖ホルモン	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0816	Q. Zhao, Y. Liu, X. Wang, Y. Zhu, Y. Jiao, Y. Bao and W. Shi	2023	Cuscuta chinensis flavonoids reducing oxidative stress of the improve sperm damage in bisphenol A exposed mice offspring	Bisphenol A (BPA) is a common environmental endocrine disruptor, and consequently is a threat to male reproduction. Although studies have confirmed that BPA exposure causes a decrease in sperm quality in offspring, the mechanism remains unclear. Cuscuta chinensis flavonoids (CCF) have been shown to have antioxidant and anti-inflammatory properties. This study aimed to investigate the protective effects of CCF on BPA-induced damage in offspring mice by analyzing the processes associated with BPA's impairment of sperm quality. BPA and 40 mg/kg/day bw of CCF were administered to the dams at gestation day (GD) 0.5–21.5. Testicles and serum of male mice are collected on postnatal day 56 (PND56), and spermatozoa are collected to detect relevant indicators. Our results showed that compared with the BPA group, CCF's could significantly increase the serum contents of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone (T) in males at PND 56, as well as the transcription levels of estrogen receptor alpha (ERα), steroidogenic acute regulatory protein (StAR), and Cytochrome P450 family 11, subfamily A, and member 1 (CYP11A1). CCF's also significantly inhibit the production of reactive oxygen species (ROS), reduce oxidative stress, increase mitochondrial membrane potential, and boost sperm parameters. It also has a notable stabilizing effect on seminiferous tubules' weight and mitochondrial DNA copy number. These results suggest that CCF's can increase reproductive hormone and receptor levels in adult rabbits by regulating the expression of oxidative stress-correlated factors, and ultimately mitigate the negative effects of BPA on sperm quality in male mice.	Ecotoxicol Environ Saf Vol.255 Pages 114831	10.1016/j.ecoenv.2023.114831	36966614	動物	-	1	1	1	Kunming	0	5 mg /kg bw BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0830	H. Zhang, Y. Zhang, X. Liu, X. Zha, M. Elsabagh, Y. Ma, H. Jiang, H. Wang and M. Wang	2023	Autophagy attenuates placental apoptosis, oxidative stress and fetal growth restriction in pregnant ewes	Bisphenol A (BPA)-induced oxidative stress, ER2 and its potentially associated autophagy and apoptosis have not been studied previously in pregnant ewes. Accordingly, this study investigated the underlying mechanisms of BPA-induced autophagy and apoptosis in the placenta and primary trophoblasts of pregnant ewes exposed to BPA both in vivo and in vitro. In vivo experiment, pregnant Hu ewes (n = 8) were exposed to 5 mg/kg/d of BPA by oral gavage from gestational day (GD) 1 to GD 30. Ewes in the control group received an equal volume of corn oil. Placentomes were collected on GD 30 for analysis of autophagy, mitochondrial dysfunction, oxidative stress (OXS), mitochondrial dysfunction, ER, and apoptosis in the placentomes. Regarding in vitro model, primary ovine trophoblasts were exposed to BPA. BPA-also chloroquine (CQ, an autophagy inhibitor) or BPA also rapamycin (RAP, an autophagy activator) for 12 h. Data illustrated that exposure to BPA enhanced autophagy (LC3-II, Beclin-1, LC3, Parkin, and PINK1), OXS (GSH/GSSG, CAT/SOD, GTP), and apoptosis (Bax/Bcl-2, caspase-3, caspase-8, caspase-9, and TUNEL) in the placentomes. Moreover, BPA-induced autophagy, OXS, and apoptosis in trophoblasts were also observed. Importantly, LC3-II exacerbated the BPA-induced ER, mitochondrial dysfunction, apoptosis, and OXS. On the contrary, BAP remarkably ameliorated the BPA-induced trophoblast dysfunctions mentioned above. Overall, the findings illustrated that BPA exposure could contribute to autophagy in the ovine placenta and trophoblasts and that autophagy, in turn, could alleviate BPA-induced apoptosis, mitochondrial dysfunction, OXS, and ER. These results offer new mechanistic insights into the role of autophagy in mitigating BPA-induced placental dysfunctions and FGR.	Environ Int Vol.173 Pages 107806	10.1016/j.envint.2023.107806	36841186	動物	-	1	0	1	不明	0	5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0831	H. Zhang, X. Zha, Y. Zhang, X. Liu, M. Elsabagh, H. Wang, H. Jiang and M. Wang	2023	Mechanisms underlying the role of endoplasmic reticulum stress in the placental injury and fetal growth restriction in an ovine gestation model	MACHINDUNDU: Exposure to bisphenol A (BPA), an environmental pollutant known for its endocrine-disrupting properties, during gestation has been reported to increase the risk of fetal growth restriction (FGR) in an ovine model of pregnancy. We hypothesized that the FGR results from the BPA-induced insufficiency and endocrine dysfunction of the placenta, oxidative stress, inflammatory responses, autophagy and endoplasmic reticulum stress (ERS). However, precise mechanisms underlying the BPA-induced placental dysfunction, and subsequently, FGR, as well as the potential involvement of placental ERS in these complications, remain to be fully elucidated. Therefore, the objective of this study was to investigate the role of ERS in BPA-induced placental injury and fetal growth restriction in an ovine gestation model. In this study, whereas the other group received BPA (5 mg/kg body bw; a subcutaneous injection) in the vehicle, pregnant ewes (n = 8/group) were exposed to 2 treatments, the control group received an equal volume of corn oil (vehicle). The OTCs were treated with 500 μM 4-PBA (chemical chaperone) and EMBA4 (7.2 complete medium (control), for 24 h. RESULTS: The results of this study revealed that BPA exposure induced ERS, OXS, inflammation, autophagy, and apoptosis in the placentomes and primary trophoblasts. Moreover, BPA-induced ERS, OXS, inflammation, autophagy, and apoptosis were found together to impair placental barrier dysfunction, ERS, inflammatory responses, autophagy, and OXS in the placentomes. In vitro experiments, the BPA-induced ERS, OXS, inflammation, autophagy, and apoptosis in trophoblasts were also observed. Importantly, 4-PBA significantly ameliorated the BPA-induced trophoblast dysfunctions mentioned above. Overall, the findings illustrated that BPA-induced ERS could contribute to placental dysfunction and gene expressions of antioxidant, anti-apoptosis, and barrier function. Moreover, treating the OTCs with 4-PBA reversed the BPA-induced dysfunction of barrier and endocrine (the increased E2 level and decreased P4 level). CONCLUSIONS: In general, the results reveal that BPA exposure can cause ERS in the ovine placenta and OTCs, and ERS induction might contribute to the dysfunction of the placental barrier and endocrine, ERS, inflammatory responses, and autophagy. These data offer novel mechanistic insights into whether ERS is involved in BPA-mediated placental dysfunction and fetal development.	J Anim Sci Biotechnol Vol.14 Issue 1 Pages 117	10.1186/s40104-023-00919-z	37691111	動物、in vitro	-	1	0	1	不明	0	5 mg/kg/day	-	-	-	-	-	-	1	0	400 μmol/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0832	H. Zhang, X. Zha, B. Zhang, Y. Zheng, M. Elsabagh, H. Wang and M. Wang	2024	Gut microbiota contributes to bisphenol A-induced maternal intestinal and placental apoptosis, oxidative stress, and fetal growth restriction in pregnant ewe model by regulating gut-placental axis	MACHINDUNDU: Bisphenol A (BPA) is an environmental contaminant with endocrine-disrupting properties that induce fetal growth restriction (FGR). Previous studies on pregnant ewes revealed that BPA exposure causes placental dysfunction and FGR by inducing oxidative stress, inflammation, autophagy, and apoptosis. However, the precise mechanisms underlying BPA-induced FGR, as well as the potential involvement of gut microbiota in these complications, remain to be fully elucidated. Therefore, the objective of this study was to investigate the role of gut microbiota in BPA-induced placental injury and FGR in an ovine model of pregnancy. In this study, whereas the other group received BPA (5 mg/kg body bw; a subcutaneous injection) in the vehicle, pregnant ewes (n = 8/group) were exposed to 2 treatments, the control group received an equal volume of corn oil (vehicle). The GFD+R treatment was initiated on GD 30 and continued until GD 130. Ewes in the GFD+R group received a gut microbiota transplantation (GMT) from the control group (n = 10) through fecal microbiota (Fm) slurry (4 g/kg body bw) via oral gavage every other day from GD 60 to GD 110 of gestation. The maternal colonic digesta and the ileum and placental tissue samples were collected to examine the biomarkers of apoptosis, oxidative stress, mitochondrial dysfunction, ERS, and IRS. To investigate the link between gut microbiota and the BPA-induced FGR in pregnant ewes, gut microbiota transplantation (GMT) was conducted in two pregnant ewe groups (n = 10/group) from day 0 to day 14 of gestation after removing their intestinal microbiota by antibiotics. The GMT was performed by orally administering the Fm from the control and BPA-exposed ewes, respectively. The results revealed that BPA exposure disturbs the gut microbiota composition in pregnant ewes. GMT-induced BPA-exposed GM also induced BPA-like maternal FGR, placental dysfunction, and oxidative stress. Moreover, BPA exposure and GM transfer altered the gut microbiota composition, which was associated with changes in the concentrations of SCFAs and BAs. Interestingly, GM transfer also induced BPA-like alterations in the expressions of genes involved in the synthesis and transport of SCFAs and BAs, as well as their receptors in the colon and placental tissues. Furthermore, BPA exposure and GM transfer-induced dysbiosis in the gut microbiota was correlated with the dysfunction of the placental barrier and endocrine, ER, inflammatory responses, and autophagy. These data offer novel mechanistic insights into whether ERS is involved in BPA-mediated placental dysfunction and fetal development.	Microbiome Vol.12 Issue 1 Pages 28	10.1186/s40168-024-01749-5	38365714	動物	-	1	0	1	不明	0	5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0833	H. Zhang, R. Yang, W. Shi, X. Zhou and S. Sun	2022	The association between bisphenol A exposure and oxidative damage in rats/mice: A systematic review and meta-analysis	Numerous studies reported that BPA could cause oxidative damage to different tissues in rats/mice. This study aimed to perform a systematic review and meta-analysis of BPA exposure on oxidative damage in rats/mice. A comprehensive literature search was conducted using PubMed, Embase, and Web of Science databases from their inception until July 26, 2021. 21 eligible articles were included in this study. The results showed that BPA could significantly increase the level of MDA (SMD, 16.88; 95%CI, 12.38–21.71), but there was a significant reduction in the contents of antioxidants, such as SOD (-10.46, -13.91 – -7.02), CAT (-8.08, -11.48 – -4.68), GPx (-9.31, -12.95 – -5.68), GST (-7.94, -14.51 – -1.37), GSH (-10.64, -13.96 – -7.33), and T-SOD (-6.48, -9.27 – -3.68) in rats/mice. Our study provided new evidence that BPA exposure could significantly induce oxidative damage in rats/mice. Entire dose found that the degree of oxidative damage was related to BPA dose, target tissue, intervention means, and exposure duration of BPA.	Environ Pollut Vol.292 Issue Pt B Pages 118444	10.1016/j.envpol.2021.118444	34742820	動物	-	1	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0834	H. Zhang, H. Kuang, Y. Luo, S. Liu, L. Meng, Q. Pang and R. Fan	2019	Low-dose bisphenol A exposure impairs learning and memory ability with alterations of neuromorphology and neurotransmitters in rats	To investigate the developmental neurotoxicity of environmental bisphenol A (BPA) exposure for infants and children, postnatal rats were used as the animal model and were divided into four groups. Then, they were exposed to 0 (control), 0.05, 5, and 50 mg/kg BPA by gavage from PND 1 to PND 21. Behavioral tests, including the Morris water maze test, open field test, and novel object recognition test, were performed. Immunohistochemistry, transmission electron microscopy (TEM), ELISA, HPLC, and western blot analysis were used to detect the hippocampal neuron morphology and neurotransmitter levels, respectively. The results showed that the BPA-exposed rats, especially the low- and high-exposed rats, needed more trials and longer times to qualify for the learned criterion than the control rats. Additionally, rats after low- or high-exposure to BPA exhibited decreased DG dendritic complexity and reduced CA1 and DG dendritic spine densities in the hippocampus. Low-dosage BPA treatment could significantly alter the neurotransmitter contents in the hippocampus. In male rats, the levels of glutamic acid (Glu) and acetylcholine increased, while the 5-hydroxytryptamine (5-HT) and γ-aminobutyric acid (GABA) levels decreased, which led to an unbalanced Glu/GABA ratio. However, in female rats, only 5-HT levels decreased. In contrast, neonatal exposure to BPA could not alter the dependently dose-dependent developmental neurotoxicity in female rats. Taken together, these results showed that

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0856	D. Wu, F. Wu, R. Lin, Y. Meng, W. Wei, Q. Sun and L. Jia	2020	Impairment of learning and memory induced by perinatal exposure to BPA is associated with ER α -mediated alterations of synaptic plasticity and PKC/ERK/CREB signaling pathway in offspring rats	The effect of bisphenol A (BPA) on learning and memory has attracted much attention recently, but its underlying mechanism remains unclear. We aimed to investigate whether the impairment of learning and memory induced by perinatal exposure to BPA was associated with the hippocampal estrogen receptor -α (ERα)-mediated synaptic plasticity and PKC/ERK/CREB signaling pathway in different sex offspring rats. Pregnant Sprague-Dawley rats were exposed to BPA (0, 0.5, 5, 50 mg/kg/day, n = 10/group) from gestation day 9 to postnatal day 21. The Morris water maze test was used to assess the learning and memory ability, place navigation and spatial memory, placement and object recognition, and step-down passive avoidance task were performed. The serum estradiol (E2) levels, histopathology of hippocampus, and the expressions of learning and memory-related proteins were measured. The results showed that spatial and recognition memory were impaired in BPA -exposed female and male offspring, but the impaired passive avoidance memory presented only in males, not in females. Moreover, BPA was found to increase in BPA -exposed females and males. BPA altered the morphology and quantity of hippocampal neurons. The levels of ERα, MAPK receptor subunit 2B (MAP2B), p-MEK, MAPK receptor 1 (ERK1), p-ERK1, PKCγ, p-PKCγ, CREB, and p-CREB protein expression were decreased in BPA -exposed females and males, and there were interactions of sex × BPA exposure in ERα, p-MEK and p-ERK levels. These findings suggested that perinatal exposure to BPA has sex-specific effects on learning and memory, which is associated with ERα -mediated impairment of synaptic plasticity and down-regulation of PKC/ERK/CREB signaling pathway.	Brain Res Bull Vol.161 Pages 43-54	10.1016/j.brainresbull.2020.04.023	32380187	動物	-	1	1	1	1	0	1、10 μg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0857	D. Wu, H. Liu, Y. Liu, W. Wei, Q. Sun, D. Wei and L. Jia	2021	Protective effect of alpha-lipoic acid on bisphenol A-induced learning and memory impairment in developing mice: nNOS and keap1/Nrf2 pathway	The adverse effects of bisphenol A (BPA) on learning and memory may be related to th oxidative stress, but the mechanisms are unclear. This study aimed to investigate the mechanism of damaged learning and memory caused by BPA through inducing oxidative stress, as well as to explore whether alpha-lipoic acid (ALA) has a protective action. Female mice were exposed to 0.1 μg/mL BPA, 0.5 μg/mL BPA, 50 mg/mL ALA and 50 + 50 mg/mL ALA (mixed drinking water for 8 weeks. The results showed that ALA protected against the impairment of spatial, recognition, and avoidance memory caused by BPA. ALA ameliorated the values of hippocampal oxidative stress parameters, including malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and total antioxidant capacity (T-AOC) induced by BPA. ALA also ameliorated the synaptic structural proteins and PKC/ERK/CREB pathway proteins, and ALA improved these indexes reductions. ALA allowed the protein levels of nNOS and keap1/Nrf2 pathway affected by BPA. Our results suggested that impairments of learning and memory caused by BPA was related to the damage of hippocampal synapses mediated by oxidative stress, and ALA protected learning and memory by reducing the oxidative stress induced by BPA through regulating the nNOS and keap1/Nrf2 pathway.	Food Chem Toxicol Vol.154 Pages 112307	10.1016/j.fct.2021.112307	34058234	動物	-	1	1	1	1	0	0.1 μg/mL BPA, 50 + 50 mg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0858	C. Wormsbaecher, A. B. Hindman, A. Avendaño, M. Cortes-Medina, C. E. Jones, A. Buchman, L. Orua, C. E. Kowalchik, A. R. Murphy, H. L. Hellier, A. Stapkins, K. Voytovich, X. Kuang, R. Aguilar-Valenzuela, J. L. Leight, J. W. Song and C. J. Burd	2020	In utero estrogenic endocrine disruption alters the stroma to increase extracellular matrix density and mammary gland stiffness	BACKGROUND: In utero endocrine disruption is linked to increased risk of breast cancer later in life. Despite numerous studies establishing this linkage, the long-term molecular changes that predispose mammary cells to tumorigenesis remain poorly understood. Bisphenol A (BPA) is a ubiquitous endocrine disrupting chemical that has been shown to increase breast cancer risk in animal models. We have utilized bisphenol A (BPA) as a model of estrogenic endocrine disruption to evaluate the long-term consequences in the stroma. Deregulated genes were identified by RNA -seq hierarchical profiling of adult primary fibroblasts, isolated from female mice exposed to in utero BPA. Collagen staining, collagen imaging techniques, and permeability assays were used to characterize changes to the extracellular matrix. Finally, gland reconstitution assays were performed to determine if changes in the stroma were sufficient to induce changes in the epithelium. RESULTS: Fibroblasts isolated from BPA -exposed mice exhibited a 3-fold increase in cell-mediated collagen matrix compaction. Multiple collagen genes were found to be expressed in the BPA -exposed fibroblasts resulting in increased collagen deposition in the adult mammary gland. This transcriptional reprogramming of BPA -exposed fibroblasts generates a less permeable extracellular matrix and a stiffer mammary gland. These phenotypes were only observed in adult (12 -week -old, but not 5 -week -old) mice. Additionally, diethylstilbestrol, known to increase breast cancer risk in humans, also increases gland stiffness, similar to BPA, while bisphenol S does not. CONCLUSIONS: As tissue stiffness, extracellular matrix density, and collagen deposition have been directly linked to breast cancer risk, these data mechanistically connect EDC exposures to molecular alterations associated with increased disease susceptibility. These alterations, starting even time and thus contributed to cancer risk in adulthood.	Breast Cancer Res Vol.22 Issue 1 Pages 41	10.1186/s13058-020-01275-w	32370801	動物	-	1	0	1	不明	0	25 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0859	C. Wormsbaecher, B. M. Cuntibia, E. G. Amrugia, L. M. Puska, M. R. Price, K. M. Ma, S. E. Knoblaugh, T. Kurtis and C. J. Burd	2023	Mammary gland development and EDC-driven cancer susceptibility in mesenchymal ERα -knockout mice	Development of the mammary gland requires both proper hormone signaling and cross-talk between the stroma and epithelium. While estrogen receptor (ER α) expression in the epithelium is essential for normal gland development, the role of this receptor in the stroma is less clear. Moreover, several lines of evidence suggest that stromal phenotypes of in utero exposure to endocrine disruption act through mesenchymal ERα in the epithelium to increase cancer risk. Here, we utilize mesenchymal ERα -knockout mice to determine the role of this receptor in the stroma during development and in response to in utero bisphenol A (BPA) exposure to alter the tumor susceptibility in the mouse mammary gland. Mesenchymal ERα -knockout mice exhibited delayed mammary gland development and reduced cancer risk. Mesenchymal ERα -knockout mice also exhibited delayed reproductive tract development and atypical cycling associated with estrous cycling. The mammary gland demonstrated mature epithelial extension within complete ERα+ lobular-like structures, but ductal extension was delayed and reduced compared to ERα -competent mice. Using the MATT (Mouse Mammary Tumor Virus -Neu -ires -Cre) model, we found that mesenchymal ERα -intact mice exposed to BPA had reduced tumor-free survival and overall survival compared to BPA -exposed mice lacking mesenchymal ERα activation. This difference is specific for BPA exposure as vehicle -treated animals had no difference in tumor development between mice expressing and not expressing mesenchymal ERα. These data demonstrate that mesenchymal ERα -expression is not required for ductal extension, nor does it influence cancer risk in this mouse model but does influence the tumor incidence associated with in utero BPA exposure.	Endocr Relat Cancer Vol.30 Issue 12	10.1530/erc-23-0062	37855322	動物	-	1	1	1	0	0	25 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0860	J. T. Wolstenhulme, Z. Drobná, A. D. Henriksen, J. A. Goldsby, R. Stevenson, J. W. Irvin, J. A. Flaws and E. F. Rissman	2019	Transgenerational Bisphenol A Causes Deficits in Social Recognition and Alters Postsynaptic Density Genes in Mice	Bisphenol A (BPA) is a ubiquitous endocrine disrupting chemical. Developmental exposure produces changes in behavior and gene expression in the brain. Here, we examined social recognition behaviors in mice from the third familial generation (F3) after exposure to gestational BPA. Six-cell generation mice were bred to one of four mating combinations to reveal whether characteristics in F3 were acquired via maternal or paternal lineage. Mice were exposed to 0 (vehicle) or 50 μg/kg BPA during gestation days 8 to 14. Social recognition was tested in adulthood (90 days) using a habituation/dishabituation task. The same mice were tested in F3 for changes in the expression of PSD genes using quantitative PCR. Differential expression in genes important for the solubility of PSDs were assessed at three developmental ages. Social recognition was impaired in BPA-lineage females and males. Gene expression was altered in the postsynaptic density (PSD) scaffolding protein Dlg4 (PSD-95). Dlg4 and Dlg2 (PSD-93) were differentially expressed in several -to-BPA-lineage males. Using a second strain of F3 inbred mice exposed to BPA, we tested the same differences in Dlg4 and F11R3 expression in C57BL/6J mice. In sum, transgenerational BPA exposure altered social interactions in mice and dysregulated normal expression of PSD genes during neural development. The fact that the same genetic effects were found in different mouse strains and in several brain regions increased potential for translation. The genetic and functional relationship between PSD and abnormal neurobehavioral disorders is well established, and our data suggest that BPA may contribute to a transgenerational reverse in neurodevelopmental disorders.	Endocrinology Vol.160 Issue 8 Pages 1854-1867	10.1210/en.2019-00196	31188430	動物	-	1	1	1	1	0	20 μg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0861	M. Wiczyńska, E. Lepiarczyk, L. Paukszto, K. G. Maksiszcenko, A. Lipka, M. A. Maldzieri, L. Polak, K. Makowska, S. Gonkowski, P. Correia-de-Sá and M. Majewska	2023	A comprehensive transcriptomic analysis of the bisphenol A affected kidney in mice	Introduction: Bisphenol A (BPA) is a substance belonging to the endocrine-disrupting chemicals, globally used in the production of polycarbonate plastics. It has been found that BPA enhances carcinogenesis, triggers obesity and exerts a pathogenic effect in several disorders, such as type 2 diabetes, asthma, or increased blood pressure. Recent studies have revealed, that BPA has a harmful impact on the kidneys function, therefore, the current research aimed to explore the specific molecular changes triggered in these organs after oral BPA exposure in mice. Materials and Methods: The experiment was carried out on 22 (5-month-old) female mice, divided into two groups: the control group (C) and the BPA group (BPA). The BPA group was exposed to BPA in drinking water at a dose of 50 mg/kg b.w./day for 28 days. The RNA-Seq analysis was used to perform RNA-seq. Results: Applied multiway bioinformatic revealed 210 differentially expressed genes (DEGs) in the BPA-treated kidneys (120 upregulated and 90 downregulated). Additionally, 99 differentially expressed long noncoding RNAs (DELs) were revealed in BPA samples. The Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) annotations indicated that BPA exposure resulted in profound changes, in several essential processes, such as: oxidative phosphorylation, mitochondrial and ribosome function, or chemical carcinogenesis. Conclusion: The obtained novel results suggest that BPA has a harmful impact on the fundamental processes of the kidney and significantly impairs its functionality reducing mitochondrial dysfunction leading to oxidative stress and reaction oxygen species production.	Front Mol Biosci Vol.10 Pages 1260716	10.3389/fmolb.2023.1260716	38074096	動物	-	1	1	1	不明	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0862	M. Wiczyńska, E. Lepiarczyk, M. A. Maldzieri, L. Paukszto, K. G. Maksiszcenko, A. Lipka, M. A. Maldzieri, L. Polak, K. Makowska, S. Gonkowski, P. Correia-de-Sá and M. Majewska	2023	The Carcinogenic Potential of Bisphenol A in the Liver Based on Transcriptomic Studies	Bisphenol A (BPA) is an environmental toxin widely used in the production of polycarbonate plastics. A correlation exists between BPA tissue contamination and the occurrence of pathological conditions, including cancer. Five-passage detoxification of high BPA amounts in the liver promotes hepatotoxicity and morphological alterations of this organ, but there is a lack of knowledge about the molecular mechanisms underlying these changes. Therefore, the current research aimed to explore the specific molecular changes triggered in the liver after oral BPA exposure in mice. Materials and Methods: The experiment was carried out on 22 (5-month-old) female mice, divided into two groups: the control group (C) and the BPA group (BPA). The BPA group was exposed to BPA in drinking water at a dose of 50 mg/kg b.w./day for 28 days. The RNA-Seq analysis was used to perform RNA-seq. Results: Applied multiway bioinformatic revealed 210 differentially expressed genes (DEGs) in the BPA-treated livers (120 upregulated and 90 downregulated). Additionally, 99 differentially expressed long noncoding RNAs (DELs) were revealed in BPA samples. The Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) annotations indicated that BPA exposure resulted in profound changes, in several essential processes, such as: oxidative phosphorylation, mitochondrial and ribosome function, or chemical carcinogenesis. Conclusion: The obtained novel results suggest that BPA has a harmful impact on the fundamental processes of the liver, which is predictive of the carcinogenic potential of this compound in this organ.	Cancers (Basel) Vol.15 Issue 20	10.3390/cancers15205014	37894381	動物	-	1	1	1	C67BL6/J/CMDB	0	50 mg/kg b.w.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0863	T. T. Wit- Shwe, R. Yanagisawa, E. Koike and H. Takano	2021	Dietary exposure to bisphenol A affects memory function and neuroimmune biomarkers in allergic asthmatic mice	Bisphenol A (BPA) is a raw material of polycarbonate and epoxy resin. It is used for various household electrical appliances, electronic equipment, office automation equipment, medical equipment, mobile phones, paints for automobiles, internal surface coating of cans, and adhesives for civil engineering and construction. BPA is a well-known endocrine disrupting chemical, and it was reported that BPA has an adverse effect on the immune system. However, the effect of BPA on the central nervous system, especially on memory function, is not well understood. Therefore, we investigated the effects of dietary exposure to BPA on brain function and biomarkers using allergic asthmatic mice. Female mice were fed rice diets containing 0 (control), 0.001, 0.01, or 1 μg/kg/day concentrations of BPA for seven consecutive weeks. Then, ovalbumin (OVA) was given by intranasal instillation every 2 weeks. Memory function was determined by a novel object recognition test. Genes related to memory and immune markers in the hippocampus were measured by real-time RT-PCR. Ovalbumin-specific IgE (OVA-IgE) in the serum was measured by ELISA. Results: Memory impairment was observed in the presence of allergen. However, upregulation of expression levels of neurotrophin biomarkers such as N-methyl-D-aspartate receptor, nerve growth factor -α, cerebral calcium binding adapter molecule -1, cyclooxygenase-2, and nerve regulation-1 in the hippocampus was observed in BPA-exposed allergic asthmatic mice. These findings show that BPA exposure can induce neuroinflammation and which triggers impairment of memory function in mice with allergic asthma. Our study	J Appl Toxicol Vol.41 Issue 10 Pages 1527-1536	10.1002/jat.4143	33474794	動物	-	1	1	1	C3H/HeJSlc	0	0.001、0.01 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0864	T. T. Wit- Shwe, R. Yanagisawa, E. Koike and H. Takano	2019	Memory Function, Neurological, and Immunological Biomarkers in Allergic Asthmatic Mice Intratracheally Exposed to Bisphenol A	Bisphenol A (BPA) is a major constituent of plastic products, including epoxy resin containers, mobile phones, dental sealants, as well as electronic and medical equipment. BPA is recognized as an endocrine system disrupting chemical which has toxic effects on the brain and reproductive system. However, little is known about the effects of co-exposure of BPA with allergens on the memory function and neurological as well as immunological biomarkers. Female mice were given 0 (control), 0.1 (low dose), or 10 (high dose) μg/kg/day BPA intratracheally (i.t.) for 5 consecutive days. Then, mice (C3H/He Jcl mice were given three doses of BPA (0.6/0.6 μmol, i.t.)) 0 and 10 μmol BPA) solution) immediately every week, and ovalbumin (OVA) intratracheally every other week from 5 to 11 weeks old. At 12 weeks of age, a novel object recognition test was conducted after the final administration of OVA, and the hippocampal and hypothalami of the animals were collected after 24 h. The expression levels of the memory function-related genes N-methyl-D-aspartate (NMDA) receptor subunits, inflammatory cytokines, microglia markers, estrogen receptor alpha, and caspase receptor were examined by real-time RT-PCR. Real-time reverse transcription polymerase chain reaction and immunohistochemical methods. Treatment of the novel object recognition ability was observed in the high dose BPA -exposed mice with allergic asthma. In addition, the expression levels of memory function-related genes were significantly decreased in the high dose BPA -exposed mice with allergic asthma. Moreover, the immunohistochemical results revealed that BPA -treated mice showed significantly increased NMDA receptor subunit 2B -immunoreactivity. These findings suggest that exposure to high dose BPA triggered impairment of memory function in the allergic asthmatic mice. This is the first study to show that, in the presence of allergens, exposure to high dose BPA may affect memory by modulating the memory function-related genes in the hippocampus.	Int J Environ Res Public Health Vol.16 Issue 19	10.3390/ijerph16193770	31597243	動物	-	1	0	1	C3Hjcl（Charles River Japan）	1	0.1 μg/kg BPA（高分子量型）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0865	M. Wieckowski, S. Ranga, D. Molson, S. Mesalam, S. Abdallah, S. Granon, R. Habert, V. Rouillier-Fabre, G. Livera and M. J. Guerquin	2021	Unexpected Interacting Effects of Physical (Radiation) and Chemical (Bisphenol A) Treatments on Male Reproductive Functions in Mice	For decades, numerous chemical pollutants have been described to interfere with endogenous hormone metabolism's/signaling altering reproductive functions. Among these endocrine disrupting substances, Bisphenol A (BPA), a widely used compound, is known to negatively impact germ and somatic cells in the testis. Physical agents, such as ionizing radiation, were also described to perturb spermatogenesis. Despite the fact that we are constantly exposed to numerous environmental chemical and physical compounds, very few studies explore the impact of combined exposure to chemical and physical pollutants on reproductive health. The aim of this study was to investigate the effects of BPA exposure (0.5 μg/mL in drinking water) on the male reproductive system of mice exposed to a sub-lethal dose of X-rays (0.5 Gy). Adult male mice were treated or not treated since birth (0.5 Gy) or only INDO at 0.15 days post conception. Co-exposure to BPA and γ -rays induces DNA damage in the germ cells in an additive manner, leading to a long-lasting decrease in sperm cell abundance. We also observed significant alteration of adult steroidogenesis by INDO exposure independently of the BPA exposure. This is illustrated by the downregulation of steroidogenic genes and the decrease of the number of adult Leydig cells. As a consequence, Leydig cells dysfunction is modified, and male alterations' ascertainments associated with infertility decreased. In conclusion, this study provides evidence for the importance of broadening the concept of endocrine disruptors to include physical agents, leading to a remodulation of risk management and regulatory decisions.	Int J Mol Sci Vol.22 Issue 21	10.3390/ijms222111808	34769238	動物	-	1	1	1	NMRI	0	0.5 μg/mL BPA（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0866	J. Weng, Y. Y. Zhu, L. Y. Liao, X. T. Yang, Y. H. Dong, W. D. Meng, D. J. Sun, Y. Liu, W. Z. Pang and Y. Jiang	2024	Distinct epigenetic modulation of differentially expressed genes in the adult mouse brain following prenatal exposure to low-dose bisphenol A	Bisphenol A (BPA) is a common component in the manufacture of daily plastic consumer goods. Recent studies have suggested that prenatal exposure to BPA can increase the susceptibility of offspring to mental illness, although the underlying mechanisms remain unclear. In this study, we performed transcriptomic and epigenomic profiling in the adult mouse brain following prenatal exposure to low-dose BPA. We observed a sex-specific transcriptional response to BPA exposure, with more differentially expressed genes (DEGs) identified in males than in females. Functional enrichment analysis revealed that the DEGs in males were significantly enriched within the downregulated genes, were significantly associated with energy metabolism pathways. More importantly, our findings supported the hypothesis that mitochondrial function included a decreased mtDNA copy number and reduced number of mitochondria in the cortical neurons of the BPA group. We further investigated the higher -order chromatin regulatory patterns of DEGs by incorporating published Hi -C data. Interestingly, we found that upregulated genes exhibited more distal interactions with multiple enhancers, while downregulated genes displayed relatively short -range interactions among adjacent genes. Our data further revealed distinct H3K4me3 signals on the distal enhancers of upregulated genes, whereas increased DNA methylation and H3K27me3 signals on the promoters of downregulated genes. In summary, our study provides compelling evidence for the potential health risks associated with prenatal exposure to BPA, and uncovers sex -specific transcriptional changes with a complex interplay of multiple epigenetic mechanisms.	Cell Biol Toxicol Vol.40 Issue 1 Pages 37	10.1007/s10565-024-09875-4	38777957	動物	-	1	1	1	1	0	40 μg/kg bw/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0867	X. Wen, M. Zhu, Z. Li, T. Li and X. Xu	2022	Dual effects of bisphenol A on wound healing, involvement of estrogen receptor β	Bisphenol A (BPA) is a ubiquitous environmental pollutant that can specifically induce estrogen receptor β (ERβ) expression, and the latter plays a crucial role during wound healing. However, no study has investigated the effects of BPA on wound healing. Therefore, we aimed to explore the effects of BPA on wound healing and the underlying mechanisms. Sprague-Dawley rats were used to establish a full-thickness skin defect model. The process of wound healing dietary intake (0 and 50 mg kg-1 and wound application (0 and 100 nM). Nine primary fibroblastoma were exposed to BPA to verify the role of BPA on the function of fibroblasts. We also applied BPA to diabetic mice to evaluate its therapy value. BPA showed dual effects on wound healing, which were dependent on the application routes. Dietary intake of BPA delayed wound healing by suppressing ovarian estrogen synthesis and circulating estrogen levels. Wound application of BPA promoted wound healing by activating ERβ. BPA enhanced the function of fibroblasts, which was blocked by ERβ inhibitor. Wound application of BPA significantly accelerated wound healing in diabetic mice but has no significant adverse effect on ovarian hormonic levels. The current study indicates that although BPA disrupts the function of the female ovaries when administered by diet, local application of BPA on wounds shows a superior role in promoting wound repair, and this may provide a novel approach for the therapy of pathologic wound healing.	Ecotoxicol Environ Saf Vol.231 Pages 113207	10.1016/j.ecoenv.2022.113207	35051763	動物	-	1	1	1	1	0	0.5, 5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0868	Y. Wei, S. Li, C. Hao , Y. Bao and W. Shi	2019	Cuscuta chinensis flavonoids alleviate bisphenol A-induced apoptosis of testicular cells in male mice offspring	Bisphenol A (BPA) is a widespread environmental endocrine disruptor that has multiple effects on reproductive organ development. To investigate the effect of Cuscuta chinensis flavonoids (CCF) on testicular apoptosis induced by BPA in male mice offspring, pregnant mice were administered intragastrically with BPA and CCF at gestational day (GD) 12-17.5. The testes of male offspring (F1 males) were collected at post-natal day (PND) 21, PND 35, and PND 56 and were subjected to TUNEL staining and immunohistochemistry. The results indicated that CCF could protect the testes against BPA-induced apoptosis. The concentrations of CCF groups, the expression levels of Bax, caspase 9 and caspase 7 proteins were significantly decreased at PND 21 and PND 56, while the expression level of bcl-2 protein was significantly increased, and testicular apoptotic cells were also decreased significantly (p < .01 or p < .05). Forty-mg/kg CCF has no significant difference compared with the control group. The results indicated that CCF could protect the testes during development of F1 male mice by alleviating the apoptosis of testicular cells induced by BPA.	Andrologia. 2019 Dec;51(11):e13427.	10.1111/and.13427	31583719	動物	精巣	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を依頼性評価へ進め、当該時点評価段階で原則に基づき解釈。

利用評価機関
●：該当

別添-2　統合文献リスト

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0882	S. Wang, Y. Yang, D. Luo, L. Zhai, Y. Bai, W. Wei, Q. Sun and L. Jia	2021	Bisphenol A increases TLR4-mediated inflammatory response by up-regulation of autophagy-related protein in lung of adolescent mice	In previous studies we found that bisphenol A (BPA) aggravated OVA-induced lung inflammation. The aim of this research was to determine whether BPA exposure alone also induced inflammatory response in the lungs, which mechanism was associated with TLR4/NF-κB signaling pathway and the activation of mTOR-mediated autophagy. Female C57BL/6 mice aged 3 weeks were randomly divided into three groups (10 /group) corresponding to 0, 50, and 500 μg/kg/day BPA exposure by gavage for 28 consecutive days. The histopathological changes in lung tissues were observed by hematoxylin-eosin staining. In addition, the RAW264.7 cell culture experiment was conducted to determine whether BPA stimulated autophagy. We found that BPA can induce autophagy flux by enhancing autophagosome formation. It was further confirmed the details of the mechanism of action with chloroquine (CQ), a compound that inhibits the fusion of autophagosomes and lysosomes) intervention. The inhibition of autophagy led to down-regulation of expression levels associated with inflammation. This research results indicated that BPA-induced inflammatory response in vitro and in vivo, and its mechanism may be related to TLR4/NF-κB signaling pathway and the activation of mTOR-mediated autophagy. After autophagy was suppressed, the inflammatory response also weakened. Our findings provide a new perspective into the mechanisms underlying inflammatory responses induced by the environmental exposure. These findings indicate that therapeutic strategies targeting autophagy may provide a new method for the treatment of inflammatory diseases.	Chemosphere. 2021 Apr;268:128837.	10.1016/j.chemosphere.2020.128837	33187652	動物、in vitro	-	1	不明	1	1	0	0.1, 0.2 μg mL	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0883	S. Wang, Y. Dong, L. Zhi, Y. Bai, Y. Yang and L. Jia	2024	Decreased Treg cells induced by bisphenol A is associated with up-regulation of PI3K/Akt/mTOR signaling pathway and Foxp3 DNA methylation in spleen of adolescent mice	The current study aimed to explore whether bisphenol A (BPA) exposure aggravated the decrease in Tregs induced by ovalbumin (OVA) in adolescent female mouse models of asthma, and whether the process was associated with mTOR-mediated signaling pathways and DNA methylation in the spleen. A 3-week-old female mice were randomly divided into three groups (10/group) corresponding to 0, 50, and 500 μg/kg/day BPA exposure by gavage for 28 consecutive days. The mice at the age of 4 weeks in the asthma model were established by ovalbumin (OVA) nasal and inhalation after 1 week of desensitization. Each group conducted of eight mice the control group, OVA group (OVA + BPA (0) 0 μg mL), CT group (OVA + BPA (50 μg mL), and OVA + BPA (0.2 μg mL) CT group). Results revealed that Foxp3 protein levels, Treg cells, and DNA methyltransferase 1 (DNMT1) mRNA levels in the spleen were significantly increased in the OVA group compared to the control group. Moreover, the OVA + BPA (0.2 μg mL) CT group exhibited significantly higher levels of these parameters than the OVA group. The mechanism was related to the activity of TLR4/NF-κB and PI3K/Akt/mTOR signaling pathways and the enhancement of Foxp3 DNA methylation. Our results, collectively, provide a new perspective for studying the mechanisms underlying BPA exposure-induced immune dysfunction. Investigation of the regulatory mechanisms of DNA methylation in the abnormal Th immune response caused by BPA exposure could help reveal the causes and molecular mechanisms underlying the high incidence of allergic diseases in children in recent years.	Chemosphere Vol.357 Pages 141957	10.1016/j.chemosphere.2024.141957	38641296	動物	-	1	不明	0	1	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0884	R. Wang, Z. H. Liu, N. Bi, K. Gu, C. Huang, R. Zhou, H. Liu and H. L. Wang	2023	Dysfunction of the medial prefrontal cortex contributes to BPA-induced depression- and anxiety-like behavior in mice	Bisphenol A (BPA), a well-known environmental endocrine disruptor, has been implicated in anxiety-like behavior. But the neural mechanism remains elusive. Herein, we found that mice exposed to 0.5 mg/kg/day BPA chronically from postnatal day (PND) 21 to PND 56 exhibited depression- and anxiety-like behavior. Further study showed that medial prefrontal cortex (mPFC) was associated with BPA-induced depression- and anxiety-like behavior, as evidenced by decreased c-fos expression in mPFC of BPA-exposed mice. Both the morphology and function of glutamatergic neurons (also called pyramidal neurons) in mPFC of mice were impaired following BPA exposure, characterized by reduced primary branches, condensed dendritic spines, and decreased mEPSC frequency. Importantly, optogenetic activation of the glutamatergic neurons in mPFC greatly reversed BPA-induced depression- and anxiety-like behavior in mice. Furthermore, we reported that microglial activation in mPFC of mice may also have a role in BPA-induced depression- and anxiety-like behavior. Taken together, the results indicated that mPFC is the brain region that is greatly damaged by BPA exposure and is associated with BPA-induced depression- and anxiety-like behavior. The study thus provides new insights into BPA-induced neurotoxicity and behavioral changes.	Ecotoxicol Environ Saf Vol.259 Pages 115034	10.1016/j.ecoenv.2023.115034	37210999	動物	-	1	1	1	不明	0	0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0885	M. Wang, Y. Wang, J. Han, Z. Duan, J. Yin, R. Ding and Q. Wang	2023	Gestational and Lactational Co-Exposure to DEHP and BPA Impairs Hepatic Function via PI3K/AKT/FOXO1 Pathway in Offspring	(2-Ethylhexyl) phthalate (DEHP) and bisphenol A (BPA) present significant environmental endocrine-disrupting chemical properties. Although studies have implied reproductive impairment from exposure to BPA and DEHP, no study to date has shown the effect and mechanism of hepatic function after gestational and lactational co-exposure to DEHP and BPA in offspring. A total of 36 perinatal rats were randomly divided into four groups, CRAP (600 mg/kg bw/kg), BPA (50 mg/kg bw/kg), DEHP combined with BPA (600 mg/kg bw + 50 mg/kg bw), and control. Notably, (1) chemical reports and network pharmacology results revealed that the disorders mainly concentrated the most severe structural damage, including vacuolization, cytoplasmic shedding, and mitochondrial degeneration. BPA exposure disrupted oxidative stress homeostasis by reducing superoxide dismutase activity and increasing malondialdehyde (MDA) content, and decreasing the activity levels of SOD, CAT, GSH, and T-AOC. BPA further induced hepatic inflammation by upregulating the gene abundance of key factors of the immune system (TLR2, IL-6, MyD88, and NF-κB); the transcriptional activity of NF-kB; and the secretion of pro-inflammatory cytokines (IL-1,β, IL-6, IL-8, and TNF-α). Moreover, apoptosis was activated by BPA, whereas cell proliferation was inhibited by BPA. Mechanistically, co-treatment of intestinal epithelial cells with BPA using the oxidative stress scavenger NAC, the NF-κB-specific inhibitor QNZ (EVP4593), and the apoptosis inhibitor Z-VAD-FMK, respectively, showed that BPA activates the innate immune response by inducing oxidative stress. Consequently, apoptosis is promoted, and cell proliferation is inhibited, ultimately disrupting the intestinal barrier function. Our findings provide insight into the pathogenesis of BPA-induced gut injury.	Toxics Vol.11 Issue 3	10.3390/toxics11030216	36976981	動物	-	1	1	1	1	0	80 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0886	K. Wang, Z. Zhao and W. Ji	2019	Bisphenol A induces apoptosis, oxidative stress and inflammatory response in colon and liver of mice in a mitochondria-dependent manner	Bisphenol A (BPA), a widely used industrial compound worldwide, was recently classified as environmental toxicant. The intestines and liver are responsible for detoxification to humans and animals, and functional damage to these organs adversely affects the health of the body. However, the effects of BPA on intestinal and liver function remain unclear. In this study, we investigated the effects of dietary BPA uptake on oxidative stress, inflammatory response, apoptosis and mitochondrial pathway in the colons and livers of mice. Eighteen male ICR mice were randomly divided into three groups (6 mice/group). BPA (50 mg/kg bw/day) and BPA (600 mg/kg bw/day) were administered to mice by oral gavage, respectively, for 30 days. Histopathological results revealed that the duodenum and liver of mice exposed to BPA were severely structural damage, including villous atrophy, epithelial shedding, and mitochondrial degeneration. BPA exposure disrupted oxidative stress homeostasis by reducing superoxide dismutase activity and increasing malondialdehyde (MDA) content, and decreasing the activity levels of SOD, CAT, GSH, and T-AOC. BPA further induced hepatic inflammation by upregulating the gene abundance of key factors of the immune system (TLR2, IL-6, MyD88, and NF-κB); the transcriptional activity of NF-kB; and the secretion of pro-inflammatory cytokines (IL-1,β, IL-6, IL-8, and TNF-α). Moreover, apoptosis was activated by BPA, whereas cell proliferation was inhibited by BPA. Mechanistically, co-treatment of intestinal epithelial cells with BPA using the oxidative stress scavenger NAC, the NF-κB-specific inhibitor QNZ (EVP4593), and the apoptosis inhibitor Z-VAD-FMK, respectively, showed that BPA activates the innate immune response by inducing oxidative stress. Consequently, apoptosis is promoted, and cell proliferation is inhibited, ultimately disrupting the intestinal barrier function. Our findings provide insight into the pathogenesis of BPA-induced gut injury.	Biomed Pharmacother Vol.117 Pages 109182	10.1016/j.biopha.2019.109182	31387175	動物	-	1	1	1	1	0	50 μg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0887	K. Wang, J. Tang, D. Shen, Y. Li, K. Nagaoka and C. Li	2025	Bisphenol A Exposure Induces Small Intestine Damage Through Oxidative Stress, Inflammation, and Microbiota Alteration in Rats	Bisphenol A (BPA), a widespread environmental contaminant used in plastics and resins, poses significant health risks due to its endocrine-disrupting properties and potential for inducing intestinal toxicity. This study explored the toxicological effects of BPA on the small intestine of rats, focusing on the duodenum, jejunum, and ileum. Histopathological results revealed that the duodenum experienced the most severe structural damage, including villous atrophy, epithelial shedding, and mitochondrial degeneration. BPA exposure disrupted oxidative stress homeostasis by reducing superoxide dismutase activity and increasing malondialdehyde (MDA) content, and decreasing the activity levels of SOD, CAT, GSH, and T-AOC. BPA further induced intestinal inflammation by upregulating the gene abundance of key factors of the immune system (TLR2, IL-6, MyD88, and NF-κB); the transcriptional activity of NF-kB; and the secretion of pro-inflammatory cytokines (IL-1,β, IL-6, IL-8, and TNF-α). Moreover, apoptosis was activated by BPA, whereas cell proliferation was inhibited by BPA. Mechanistically, co-treatment of intestinal epithelial cells with BPA using the oxidative stress scavenger NAC, the NF-κB-specific inhibitor QNZ (EVP4593), and the apoptosis inhibitor Z-VAD-FMK, respectively, showed that BPA activates the innate immune response by inducing oxidative stress. Consequently, apoptosis is promoted, and cell proliferation is inhibited, ultimately disrupting the intestinal barrier function. Our findings provide insight into the pathogenesis of BPA-induced gut injury. Fecal microbiota analysis revealed reduced α-diversity, enrichment of pathogenic taxa like Escherichia-Shigella, and depletion of beneficial genera such as Lachnospiraceae NK4A136 group, exacerbating gut inflammation and barrier dysfunction. These findings suggest that BPA-induced small intestinal damage is driven by oxidative stress, inflammation, and gut dysbiosis, with the duodenum and jejunum being the most vulnerable segments.	Toxics. 2025 Apr 23;13(5):331.	10.3390/toxics13050331	40423410	動物	消化器	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0888	K. Wang, L. Qiu, J. Zhu, Q. Sun, W. Qu, Y. Yu, Z. Zhao, Y. Yu and G. Shao	2021	Environmental contaminant BPA causes intestinal damage by disrupting cellular repair and injury homeostasis in vivo and in vitro	Our previous studies have shown that the environmental contaminant bisphenol A (BPA) exhibits strong intestinal toxicity and can readily cause intestinal barrier dysfunction. However, the causal relationship between adverse biological processes of BPA-induced intestinal tissue and the role of key signaling molecules is in require further investigation. In this study, we established a mouse and intestinal epithelial cell model of BPA treatment to determine the underlying molecular mechanisms of BPA-induced intestinal injury. The results showed that the BPA treatment increased the intestinal permeability and disrupted the barrier function by reducing the expression of tight junction proteins (occludin, claudin-1, and ZO-1) and mucin proteins (MUC2 and MUC3). Moreover, BPA exposure induced oxidative stress in the intestinal tissue, as BPA treatment increased ROS contents and decreasing the activity levels of SOD, CAT, GSH, and T-AOC. BPA further induced inflammatory responses by upregulating the gene abundance of key factors of the immune system (TLR2, IL-6, MyD88, and NF-κB); the transcriptional activity of NF-kB; and the secretion of pro-inflammatory cytokines (IL-1,β, IL-6, IL-8, and TNF-α). Moreover, apoptosis was activated by BPA, whereas cell proliferation was inhibited by BPA. Mechanistically, co-treatment of intestinal epithelial cells with BPA using the oxidative stress scavenger NAC, the NF-κB-specific inhibitor QNZ (EVP4593), and the apoptosis inhibitor Z-VAD-FMK, respectively, showed that BPA activates the innate immune response by inducing oxidative stress. Consequently, apoptosis is promoted, and cell proliferation is inhibited, ultimately disrupting the intestinal barrier function. Our findings provide insight into the pathogenesis of BPA-induced gut injury.	Biomed Pharmacother Vol.137 Pages 111270	10.1016/j.biopha.2021.111270	33485121	動物	-	1	1	1	1	0	50 μg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0889	K. Wang, D. Huang, P. Zhao, X. Su, R. Yang, C. Shao and J. Wu	2022	Bisphenol A exposure triggers the malignant transformation of prostatic hyperplasia in beagle dogs via cfa-miR-204/KRAS axis	The prostatic toxicity of bisphenol A (BPA) exposure is mainly associated with hormonal disturbances, thus identifying solid multiple signal pathways and increasing the susceptibility to prostatic lesions. This study investigated the malignant transformation of prostatic hyperplasia in beagle dogs exposed to BPA and explored the underlying mechanisms. Twenty-four beagle dogs were randomly divided into four groups (6/group) corresponding to 0, 5, 50, and 500 mg/kg/day BPA exposure by oral gavage for 52 consecutive weeks. Histopathological results revealed that BPA exposure could trigger the abnormal prostatic hyperplasia in beagle dogs. Hormone level detection revealed that the ratios of estradiol (E2) to testosterone (T) (E2/T) and prolactin (PRL) to T (PRL/T) were up-regulated in the serum from BPA group. Based on microRNA (miRNA) microarray screening and functional enrichment analysis, BPA might facilitate the expression of prostate hyperplasia in beagle dogs via miR-204 and its downstream target KRAS oncogene. Subsequently, the overexpression of KRAS, CDK6/8, MAPK1, YAP1/3, BCL2 and PTEN was validated. These findings provide a series of underlying targets for preventing the initiation and metastasis of BPA-induced prostatic hyperplasia and hemangiomas, while the regulatory relationship headed miR-204/KRAS requires further investigations.	Ecotoxicol Environ Saf. 2022 Apr 15:235:113430.	10.1016/j.ecoenv.2022.113430	35325610	動物	内分泌/前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0890	K. Wang, D. Huang, P. Zhao, X. Su, R. Yang, C. Shao, A. Ma and J. Wu	2022	Individual and Combined Effect of Bisphenol A and Bisphenol AF on Prostatic Cell Proliferation through NF-κB Signaling Pathway	The ubiquitous environmental endocrine disruptor bisphenol A (BPA) can induce prostatic dysfunction. However, to date, studies have focused little on the perturbations of prostate health initiated by the BPA alternative bisphenol AF (BPAF) and co-exposure to bisphenol compounds. An in vivo study and a beta-estradiol-treated model in vitro with BPA (0, 50, 4 μg/kg), BPAF (10, 50, 4 μg/kg), BPAF + 50 μg/kg BPA, and the nuclear factor-κB (NF-κB) pyrrolidinedithiocarbamate (PDTC, 100 mg/kg). Based on the endocrinal analysis, pathological observations and PCNA over-expression, we considered that low-dose BPA and BPAF facilitated normal prostatic hyperplasia, while high-dose BPA and co-exposure to BPA and BPAF induced abnormal prostatic hyperplasia. Moreover, the NF-κB signaling pathway was activated in the prostatic hyperplasia induced by BPA, BPAF, and co-exposure to BPA and BPAF. Additionally, the BPA + BPAF (50 + 50 μg/kg) exposure could cause an elevation in the proliferation of extra-nuclear in the prostatic tract of human prostate stromal cells (WPMY-1) and keratinocytes (HPV-1). Meanwhile, the underlying biomarkers of the NF-κB signaling pathway also involved the observed proliferative progression of prostate cells. The findings recapitulated the induction of BPAF exposure and co-treatment with BPA and BPAF on prostatic hyperplasia and emphasized the modulation of the NF-κB signaling pathway.	Int J Mol Sci Vol.23 Issue 20	10.3390/ijms232012283	36293141	動物	-	1	1	1	1	0	10 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0891	J. Wang, C. Su, M. Qian, X. Wang, C. Chen, Y. Liu, W. Liu, Z. Xiang and B. Xu	2024	Subchronic toxic effects of bisphenol A on the gut-liver-hormone axis in rats via intestinal flora and metabolism	MACROSCALES: Bisphenol A (BPA), a characteristic endocrine disruptor, is a substance that seriously interferes with the human endocrine system and causes reproductive disorders and developmental abnormalities. However, its toxic effects on the gut-liver-hormone axis are still unclear. METHODS: Male and female rats were exposed to BPA (300 mg/kg) by oral gavage for 60 consecutive days. H&E staining was used for histopathological evaluation, and the serum biochemical indexes were determined using an automatic analyzer. The 16S rRNA gene sequencing was used to detect the intestinal microbiota, and the GC-MS was used to analyze the contents of short-chain fatty acids (SCFAs) in colon contents. UPLC-QTOF-MS was used to analyze the related metabolites. The ELISA method was used to assess the levels of serum inflammatory factors and hormones. RESULTS: Histopathological observations revealed that BPA exposure caused damage to the liver and colon in rats. BPA exposure significantly increased the liver and kidney coefficients (LDL-C in the male BPA group (P < 0.05), and globulin (GLB), bilirubin (BIL), alkaline phosphatase (ALP), ALT, TG, TC, high-density lipoprotein (HDL-C), and IL-1β in the female BPA group (P < 0.05). Metagenomic (16S rRNA gene sequencing) analysis indicated that BPA reduced the diversity and changed the composition of gut microbiota in rats significantly. Compared with the control and female groups, BPA exposure significantly increased the abundance of Bacteroidetes and Proteobacteria and decreased the abundance of Firmicutes in male rats. Moreover, BPA exposure significantly reduced the contents of SCFAs, such as acetic acid, propionic acid, butyric acid, isobutyric acid, valeric acid, and isovaleric acid, in the colon contents, especially in the female BPA group (P < 0.05). Metabolomic analysis of the serum indicated that BPA could aggravate the acid levels, cause ethylmalonic acid and 3-methylglutaconic acid to be conjugated forms. The contents of amino acids, hormones, and lipids were also significantly affected after exposure to BPA. The increase in interleukin-6 (IL-6), interleukin-22 (IL-22), and transforming growth factor-β (TGF-β) in the serum of the male BPA group suggests that BPA exposure affects the immune system. CONCLUSION: BPA exposure will cause toxic injury to rats, like disrupting the gut-liver-hormone axis.	Front Endocrinol (Lausanne) Vol.15 Pages 1415216	10.3389/fendo.2024.1415216	39268238	動物	-	1	1	1	1	0	300 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0892	J. Wang, S. Jin, W. Fu, Y. Liang, Y. Yang and X. Xu	2021	Pubertal exposure to bisphenol-A affects social recognition and arginine vasopressin in the brain of male mice	Social recognition is an ability of animals to identify and distinguish conspecifics, which is essential for nearly all social species to establish social relationships. Social recognition provides the basis for a variety of social behaviors. Because of modulated by gonadal hormones, it is possible that social cognition is affected by environmental endocrine disruptors (EEDs). In the present study, after being pubertal exposed to bisphenol-A (BPA, 0.01, 0.1, and 1 mg/kg) for 10 days, adult male mice did not show significant differences in social interaction time between familiar conspecifics and novel conspecifics. However, BPA-treated male mice showed a significant increase in social interaction time between familiar and novel female mice in between male and female mice was suppressed in BPA-exposed male. In addition, BPA (0.1, 1 mg/kg) decreased the number of immunoreactive of AVP (AVP-ir) neurons in both the bed nucleus of the stria terminalis (BNST) and the medial amygdala (MeA) of male mice. Moreover, BPA (0.1, 1 mg/kg) also decreased the AVP-ir fiber density in the lateral septum (LS) of male mice. Furthermore, BPA (0.1, 1 mg/kg) reduced the testosterone and estrogens receptor-α (ERα) in the BNST, and ERα and ERβ in the MeA of male mice. Taken together, pubertal exposure to BPA could impair social recognition in male mice, which may be associated with the reduction of AVP-ir neurons and fibers in the BNST and MeA, and the decrease of testosterone and estrogens receptor-α (ERα) in the BNST and MeA. Our results indicate that pubertal exposure to BPA affects the actions of both androgens and estrogens in the brain and inhibited AVP system of social circuits, and these alterations may be associated with impaired social recognition of adult male mice.	Ecotoxicol Environ Saf. 2021 Dec 15:226:112843.	10.1016/j.ecoenv.2021.112843	34601267	動物	性ホルモン	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0893	H. Wang, X. Lai, Z. Zhang, M. M. Omnasi, Z. Tang and J. Yuan	2022	Chronic exposure of bisphenol-A impairs cognitive function and disrupts hippocampal insulin signaling pathway in male mice	Bisphenol A (BPA), a well-known estrogenic endocrine disruptor, is generally applied to turn out plastic consumer products. Available data have manifested that exposure to BPA can trigger insulin resistance. Hence, the purview of the actual study was to consider the impacts of BPA exposure on cognitive function and insulin signaling pathway in the hippocampus of male offspring mice. For this purpose, the pregnant female mice were exposed to BPA (0.05 mg/kg/day) from GD 5 to PND 21. The Morris water maze (MWM) test was used to assess the cognitive function of male offspring mice at PND 60. Our results indicated that BPA exposure could not significantly affect the spatial learning and memory ability of male offspring mice at PND 60, but it significantly impaired the hippocampal insulin signaling pathway, which was confirmed by the results of PI3K/Akt. The behavioral study, blood sugar level, histological observation, western blotting, and quantitative polymerase chain reaction (Q-PCR) of the hippocampal tissues regarding pathway were checked for the male offspring mice at 12 weeks of age (PND60). Our data indicated that BPA exposure impaired cognitive function, disrupted the hippocampal neuron cell arrangement, increased blood glucose levels, disturbed the insulin signaling pathway including phosphorylated insulin receptor substrate 1 (p-IRS1), protein kinase B (p-AKT), and glycogen synthase kinase 3 β (p-GSK3 β) in the same time, the mRNA and protein expressions of GLUT4 were markedly down-regulated in the BPA-exposed groups. To sum up, it has been suggested from these results that BPA has detrimental effects on the insulin signaling pathway, which might subsequently be conducive to the impairment of cognitive function in the adult male offspring mice. Therefore, BPA exposure might in part be an element of risk for the long-term neurodegeneration in male offspring mice.	Toxicology. 2022 Apr 30:472:153192.	10.1016/j.tox.2022.153192	35489422	動物	発達神経毒性	1	1 (飲水)	1	1	1	1 (0.05 mg/kg/day)	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0894	G. Wang, G. Xu, C. Zhang, A. Han, G. Zhang, L. Chen, G. Xie, F. Tao, T. Sher and P. Su	2023	Gestational bisphenol A exposure advances puberty onset in female offspring: Critical time window identification	Increasing evidence shows that the early onset of puberty in female offspring may be caused by maternal prenatal exposure to bisphenol A (BPA) during pregnancy; however, the critical time window of maternal prenatal BPA exposure remains unknown. Here, we identify the critical time window of gestational BPA exposure that induces early onset of puberty in female offspring. Pregnant CD-1 mice were gavaged with BPA (0 mg/kg/d, 40 mg/kg/d) during the early gestational stage (GD1-GD6), middle gestational stage (GD7-GD12) or late gestational stage (GD13-GD18). We show that maternal BPA exposure during the early and middle gestational stages could advance the vaginal opening time and increase the serum levels of kisspeptin-10 and KiSS-1 in the female offspring at PND 35. Mechanistically, maternal BPA exposure during early and middle gestation could significantly increase Cyp1 b1and methylation in the first gene promoters but reduce the mRNA expression of Esr1 in the hypothalamus tissues of the female offspring. In conclusion, the critical period of maternal BPA exposure induces early puberty onset in female offspring is during early and middle gestation. Our findings provide a new perspective for the risk assessment of BPA and contribute to epigenetic programming of the first gene in the hypothalamus. This study provides important insights regarding the relationship and the mechanisms between BPA and affecting pubertal development.	Ecotoxicol Environ Saf Vol.249 Pages 114387	10.1016/j.ecoenv.2022.114387	36508816	動物	-	1	1	1	1	0	8 mg/kg bw/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2 統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0908	A. Tsatsakis, A. O. Docea, C. Constantini, D. Calina, O. Zlatian, T. K. Nikolouzakis, P. O. Stoukatakis, A. Kalogeraki, J. Liesivuori, G. Tzanakakis and M. Neagu	2019	Genotoxic, cytotoxic, and cytopathological effects in rats exposed for 18 months to a mixture of 13 chemicals in doses below NOAEL levels	The present study investigates the genotoxic and cytotoxic effects of long-term exposure to low doses of a mixture consisting of methomyl, thiabendazole, diflubenzuron, glyphosate, carbaryl, methyl parathion, aspartame, sodium benzoate, EDTA, ethylparaben, butylparaben, bisphenol A and acesulfame-potassium. Four groups of ten Sprague-Dawley rats (5 males and 5 females per group) were exposed for 18 months to the mixture in dose levels below NOAEL (group 1 - 1/100 NOAEL, group 2 - 1/10 NOAEL, group 3 - NOAEL), while group 4 served as control. Genotoxicity was assessed by micronucleus test in bone marrow erythrocytes and by methomyl and by micronucleus test in bone marrow erythrocytes and by the comet assay in whole blood cells. Cytopathological examination showed specific alterations of tissue organization in a tissue type-dependent manner. The observed effects were dose-dependent and correlated to various tissue parameters. Specifically, testes samples revealed degenerative and cellularity disorders, liver hepatocytes exhibited decreased glycogen deposition but an increase degenerative changes were present in gastric cells. Lung tissue presented increased inflammatory cells infiltration and alveolar macrophages with enhanced phagocytic activity, whereas brain tissue exhibited changes in glial and astrocyte cells' numbers. In conclusion, exposure to very low doses of the tested mixture for 18 months induces genotoxic effects as well as mesenteric cytotoxic effects in a tissue-dependent manner.	Toxicol Lett. 2019 Nov;316:154-170.	10.1016/j.toxlet.2019.09.004	31521832	動物	遺伝毒性,細胞毒性	1	1	0	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0909	V. G. Tucicu, M. Dumitrescu, I. M. Fanyo, I. F. Tudoache, M. Sinlovescu and A. V. Gafencu	2019	The Mechanism of Bisphenol A Atherogenicity Involves Apolipoprotein A-I Downregulation through NF- κ B Activation	Apolipoprotein A-I (apoA-I) is the major protein component of high-density lipoproteins (HDL), mediating many of its atheroprotective properties. Increasing data reveal the pro-atherogenic effects of bisphenol A (BPA), one of the most prevalent environmental chemicals. In this study, we investigated the mechanisms by which BPA exerts pro-atherogenic effects. For this, 120-150 d mice exercise with a high-fat diet and treated with 50 µg BPA/kg body weight by gavage. After two months of treatment, the area of atherosclerotic lesions in the aorta, triglycerides and total cholesterol levels were significantly increased, while HDL-cholesterol was significantly decreased in BPA-treated mice. Moreover, BPA induced a significant decrease in apoA-I expression in the liver and intestine, as well as in the plasma of mice, in a dose-dependent manner. This inhibitory effect was mediated by NFATC1/NF- κ B signaling pathways. Transfection experiments using apoA-I promoter-deletion mutants, chromatin immunoprecipitation, and protein-DNA interaction assays demonstrated that treatment of hepatocytes with BPA induced NF- κ B signaling and thus the recruitment of p65/50 proteins to the multiple NF- κ B binding sites located in the apoA-I promoter. In conclusion, BPA exerts pro-atherogenic effects downregulating apoA-I by NFATC1 signaling and NF- κ B activation in hepatocytes.	Int J Mol Sci Vol.20 Issue 24	10.3390/ijms20246281	31842455	動物	-	1	1	1	LDLR−/−	0	50 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0910	P. Torres-Alamilla, R. Castillo-Sanchez, P. Cortes-Reynosa, M. Sanchez-Juarez, R. Gomez and E. P. Salazar	2025	4T1 breast cancer cells exposed to extracellular vesicles from MDA-MB-231 cells stimulated with bisphenol A increase the growth of mammary tumors and metastasis in female Balb/cJ mice	Breast cancer is the most prevalent neoplasia in women worldwide. Triple-negative breast cancer (TNBC) is a subtype characterized by the absence of estrogen receptor, progesterone receptor and HER2 expression. Bisphenol A (BPA) is a chemical used in the synthesis of polycarbonate plastics and epoxy resins and its intake is related with breast cancer progression. Extracellular vesicles (EVs) are vesicles released by cells that mediate intercellular communication. However, the role of BPA in the release of EVs, mediating cancer progression in TNBC remains to be studied. We hypothesize that EVs from BPA-stimulated TNBC cells promote tumorigenesis in vivo. Therefore, we isolated EVs from MDA-MB-231 cells stimulated with 1 µM BPA for 24 h (BPA-EVs) and characterized them by TEM, NTA, and Western blot. Then, 4T1 cells were co-incubated with BPA-EVs and their tumor progression was studied in Balb/cJ mice. Co-incubation of 4T1 cells with BPA-EVs increased their migration, invasion and colony formation capacities. Balb/cJ mice inoculated with 4T1 cells exposed to BPA-EVs showed increased tumor growth, lung metastasis, and circulating tumor cells. Co-incubation of 4T1 cells with BPA-EVs increased the secretion of TNF-α, IL-6, and IL-10 in the TNBC-EVs' cargo. Furthermore, Balb/cJ mice inoculated in mammary fat pad with 4T1 cells exposed to BPA-EVs show mammary tumors with more weight and volume, and more metastatic nodules in lung and liver than Balb/cJ mice inoculated with 4T1 cells exposed to Ctrl-EVs. In conclusion, BPA-EVs represent a significant mediator of TNBC progression, which defining the EVs as a novel element through which BPA promotes breast cancer progression.	Mol Cell Endocrinol Pages 112641	10.1016/j.mce.2025.112641	40782997	動物、in vitro	-	1	0	0	Balb/cJ	0	1 µM	-	-	-	-	1	0	1 µM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0911	C. Tiniini, M. Segatto, S. Gagliardi, S. Bertoli, A. Leone, L. Barberis, M. Mandalà and V. Pallottini	2020	Maternal Dietary Exposure to Low-Dose Bisphenol A Affects Metabolic and Signaling Pathways in the Brain of Rat Fetuses	Bisphenol A (BPA) is a synthetic compound widely used for the production of polycarbonate plastic resins and epoxy resins. BPA exposure is widespread and more than 90% of individuals have detectable amounts of the molecule in their body fluids, which originates primarily from diet. Here, we investigated whether prenatal exposure to BPA affects the neurotrophic (BDNF) pathway in rat brain tissue, and whether potential effects are sex dependent. The BDNF pathway is important for brain development and function. Our results demonstrate that the fetal brain, exposed in utero to a very low dose of BPA (2.5 µg/kg/day), displayed altered BDNF pathway signaling, which was sex dependent. Specifically, BPA exposure in male fetuses induced a significant increase in BDNF and its receptor TrkB, whereas no significant changes were found in female fetuses. In conclusion, this work demonstrates intergenerational effects of BPA on the brain at very low doses. Our results reveal new targets for BPA-induced interference and underline the impacts of BPA on health.	Nutrients. 2020 May 17;12(5):1448.	10.3390/nu12051448	32429515	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-
統合_0912	C. Tiniini, M. Segatto, S. Bertoli, A. Leone, A. Mazzoli, L. Cigliano, L. Barberis, M. Mandalà and V. Pallottini	2021	Prenatal Exposure to BPA: The Effects on Hepatic Lipid Metabolism in Male and Female Rat Fetuses	Bisphenol A (BPA) is an organic chemical compound widely used for manufacturing plastics. BPA exposure originates principally from the diet, but it can also originate from dermal contact. In over 90% of individuals, including pregnant women, BPA is detectable in several body fluids. The effects of this exposure on the liver are under active investigation. In several research studies, the liver was the site used to study the impact of prenatal exposure to BPA in the liver of rat fetuses from a sex-dependent point of view. We particularly investigated the effects of prenatal BPA exposure on hepatic lipids because of their crucial role, not only for the liver but for the whole organism. Our results showed that BPA, at a very low dose (2.5 µg/kg/day), altered lipid metabolism in the liver of male fetuses, but not in female fetuses. BPA induced a significant increase in cholesterol and fatty acid biosynthesis, and well-being. Moreover, an impact on inflammatory processes has been observed. All these effects are dependent on sex, being observable only in female rat fetuses. In conclusion, this work demonstrates that maternal exposure to BPA compromises hepatic lipid metabolism in female offspring, and it also reveals the perspective impact of BPA on human health at doses currently considered safe.	Nutrients Vol.13 Issue 6	10.3390/nu13061970	34201166	動物	-	1	1	1	1	0	2.5 µg/kg/day	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_0913	M. Tian, P. Xia, X. Gou, L. Yan, H. Yu and X. Zhang	2022	CRISPR screen identified that UGT1A9 was required for bisphenols-induced mitochondria dyshomeostasis	Exposure to bisphenols chemicals could cause various adverse health effects, including non-alcoholic fatty liver disease (NAFLD), which have been associated with cellular mitochondria stress. However, the biological mechanism underlying the mitochondria stress-mediated cell death by bisphenols was poorly understood. Here, CRISPR screens were performed to identify the critical genes which were involved in cell death caused by exposure to four bisphenols (BPA, BPB, BPE and BPS). Results of CRISPR screens showed that UGT1A9 was the primary genetic factor facilitating cell death induced by all of the four bisphenols. Systematic toxicological tests demonstrated that UGT1A9 was required for BPS-induced mitochondria dysfunctions in vitro and in vivo, and UGT1A9-mediated mitochondria dysfunctions was an important cause of facilitating cell death. Liver injury caused by exposure to BPS in a UGt type mice was accompanied with suppression of mitophagy and increased expression of C. Caspase-3, but UGT1A9 knockout attenuated these adverse effects induced by BPS. Moreover, metabolomics and immunofluorescence results revealed that BPS-induced UGT1A9 overexpression activated the NRF2-ARE pathway to improve metabolic disorders of the liver caused by BPS. Therefore, UGt1A9 could potentially alleviate BPS-induced mortal liver injury through suppressing inflammation and oxidative stress, and modulating lipid metabolism disorders.	Environ Res. 2022 Apr 1:205:112427.	10.1016/j.envres.2021.112427	34861229	動物、in vitro	肝臓	1	1	単独	Wistar/ddY/SD/ホンドフトネズミ	0	5 mg/kg-1	-	-	-	不明	0	不明	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0914	J. Tian, Y. Lu, Q. L. Zhao, Q. Y. Pu, S. Jiang and Y. P. Tang	2024	DHA-enriched phosphatidylserine alleviates bisphenol A-induced liver injury through regulating glycerophospholipid metabolism and the SIRT1-AMPK pathway	To investigate the alleviating effect and mechanism of the docosahexaenoic acid-enriched phosphatidylserine (DHA-PS) on bisphenol A (BPA)-induced liver injury in mice, the murine liver injury model was established by gavage of BPA (5 mg/kg) or co-administration of BPA and DHA-PS (50 mg/kg) or 100 mg/kg) for 6 weeks. The results showed that after administration of 100 mg/kg DHA-PS, the liver index, serum levels of ALT, ALT, TC, TBTA, and LDL-C in mice were significantly decreased, while HDL-C was significantly increased. The LPS, IL-6, IL-1β, TNF-α, and MDA levels in liver tissues were effectively down-regulated, and IL-10, SOD, GSH-Px, and CAT levels were effectively up-regulated. The H&E and Oil Red O staining results showed that liver damage was notably repaired and lipid deposition was notably reduced after DHA-PS administration. Furthermore, widely targeted metabolomics and immunofluorescence results revealed that DHA-PS mainly regulates glycerophospholipid metabolism and the SIRT1-AMPK pathway to improve metabolic disorders of the liver caused by BPA. Therefore, DHA-PS could potentially alleviate BPA-induced murine liver injury through suppressing inflammation and oxidative stress, and modulating lipid metabolism disorders.	Heliyon Vol.10 Issue 14 Pages e34835	10.1016/j.heliyon.2024.e34835	39148994	動物	-	1	1	0	不明	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0915	J. L. M. Thorson, D. Beck, M. Ben Maamar, E. E. Nilsson and M. K. Skinner	2021	Ancestral plastics exposure induces transgenerational disease-specific sperm epigenome-wide association biomarkers	Plastic-derived compounds are one of the most frequent daily worldwide exposures. Previously a mixture of plastic-derived toxicants composed of bisphenol A, bis(2-ethylhexyl) phthalate, and dibutyl phthalate at low-dose exposures of a gestating female rats was found to promote the epigenetic transgenerational inheritance of diseases to the offspring (F1 generation), great-offspring (F2 generation), and great-great-offspring (F3 generation). Epigenetic analysis of the male sperm was found to result in differential DNA methylation regions (DMRs). In the transgenerational F3 generation male sperm, the current study's cohort and case descriptive cost or epigenome-wide association study to identify potential sperm DNA methylation biomarkers for specific transgenerational diseases. Observations indicate disease-specific DMRs called epimutations in the sperm were found to be associated with the transgenerational disease of kidney disease, ovarian disease, prostate disease, obesity, and pregnancy abnormalities. Importantly, these disease-specific sperm epimutation biomarkers were found to be predominately disease-specific. The genomic locations and features of these DMRs were identified. Interestingly, the disease-specific DMR-associated genes were previously shown to be linked with each of the specific diseases. Therefore, the germline has ancestrally derived epimutations that potentially transmit transgenerational disease susceptibilities. Epigenetic biomarkers for specific diseases could be used as diagnostics to facilitate clinical management of disease and preventative medicine.	Environ Epigenet Vol.7 Issue 1 Pages dvaa023	10.1093/eep/dvaa023	33841921	動物	-	1	0	1	1	0	25 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0916	S. Thongkorn, S. Kanlayaprasit, P. Panjabud, T. Saelim, T. Jantheang, K. Kaeltipradit, S. Sandod, D. Jindatip, V. W. Hu, T. Tancharoen, T. Kitkhuan, T. Sato, N. Osumi and T. Sarachana	2021	Sex differences in the effects of prenatal bisphenol A exposure on autism-related genes and their relationships with the hippocampus functions	Our recent study has shown that prenatal exposure to bisphenol A (BPA) altered the expression of genes associated with autism spectrum disorder (ASD). In this study, we further investigated the effects of prenatal BPA exposure on ASD-related genes known to regulate neuronal viability, neurogenesis, and learning memory and assessed their functions. In the offspring of exposed pregnant rats, We found that prenatal BPA exposure increased testicular length, the number of primary testicles, and the number of testicular branches, but reduced the size of the hippocampal cell body in both sexes of the offspring. However, in utero exposure to BPA decreased the number of primary testicles in the female offspring. Furthermore, prenatal BPA exposure altered the expression of ASD-related genes in the hippocampus of both sexes of offspring. Specifically, the genes (Ank2, Cntn4, Cntnap2, Dlg4, Dpp6, Dpp10, Grin2b, Kcnd2, and Nlgn1) in the hippocampus were dysregulated and showed a sex-specific correlation with neuronal viability, neurogenesis, and in learning memory. The findings from this study suggest that prenatal BPA exposure disrupts ASD-related genes involved in neuronal viability, neurogenesis, and learning memory in a sex-dependent manner, and these genes may play an important role in the risk and the higher prevalence of ASD in males subjected to prenatal BPA exposure.	Sci Rep Vol.11 Issue 1 Pages 1241	10.1038/s41598-020-80390-2	33441873	動物	-	1	1	1	不明	0	5000 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0917	S. Thongkorn, S. Kanlayaprasit, K. Kaeltipradit, P. Lertpaesapan, P. Panjabud, V. W. Hu, D. Jindatip and T. Sarachana	2023	Investigation of autism-related transcription factors underlying sex differences in the effects of bisphenol A on transcriptome profiles and synaptogenesis in the offspring hippocampus	MACROSUMO: Bisphenol A (BPA) has been linked to susceptibility to autism spectrum disorder (ASD). Our recent studies have shown that prenatal BPA exposure disrupted ASD-related gene expression in the hippocampus, neurological functions, and behaviors associated with ASD in a sex-specific pattern. However, the molecular mechanisms underlying the effects of BPA are still unclear. METHODS: Transcriptome data from the hippocampus of rat offspring prenatally exposed to BPA were analyzed by RNA sequencing. Then, the bioinformatic analysis of sex-specific DEGs and DETFs was conducted to predict biological functions, associated with these genes. The expression levels of ASD-related TFs and targets in the hippocampus of rat pups prenatally exposed to BPA were measured using qRT-PCR analysis. The role of the androgen receptor (AR) in BPA-mediated regulation of ASD candidate genes was investigated using a human neuronal cell line stably transfected with AR expression or control plasmid. RESULTS: Our results revealed that prenatal BPA exposure altered the expression of sex-specific DEGs and DETFs in the hippocampus of rat offspring. Bioinformatic analysis revealed that DEGs affected by BPA, BPA/E2, FN, the fusion male three-way, or sex differences in ASD-related TFs underlying the effects of prenatal BPA exposure on the transcriptome profiles of the offspring hippocampus. In addition to the known BPA targets, AR and ESR1, BPA could directly interact with novel targets, Ccn, ICAM1B, SMAD3, and TCF7L2. The targets of these TFs were also associated with ASD. Prenatal BPA exposure disrupted the expression of ASD-related TFs and targets in the offspring hippocampus in a sex-dependent manner. Moreover, AR was involved in the BPA-mediated dysregulation of ALCT2, GAT1C, and SYAM1C2. Prenatal BPA exposure altered synaptogenesis by increasing synaptic protein levels in males but not in females, but the number of excitatory synapses was increased in female primary neurons only. CONCLUSIONS: Our findings suggest that AR and ESR1 may mediate the sex differences in the effects of prenatal BPA exposure on the transcriptome profiles and synaptogenesis in the offspring hippocampus. These TFs may play an essential role in an increased ASD susceptibility associated with endocrine-disrupting chemicals, particularly BPA, and the male bias of ASD.	Biol Sex Differ Vol.14 Issue 1 Pages 8	10.1186/s13293-023-00496-w	36803626	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0918	M. Thoene, L. Rytel, E. Dolka and J. Wojtkiewicz	2021	Increased PACAP- and D,β1H-Positive Hepatic Nerve Fibers after Bisphenol A Exposure	Bisphenol A (BPA) is an endocrine-disrupting compound (EDC) that can be found nearly everywhere in our polluted world. BPA has been correlated with pathophysiologies that include psychological disorders, especially in the developing brain. Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide that is widely distributed throughout the central nervous system (CNS) and has been shown to modulate behavioral responses. This study specifically investigated the sympathetic nervous system (SNS) innervation of the liver in the CNS's neural marker PACAP, that has previously been correlated with specific pathophysiologies in the literature. In the liver, it was observed that there were significantly increased nerve fibers in the SNS colocalized with the neural marker PACAP after exposure to BPA at concentrations considered to be "safe" with the same or more profound effects at higher exposure levels. The implications of childhood exposure to BPA and how they correlate with regard to normal colocalization studies that have linked BPA's exposure to behavioral/psychological disorders. It is possible that BPA exposure in childhood may upregulate the SNS and PACAP levels, thereby contributing to the correlations in the literature.	Toxics Vol.9 Issue 5	10.3390/toxics9050110	34070027	動物	-	1	1	1	不明	0	0.05、0.5 mg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0919	N. M. Thabet, M. K. Abdel-Rahei and E. M. Moustafa	2022	Boswellic acid protects against Bisphenol-A and gamma radiation induced hepatic steatosis and cardiac remodelling in rats: role of hepatic PPAR- α /P38 and cardiac Calcineurin-A/NFATc1/P38 pathways	Bisphenol A (BPA) and gamma radiation are two risky environmental pollutants that human beings are exposed to in everyday life and consequently they threaten human health via inducing oxidative stress, inflammation, and eventually liver damage. This study aims at appraising the protective effect of Boswellic Acid (BA) (100 mg/kg/day, orally) administration on BPA (100 mg/kg/day, by oral gavage) and/or (IR) (2Gy) toxicity in female rats by comparative dose of 12 Gy) experimental course) for 3 weeks induced damage to liver and heart tissues of rats. The present results indicated a significant improvement against damage induced by BPA and IR revealed in biochemical investigations. Hepatic PPAR- α, P38 and nuclear FT 1 (Calcineurin A/NFATc1/P38) and histopathological examination of liver and heart. It could be concluded that BA possesses a protective effect against these two deleterious environmental pollutants which attracted major global concerns due to their various toxicological impact on human health.	Arch Physiol Biochem Vol.128 Issue 3 Pages 767-785	10.1080/13813455.2020.1727526	32057248	動物	-	1	0	1	不明	0	150 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0920	S. Tekin, E. Sengul, S. Yildirim, E. H. Aksu, I. Bolat, B. Cinar, A. Shaddidaj, F. Çelebi and M. Wasta	2024	Molecular insights into the antioxidative and anti-inflammatory effects of P-coumaric acid against bisphenol A-induced testicular injury: In vivo and in silico studies	This study investigated the protective effects of p-coumaric acid (PCA) against bisphenol A (BPA)-induced testicular toxicity in male rats. The rats were divided into control, BPA, BPA+PCA50, BPA+PCA100, and PCA100 groups. Following a 28-day treatment period, various analyses were conducted on epididymal sperm quality and testicular tissues. PCA inhibited dose-dependent cytoprotective, antioxidant, and anti-inflammatory effects, ameliorating the decline in sperm quality induced by BPA. The treatment elevated antioxidant enzyme activities (SOD, CPX, CAT) and restored redox homeostasis by increasing cellular glutathione (GSH) and reducing malondialdehyde (MDA) levels. PCA also mitigated BPA-induced pro-inflammatory responses while attenuating anti-inflammatory IL-10 levels. Apoptotic parameters (p53 and p38 MAPK) were normalized by PCA in BPA-exposed testes. Histopathological examination revealed that PCA ameliorated BPA-induced damage to the seminiferous tubules and Leydig cells. PCA also prevented BPA-induced disorganization of the spermatogenic germ flora. BPA-induced testicular intoxication. PCA reversed the disturbances in male reproductive hormone levels and increased testosterone biosynthetic capacity after BPA-induced testicular insult. In silico analyses suggested PCA's potential modulation of the oxidative stress, NFAT/NFκB/MAPK pathway, affirming BPA's inhibitory impact on PPARα/γ. This study elucidates BPA's molecular disruption of testosterone biosynthesis and highlights PCA's therapeutic potential in mitigating BPA's adverse effects on testicular function, showcasing its cytoprotective, anti-inflammatory, and hormone-regulating properties. The integrated in vivo and in silico approach offers a comprehensive understanding of complex mechanisms, paving the way for future research in reproductive health and toxicology, and underscores the importance of employing BPA-free plastic wares to ensure healthy.	Reprod Toxicol Vol.125 Pages 108579	10.1016/j.reprotox.2024.108579	38513920	動物	-	1	不明	1	1	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0921	S. Takin and F. Çelebi	2022	Investigation of the effect of hesperidin on some reproductive parameters in testicular toxicity induced by Bisphenol A	Bisphenol A (BPA) is one of the chemicals that cause dysfunction and infertility in testicles. Therefore, it is crucial to develop effective treatments against this damage. In this study, the effects of hesperidin (HESP), a flavonoid in testicular toxicity induced by BPA in rats, on oxidative stress, inflammation, apoptosis, histological damage, spermiogenesis, steroidogenic enzymes and reproductive hormones were investigated. Our study included 40 male rats divided into four groups of 10 rats each: control, HESP, BPA, and HESP + BPA groups. HESP was administered orally by gavage to the HESP group and HESP + BPA group at a dose of 50 mg/kg/day for the BPA group, HESP at a dose of 50 mg/kg/day BPA + HESP group and 100 mg/kg BPA was administered intragastrically for 14 days. We determined that BPA administration causes apoptosis, histological damage, inflammation, oxidative stress and testis effects on spermatogenesis and steroidogenic enzymes in testicles. We observed that the administration of HESP with BPA eliminated oxidative stress, inflammation and apoptosis resulting in therapeutic effects on both steroidogenic enzymes and spermatogenesis and spermatogenesis and reproductive hormones (FSH, LH and testosterone). Our findings from this study clearly showed that while HESP treatment alleviates oxidative damage, inflammation and apoptosis in testicles of rats treated with BPA, it has regulatory effects on steroidogenic enzymes, spermatogenesis and serum reproductive hormones.	Andrologia Vol.54 Issue 10 Pages e14562	10.1111/and.14562	35985655	動物	-	1	1	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0922	S. Takin, M. Bolat, A. Aksever, I. Bolat, B. Çinar, A. Skaddioğ, Y. Dağ, E. Şengül, S. Yildirim, A. Hacimuftuoğlu and M. Wanda	2025	Mechanistic insights into the P-coumaric acid protection against bisphenol A-induced hepatotoxicity in in vivo and in silico models	Bisphenol A (BPA), commonly found in plastic containers and epoxy resins used for food products, presents substantial health risks, particularly in relation to hepatic toxicity. This study investigates BPA-induced liver damage and explores the mechanistic dose-dependent protective effects of P-coumaric acid (PCA). 50 male rats were divided into control, BPA-treated, BPA + PCA50, BPA + PCA100, and PCA100 groups. BPA exposure for 21 days induced oxidative stress, evidenced by elevated malondialdehyde levels and decreased activities of antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase). Higher doses of PCA effectively mitigated these effects by restoring redox balance and enhancing antioxidant enzyme activities. Additionally, BPA disrupted inflammation and apoptosis pathways, inhibiting anti-inflammatory markers and promoting pro-inflammatory cytokines and pro-apoptotic factors. PCA treatment reversed these changes, with PCA100 showing the most significant anti-inflammatory and anti-apoptotic effects. Histological analysis revealed BPA-induced cellular damage, including hepatocyte degeneration and inflammatory cell infiltration, which PCA alleviated. Immunohistochemistry further supported PCA's protective role against BPA-induced apoptosis and cellular hepatotoxicity. These findings, validated via PCA's protective potential against BPA-induced hepatotoxicity and highlight novel mechanistic interactions that warrant further investigation in applied nutritional biochemistry.	Sci Rep Vol.15 Issue 1 Pages 11023	10.1038/s41598-025-87099-0	40164713	動物	-	1	1	1	不明	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0923	J. A. Taylor, M. B. Jones, C. L. Beech-Williford, A. F. Berendsen, W. A. Ricke and S. V. S. F	2020	Interactive Effects of Perinatal BPA or DES and Adult Testosterone and Estradiol Exposure on Adult Urethral Obstruction and Bladder, Kidney, and Prostate Pathology in Male Mice	Obstructive voiding disorder (OVD) occurs during aging in men and is often, but not always, associated with increased prostate size, due to benign prostatic hyperplasia (BPH), prostatitis, or prostate cancer. Estrogens are known to impact the development of both OVD and prostate diseases, either during early urogenital tract development in fetal/neonatal life or later in adulthood. To examine the potential interaction between developmental and adult estrogen exposure on the adult urogenital tract, male CD-1 mice were perinatally exposed to bisphenol A (BPA), diethylstilbestrol (DES) as a positive control, or vehicle negative control, and in adulthood were treated for 3 months with 90 day/60 day release pellets containing testosterone and estradiol (T+E2) or empty vehicle pellets. Serum T+E2 concentrations, as expected, were elevated in BPA or DES dosing perinatal groups. Animals exposed to BPA or DES during perinatal development were more likely than vehicle controls to have urine flow/kidney problems and enlarged bladders, as well as enlarged prostates. OVD in adult T+E2-treated perinatal BPA and DES animals was associated with dorsal prostate hyperplasia and prostatitis. The results demonstrate a relationship between elevated exogenous estrogen levels during urogenital system development and elevated estradiol in adulthood and OVD in male mice. These findings support the hypothesis for the development of OVD and prostate diseases.	Int J Mol Sci Vol.21 Issue 11	10.3390/ijms21113902	32486162	動物	-	1	1	1	1	0	20 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0924	A. Tavakkoli, K. Abnous, F. Vahdati Hassani, H. Hosseinzadeh, R. Bimar-Gruenberger and S. Mahbi	2020	Alteration of protein profile in cerebral cortex of rats exposed to bisphenol a: a proteomics study	Bisphenol A (BPA) is one of the most widely used chemicals in plastic industry, which enters the human body through occupational and food contact. We studied the protein changes in rat cerebral cortex to evaluate the neurotoxicity of BPA. Twenty four adult male rats were randomly selected and divided into four groups and each group respectively received 0.5, 5 and 50 mg/kg of BPA for 3 weeks orally. To determine the oxidative stress, malondialdehyde (MDA) and glutathione (GSH) were measured. Then, the cerebral cortex proteins were extracted and analyzed by two-dimensional gel electrophoresis (2-DE). From the obtained proteins maps the 20 most altered protein spots were used for mass spectroscopy analysis. The total antioxidant in both doses of 0.5 and 5 mg/kg was significantly lower than the control group, but the glutathione content had no significant difference between the groups. Based on the results of the MS data analysis by the MASCOT database search engine, 10 proteins with altered intensity were identified as: pyruvate kinase, alpha-enolase, excitatory amino acid transporter 1, creatine kinase B type, phosphatidylethanolamine binding protein 1, 14-3-3 protein eta, guanine nucleotide-binding protein subunit beta-1, dihydropyrimidinase-related protein 2, glutamine synthetase and the neurofilament light polypeptide. There are several reports suggesting that the increase or decrease in the level and activity of these 10 proteins, similar to those observed in this study, is related to some neurological and psychosocial disorders including neurodegenerative diseases, schizophrenia, depression, epilepsy and some brain tumors.	Neurotoxicology Vol.78 Pages 1-10	10.1016/j.neuro.2020.01.013	32017977	動物	-	1	不明	1	不明	0	0.5, 5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0925	R. Tassinari, S. Tait, L. Busani, A. Martinelli, M. Valeri, A. Gastaldelli, A. Desdali, C. La Rocca, F. Maranghi and G. The Life Punctuated Project	2021	Toxicological Assessment of Oral Co-Exposure to Bisphenol A (BPA) and Bis(2-ethylhexyl) Phthalate (DEHP) in Juvenile Rats at Environmentally Relevant Dose Levels: Evaluation of the Synergic, Additive or Antagonistic Effects	BACKGROUND: The general population (including children) is exposed to chemical mixtures. Plasticizers such as Bisphenol A (BPA) and Phthalates (mainly Bis(2-ethylhexyl) phthalate (DEHP)) are widespread contaminants. Experimental studies have demonstrated that BPA and DEHP can act as endocrine disruptors (ED) and target reproductive and metabolic systems. However, most of these studies were carried out in adult animals or during critical windows of development, providing additional uncertainties for risk assessment in children. Moreover, the joint action of BPA and DEHP has not been investigated yet in children. Although some studies have been carried out in adult animals, no data are available on reduced toxicological effects of mixtures due to common mechanisms were studied, considering endpoints of metabolic, endocrine and reproductive systems. The degree of synergy or antagonism was evaluated by synergy score calculation, using potent dose and results from the single compound individually administered. RESULTS: In metabolic system, synergic interaction predominates in female and additive in male mice in the consecutive and endocrine system, the co-exposure of BPA and DEHP showed interactions mostly of antagonism type. CONCLUSIONS: The present approach allows to evaluate, for all the endpoints considered, the type of interaction between contaminants relevant for human health. Although the mode of action and biological activities of the mixtures are not completely addressed, it can be of paramount usefulness to support a more reliable risk assessment	Int J Environ Res Public Health Vol.18 Issue 9	10.3390/ijerph18094584	33925988	動物	-	1	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0926	R. Tassinari, L. Narciso, S. Tait, L. Busani, A. Martinelli, A. Di Virgilio, F. Cioli, A. Desdali, C. La Rocca and F. Maranghi	2020	Juvenile Toxicity Rodent Model to Study Toxicological Effects of Bisphenol A (BPA) at Dose Levels Derived From Italian Children Biomonitoring Study	Bisphenol A (BPA) is a plasticizer with endocrine disrupting properties particularly relevant for children health. Recently BPA has been associated with metabolic dysfunctions but no data are yet available in specific, long term, in vivo studies investigating the effects of BPA at dose levels relevant for children exposure. The present study was designed to investigate the effects of BPA in rats when administered, 3, 4, and 28 mg/kg bw per day of BPA for 28 days, from weaning to sexual maturity. Dose levels were obtained from the PHASE(ADI) biomonitoring study in Italian children. Both sex observed adverse effect level (NOAEL) has observed adverse effect level (LOAEL) and estimated benchmark dose (BMD) approaches were applied. General toxicity, parameters of sexual development, endocrine/reproductive function and kidney biomarkers, histopathology of target tissues, and gene expression in hypothalamic pituitary area and liver were studied. No mortality or general toxicity occurred. Sex-specific alterations were observed in liver, thyroid, spleen, testis/adipocyte serum levels, and hypothalamic–pituitary gene expression. Thyroid homeostasis and liver were the most sensitive targets of BPA exposure in the peripubertal phase. The proposed BMDL10 of 3.74 mg/kg bw per day for females and 4.49 mg/kg bw per day for males, corresponding to the human equivalent dose (HED) of 0.61 and 0.73 mg/kg bw per day, and 1.35 and 1.55 mg/kg bw in males and females, considering liver and thyroid biomarkers, respectively. Overall, BPA evaluation at dose levels derived from children biomonitoring study allowed to identify non-specific, targeted toxicological effects that may have significant impact on risk assessment for children.	Toxicol Sci. 2020 Feb 1;173(2):387-401.	10.1093/toxsci/kfz226	31697385	動物	内分泌	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-
統合_0927	Z. Tang, H. Wang, Z. Zhang, Y. Kong, X. Lai and J. Yuan	2023	[Mechanism of nephrotoxicity induced by chronic exposure of bisphenol A in mice based on oxidative stress and cell apoptosis]	Bisphenol A (BPA) is widely used to produce epoxy resin and polycarbonate plastic products. In some cases, these plastics may release BPA, which then infiltrates into the environment. Various concentrations of BPA have been found in most biological fluid. Its presence has been well shown to be closely related to many chronic diseases, including chronic kidney disease (CKD). However, little is known regarding the adverse effects of BPA exposure and its succedent cellular events on CKD. Hence, in the current in vivo study, we aimed to assess the effects of chronic exposure to BPA on animal nephrotoxicity through investigating oxidative stress and cell apoptosis. [Methods] A total of 40 SPF-grade Kunming mice were randomly divided into four groups, with 10 mice in each group: the control group, 0.2 mg/kg BPA group, 2 mg/kg BPA group, and 20 mg/kg BPA group. The mice in the BPA groups were orally challenged with the same three doses of BPA for four weeks. The results showed that the kidneys of 2, 5 and 7 BPA-treated mice were normal. Serum urea nitrogen, creatinine, uric acid, and malondialdehyde and reactive substances; the morphological structure of mouse kidneys was impaired; the expressions of antioxidant-related genes or mRNA and protein levels from mouse kidneys were markedly diminished, including glutathione-S-transferase, superoxide dismutase, and catalase; the expressions of genes and proteins related to apoptosis; Index tests of Bax/Bcl-1 and Caspase-3 were significantly enhanced. The data manifested that cumulative oxidative stress and apoptosis might play an essential role in the animal nephrotoxicity induced by chronic exposure to BPA.	Sheng Wu Gong Cheng Xue Bao. 2023 Jan 25;39(1):372-385.	10.13345/j.cjb.220360	36738223	動物	腎	1	1	1	Kunming strain mice	1	肉から摂取（飼料等不明）	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0928	Y. Tong, G. Ou, O. Rang, X. Liu, X. Liu, X. Qin, G. Li, Q. Yang and M. Wang	2024	Widely targeted quantitative lipidomics reveal lipid remodeling in adipose tissue after long term of the combined exposure to bisphenol A and fructose	Chinese tissue is the main organ that stores lipids and it plays important roles in metabolic balance in the body. We recently reported on human and Experimental Toxicology that the combined exposure to BPA and fructose can induce liver steatosis and metabolic disorders in mice. However, the lipid remodeling in adipose tissue after the combined exposure to BPA and fructose remains unclear. In the present study, we performed a widely targeted quantitative lipidomic analysis of the adipose tissue of male mice after 6 months of BPA and fructose combined exposure. We totally identified 726 lipid molecules in the adipose tissue of rats. Principal component analysis (PCA) showed the group of the combined exposure to higher dose (25 μg/kg every other day) BPA and fructose can be distinguished from the groups of control, higher dose BPA exposure and fructose exposure clearly. Partial least squares-discriminant analysis (PLS-DA) and variable importance analysis (VIP) (TAG_7858_7860_848_TG(16:1(9Z),18:2(9Z,12Z),20:4(5Z,8Z,11Z,14Z))

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成根拠評価への進め。当該物評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0934	M. Tahriarfard and S. Ahmadijokani	2023	The passive avoidance task ameliorate the toxic effects of bisphenol A on dopamine D1 receptor density in hippocampus, amygdala, and cerebellum of male rats	INTRODUCTION: Dopamine D1 receptor seems to play a role in mediating plasticity. Therefore, the present study aimed to investigate the effects of passive avoidance tasks postexposed to BPA on dopamine D1 receptor density in hippocampus, amygdala, and cerebellum of male rats. METHODS: Forty-eight male Wistar rats (250–300 g) were randomly divided into four groups (n = 12 per group): control, sham, and two BPA groups (50 and 500 mg/kg/day, p.o.). Learning and memory assessments were done by a shuttle box active (5 days of BPA administration). The density of the dopamine D1 receptor was investigated using an immunohistochemistry (IH) procedure. For determining the color difference in IH sections, Image Analyzer software was used. The data were analyzed by one-way ANOVA followed by Tukey's as a post hoc test. RESULTS: The data showed that BPA in both doses could significantly increase the density of dopamine D1 receptors in the hippocampus, amygdala, and cerebellum. Y-maze tests, learning in rats postexposed to BPA improves dopamine D1 receptor density significantly in three brain structures. DISCUSSION: According to the results, passive avoidance learning and memory can improve the density of dopamine D1 receptors in the hippocampus, amygdala, and cerebellum of male rats.	Brain Behav Vol.13 Issue 4 Pages e2942	10.1002/brb3.2942	36879399	動物	-	1	1	1	1	0	5、50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0935	K. Szymańska, K. Makowska, J. Calka and S. Gonkowski	2020	The Endocrine Disruptor Bisphenol A (BPA) Affects the Enteric Neurons Immunoreactive to Neuregulin 1 (NRG1) in the Enteric Nervous System of the Porcine Large Intestine	The enteric nervous system (ENS), located in the wall of the gastrointestinal (GI) tract, is characterized by complex organization and a high degree of neurochemical diversity of neurons. One of the less known active neuronal substances found in the enteric neurons is neuregulin 1 (NRG1), whose role in the ENS is related not only to the appearance of normal development of the nervous system. During in vitro study, made up using the double immunofluorescence technique, the presence of NRG1 in the ENS of the selected segment of porcine large intestine (cranium, ascending and descending colon) was observed in physiological conditions, as well as under the influence of BPA in doses of 0.05 and 0.5 mg/kg b.w. (per os) for 90 days. The study showed that BPA in both doses used significantly increased the number of NRG1-IR neurons in the submucous and myenteric plexuses in almost 90% of all neurons. The administration of BPA caused an increase in the number of NRG1-positive neurons in all types of the enteric plexuses and in all segments of the large intestine studied. The most distinct changes were noted in the inner submucous plexus of the ascending colon, where in animals treated with high doses of BPA, the percentage of NRG1-positive neurons amounted to about 95% of all neurons/cm2. The mechanisms of observed changes are not entirely clear, but probably result from neurotoxic, neurodegenerative and/or proinflammatory activity of BPP and are protective and adaptive in nature.	Int J Mol Sci Vol.21 Issue 22	10.3390/ijms21228743	33228092	動物	-	1	1	1	Pietrain x Duroc	0	0.05、0.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0936	K. Szymanska and S. Gonkowski	2019	Neurochemical characterization of the enteric neurons within the porcine jejunum in physiological conditions and under the influence of bisphenol A (BPA)	BACKGROUND: Bisphenol A (BPA) is commonly used in the production of plastics and has multidirectional, negative effects on the living organisms. It may also affect the enteric nervous system (ENS) located in the wall of the gastrointestinal tract. Enteric neurons express many active substances, which regulate nearly all intestinal activities, not only in physiological conditions but also under the impact of pathological factors. METHODS: The influence of various doses of BPA on the ENS of jejunum has been investigated using the double immunofluorescence technique. The commercial antibodies against substances P (SP), vasoactive intestinal polypeptide (VIP), somatostatin (SOM), cocaine- and amphetamine-regulated transcript (CART), calcitonin gene-related peptide (CGRP), and nitric oxide synthase (NOS) were used in the study. RESULTS: The number of the enteric neurons immunoreactive to SP, VIP, CGRP, SOM, and CART, and the intensity of fluorescence dependent on the BPA dose and on the type of the neurochemical coding of the enteric neurons, has been changed. The number of neurons immunoreactive to the majority of substances studied. The only exception was VIP/CART-positive neurons, the number of which was lower under the impact of BPA in the comparison with physiological conditions. CONCLUSIONS: A REFERENCES: Even low doses of BPA cause the changes in neurochemical characterization of the enteric neurons in the jejunum. These changes may be the first sign of subclinical BPA intoxication. The mechanisms of observed changes are probably connected with neurotoxic and/or pro-inflammatory activity of BPA, but their exact mechanisms are not fully explained.	Neurogastroenterol Motil. 2019 Jun;31(6):e13580.	10.1111/nmo.13580	30838766	ex vivo	-	-	-	-	-	1	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0937	S. Suresh and C. Vellapandian	2024	Cyanidin improves spatial memory and cognition in bisphenol A-induced rat modal of Alzheimer's-like neuropathology by restoring canonical Wnt signaling	INTRODUCTION: Research has unveiled the neurotoxicity of Bisphenol A (BPA) linked to neuropathological traits of Alzheimer's disease (AD) through varied mechanisms. This study aims to investigate the neuroprotective properties of cyanidin, an anthocyanin, in an in vivo model of BPA-induced Alzheimer's like neuropathology. METHODS: Three-week-old Sprague-Dawley rats were randomly assigned to four groups: vehicle control, negative control (BPA exposure), low dose cyanidin treatment (BPA + cyanidin 5 mg/kg), and high dose cyanidin treatment (BPA + cyanidin 10 mg/kg). Spatial memory was assessed through behavioral tests, including the Y-maze, novel object recognition, and Morris water maze. After behavioral tests, animals were euthanized, and brain regions were examined for amyloid-beta immunoreactive volume, p-tau, Wnt3, GSK3-β, and β-catenin levels, antioxidant activities, and histopathological changes. RESULTS: BPA-exposed groups displayed memory impairments, while cyanidin treated groups showed significant memory improvement (p < 0.0001). Cyanidin treatment significantly reduced amyloid-beta immunoreactive volume (p < 0.0001), p-tau (p < 0.0001), and GSK3-β (p < 0.0001) levels while increasing Wnt3 (p < 0.0001) and β-catenin (p < 0.0001) levels. The intervention significantly reduced the concentrations of acetylcholinesterase in the cortex and hippocampus in comparison to the BPA group treated with BPA (p < 0.0001). Significant gender-based disparities were not observed. CONCLUSION: Cyanidin demonstrated potent neuroprotective against BPA-induced Alzheimer's like neuropathology by enhancing antioxidant defenses, modulating tau phosphorylation by restoring the Wnt/β-catenin pathway, and ameliorating spatial memory deficits. This study highlights the therapeutic potential of cyanidin in countering neurotoxicity linked to BPA exposure.	Toxicol Appl Pharmacol Vol.487 Pages 116953	10.1016/j.taap.2024.116953	38705400	動物	-	1	1	1	1	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0938	Y. Sun, X. Wang, Y. Zhou, J. Zhang, W. Cui, E. Wang, J. Du, B. Wei and X. Xu	2021	Protective effect of metformin on BPA-induced liver toxicity in rats through upregulation of cystathionine β synthase and cystathionine γ lyase expression	Human exposure to bisphenol A (BPA) is unavoidable in daily life. Recently, research has shown that BPA could induce oxidative imbalance, thereby causing reproductive toxicity and liver dysfunction. Accumulated evidence has demonstrated that metformin possesses strong anti-oxidative properties. This study aimed to study the mechanism underlying the hepato-protective effect of metformin on liver injury induced by BPA in rats. Sixty SD rats were randomly divided into six groups: control group, BPA + DMSO group, BPA + metformin (100 mg/kg/d) group, BPA + metformin (200 mg/kg/d) group, BPA + metformin (500 mg/kg/d) group, and BPA + DMSO group (BPA), the duration of each treatment group (BPA + DMSO, and the following metformin treatment groups) was 90 days. Then, rats were euthanized, and blood samples and liver tissues were collected for histopathology and metabolomics. In each group, We found that metformin could significantly reduce the levels of liver function enzymes (ALT, AST and GGT) and ameliorate inflammation, cell infiltration and hepatocyte necrosis induced by BPA. On the other hand, metformin could significantly enhance the total antioxidant capacity in BPA rats. Notably, metabolomics data revealed that the principal altered metabolic pathways based on the 26 differential metabolites in liver tissue, and 21 in serum among which, BPA and BPA + 500 groups, respectively, including cysteine and methionine metabolism, glutathione metabolism, and arginine and proline metabolism. Additionally, metformin significantly increased cystathionine β synthase (CBS) and cystathionine γ lyase (CSE) in liver, thus leading serum levels of homocysteine and increasing hepatic levels of cysteine and glutathione in BPA-treated rats. Overall, this study results provided clue, insights, into the role and mechanism of metformin in BPA-induced liver injury in rats.	Sci Total Environ. 2021 Jan 1;750:141685.	10.1016/j.scitotenv.2020.141685	32862004	動物	肝	1	1	1	SD rat	0	500 mg/kg/d;0	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0939	Y. Sun, M. Sha, Y. Qin, J. Xiao, W. Li, S. Li and S. Chen	2024	Bisphenol A induces placental ferroptosis and fetal growth restriction via the YAP/TAZ-ferritinophagy axis	Exposure to bisphenol A (BPA) during gestation leads to fetal growth restriction (FGR), whereby the underlying mechanisms remain unknown. Here, we found that FGR patients showed higher levels of BPA in the urine, serum, and placenta; meanwhile, trophoblast ferroptosis was observed in FGR placentas, as indicated by accumulated intracellular iron, impaired antioxidant molecules, and increased lipid peroxidation products. To investigate the role of ferroptosis in placental and fetal growth, BPA stimulation was performed both in vivo and in vitro. BPA exposure during gestation was associated with FGR in mice also, it induces ferroptosis in mouse placentas and human placental trophoblasts. Pretreatment with ferroptosis inhibitor ferrostatin-1 (Fer-1) attenuated BPA-induced oxidative damage and cell death. Notably, BPA reduced the trophoblastic expression of yes-associated protein (YAP) and transcriptional co-activator with PDZ-binding motif (TAZ), which are the key regulators of the Hippo signaling pathway. Moreover, the ferroptosis induced by BPA in human trophoblast hemostasis is dependent on YAP/TAZ downregulation after BPA stimulation. Consistently, the protein levels of YAP/TAZ were also reduced in FGR placentas. Further results revealed that silencing YAP/TAZ promoted BPA-induced ferroptosis through autophagy. Pretreatment with autophagy inhibitor chloroquine (CQ) attenuated BPA-induced trophoblastic ferroptosis. Terribendiagy, an autophagy degradation of ferritin (FTH1), was observed in FGR placentas. Similarly, BPA mediated the autophagic degradation of FTH1 in placental trophoblast. Pretreatment with low-dilution deoferrioxamine (DFO) and NCOA4 (an autophagy cargo receptor) siRNA weakened the ferroptosis of trophoblast after exposure to BPA, indicating that autophagy mediates ferroptosis in BPA-stimulated trophoblast by degrading ferritin. In summary, ferroptosis was featured in BPA-associated FGR and trophoblast injury; the regulation of ferroptosis involved the YAP/TAZ-autophagy-ferritin axis.	Free Radic Biol Med. 2024 Feb 1;211:127-144.	10.1016/j.freeradbiomed.2023.12.013	38103660	動物	生殖発生毒性	1	1	1	1	0	0	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0940	F. Sun, Y. Huang, H. Chen, J. Huang, L. Zhang, S. Wei, F. Liu, D. Chen and W. Huang	2023	BPA and its alternatives BPF and BPAF exaggerate hepatic lipid metabolism disorders in male mice fed a high fat diet	Alternatives to Bisphenol A (BPA), such as BPF and BPAF, have found increasing industrial applications. However, toxicological research on these BPA analogues remains limited. This study aimed to investigate the effects of BPA, BPF, and BPAF exposure on hepatotoxicity in mice fed with high-fat diets (HFD). Male mice were exposed to the bisphenols at a dose of 0.05 mg per kg body weight per day (mg/kg/day) for eight consecutive weeks, or 5 mg/kg/day for the first week followed by 0.05 mg/kg/day for seven weeks under HFD. The low dose (0.05 mg/kg/day) was corresponding to the tolerable daily intake (TDI) of BPA set by the EFSA. The results showed that exposure to BPA, BPF, and BPAF induced hepatic steatosis, with BPF and BPAF causing more severe lipid accumulation than BPA. Moreover, BPF and BPAF induced disturbances of fatty acid and bile acid metabolism in bisphenol-exposed mice livers. BPF and BPAF exposure induced lipid accumulation in HFD mice may be caused by glycerolipid and cholesterol levels. Transcriptomics analysis demonstrated that exposure levels of genes related to fatty acid synthesis and metabolism were changed, which might be related to the activation of the PPAR signaling pathway. Besides, a feedback regulation mechanism might exist in maintain hepatic metabolic homeostasis. For the first time, this study demonstrated the effects of BPF and BPAF exposure to HFD mouse livers. Considering the reality of the high prevalence of obesity nowadays and the ubiquitous environmental distribution of bisphenols, this study provides insight and highlights the adverse effects of BPA alternatives, further contributing to the consideration of the safe use of such compounds.	Sci Total Environ Vol.867 Pages 161521	10.1016/j.scitotenv.2023.161521	36632902	動物	-	1	不明	1	不明	0	0.05、5 mg/kg/日	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0941	S. Sukjamnong, S. Thongkorn, S. Kanlayaprasit, T. Saelee, K. Hussem, W. Wanayanon, V. W. Hu, T. Tancharoen and T. Sarachana	2020	Prenatal exposure to bisphenol A alters the transcriptome-interactome profiles of genes associated with Alzheimer's disease in the offspring hippocampus	Our recent study revealed that prenatal exposure to bisphenol A (BPA) disrupted the transcriptome profiles of genes in the offspring hippocampus, in addition to genes linked to autism, several genes associated with Alzheimer's disease (AD) were also dysregulated. Therefore, in the present study, we further investigated the effects of prenatal BPA exposure on the transcriptome-interactome profiles of AD-associated genes and determined whether prenatal BPA exposure also dysregulated the transcriptome profiles of genes that are associated with neurodevelopmental disorders (NDD) in the hippocampus. The level of BP, a BPA analog, and the AD-associated target gene Bace1 were significantly increased in the offspring hippocampus in a sex-dependent manner. Quantitative RT-PCR analysis also observed an increase in the expression of Tet gene. Moreover, the reanalysis of transcriptome profiling data from normal previously published BPA studies consistently showed that BPA-responsive genes were significantly associated with top AD candidate genes. The findings from this study suggest that maternal BPA exposure may increase AD risk in offspring by dysregulating genes associated with AD neuropathology and inflammation and reveal a possible relationship between AD and autism, which are linked to the same environmental factor. Sex-specific effects of prenatal BPA exposure on the susceptibility of AD deserve further investigation.	Sci Rep Vol.10 Issue 1 Pages 9487	10.1038/s41598-020-65229-0	32528016	動物	-	1	1	1	1	0	5,000 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0942	S. Škurn, K. Weber, P. Klinc, E. Spömdly-Nees, A. Fakhrzadeh, T. Križo, A. Šalkin, V. Fiatovi, Y. Okazaki, T. Rutinger, J. Lachi, R. Knezzer, M. Pogačnik, T. Šuara and V. Cetkovnik-Flajs	2022	Basic Exploratory Study of Bisphenol A (BPA) Dietary Administration to Istrian Pramenka Rams and Male Toxicity Investigation	Bisphenol A (BPA), an endocrine-disrupting chemical and environmental pollutant, has been reported by many researchers to induce male reproductive toxicity in different experimental models. In this study, we investigated whether long-term exposure to low months to 25 μg/kg/body/day (about 1/4 of BPA effective dose) had teratogenesis or sperm toxicity in young Istrian Pramenka rams and could be the evaluated body and testicular weights, histopathology of testes and epididymides, and sperm analyses, and compared these parameters between the group of treated rams and the control group of rams. Although there were some differences between the two groups, these differences were not large or statistically significant. The only statistically significant difference was the lower epididymal height of semitendinosus tubules in treated rams, compared to control rams. In addition to assessing toxicity, BPA concentrations in the blood plasma of treated rams were determined after the first administration, and the toxicokinetic parameters of total BPA were calculated. In this study, no major signs of altered reproduction in rams were detected.	Toxics Vol.10 Issue 5	10.3390/toxics10050224	35622638	動物	-	1	1	1	Istrian Pramenka	0	25 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0943	S. Škurn, I. Grabar, A. Šalkin, M. Pogačnik and V. Cetkovnik-Flajs	2020	Preliminary toxicokinetic study of BPA in lactating dairy sheep after repeated dietary and subcutaneous administration	Dietary intake is the predominant route of human exposure to bisphenol A and one of the important food commodities is milk. The aim of our study was to preliminarily evaluate the bisphenol A exposure and disposition in lactating dairy sheep after repeated dietary and subcutaneous administration. Twelve Istrian Pramenka ewes in the mid-lactation period were randomly divided into two groups and developed the toxicokinetic model. With the toxicokinetic model we observed that most (fully only) free bisphenol A passes into the mammary gland and is subsequently conjugated there. The percentage of the dose eliminated in milk was less than 0.1%, regardless of the route of bisphenol A administration. It is proven that the bisphenol A is eliminated through the milk of lactating sheep. However, the amounts excreted in the milk that were detected in this study are minimal.	Sci Rep Vol.10 Issue 1 Pages 6498	10.1038/s41598-020-63286-z	32300131	動物	-	1	1	1	Istrian Pramenka	0	100 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0944	C. Skoker, M. F. Andreoli, L. Kass, V. L. Bonquiazzo, M. F. Rossetti, G. Canesini, E. H. Luque and J. G. Ramos	2020	Perinatal exposure to bisphenol A (BPA) impairs neuroendocrine mechanisms regulating food intake and kisspeptin system in adult male rats. Evidences of metabolic disruptor hypothesis	Bisphenol A (BPA) is a compound used in the polymerization of plastic polycarbonates. It is an endocrine disruptor and it has been postulated to be an obesogen. Our objective was to determine the influence of perinatal exposure to BPA on body weight, hormone levels, metabolic parameters and hypothalamic kisspeptin system. Male rats were exposed to BPA (50 μg/kg/day) BPA in drinking water from day 9 of gestation to weaning in the drinking water. Since weaning, they were fed with control or high fat diet for 20 weeks. Perinatal exposure to BPA impaired glucose homeostasis, induced obesity and increased food intake in male rats, core clearing hypothalamic signals, partially mediated by central leptin resistance. BPA also induced an increase in kisspeptin expression by BPA exposure. Evidences shown in this work support the metabolic disruptor hypothesis for BPA.	Mol Cell Endocrinol Vol.499 Pages 110614	10.1016/j.mce.2019.110614	31606416	動物	-	1	1	1	不明	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0945	O. P. Stoddard, K. Berger, B. Eskenazi, K. Kogut, N. T. Holland, S. Rauch and K. G. Harley	2025	In utero exposure to a mixture of phthalates, parabens, and other phenols and menstrual cycle characteristics in adolescents	Phthalates, parabens, and other phenols are present in consumer products humans use every day, including personal care products and food packaging. Exposure to these chemicals may have endocrine disrupting effects, but few studies have examined associations with menstrual cycle characteristics in adolescents. We measured 11 phthalate metabolites, 4 parabens, triclosan, benzophenone-3, and bisphenol A in spot urine samples from 338 participants in a cohort of Mexican girls who were followed from ages 6–8 years old to 14–16 years old. We examined six potentially adverse menstrual cycle characteristics: irregular cycles, long cycles, short cycles, prolonged bleeding, heavy bleeding, and severe cramps. We used multivariable log-binomial regression models with generalized estimating equations to estimate associations between exposure biomarker concentrations and each characteristic, averaged across age, using logistic regression. Bayesian hierarchical modeling was used to model the chemical mixture's associations with each outcome. All models were adjusted for poverty level during pregnancy, maternal pre-pregnancy BMI, and their food consumption at adolescent age 9. Results showed a positive association between mono-(3-carboxypropyl) phthalate, propylparaben, and bisphenol A and heavy menstrual flow. Exposure to 2,2'-dichlorophenol was positively associated with short cycle length. Mono(3-carboxypropyl) phthalate and di-(2-ethylhexyl) phthalate were positively associated with long cycle length. These results suggest in utero exposure to phthalates, parabens, and other phenols may be associated with abnormal menstrual cycle characteristics in adolescents.	Int J Hyg Environ Health. 2025 Jul;268:114612.	10.1016/j.ijheh.2025.114612	40587922	ヒト	生殖発生	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_0946	M. L. Sowers, H. Tang, B. Tian, R. Goldblum, T. Midoro-Horiuti and K. Zhang	2020	Bisphenol A Activates an Innate Viral Immune Response Pathway	Bisphenol A (BPA) is a ubiquitous component in the manufacturing of plastic. It is commonly found in food and beverage containers. Because of its broad exposure and evidence that it may act as an estrogen like molecule, many have studied its potential effects. For example, epidemiological studies have found an association between in utero BPA exposure and onset of childhood asthma. One previous work suggested BPA induces mice infected asthma like symptoms. In both mothers and their pups. In order to better understand the consequences of BPA exposure and potential mechanisms, we used a proteomic approach. Using both CD1 (-/-) and mice in vivo model of BPA exposure and an in vitro epithelial cell model, we identified activation of both innate and adaptive immune signaling following BPA exposure. Furthermore, our proteomic results from our multigenerational mouse model study implicates aberrant immune activation across several generations. We propose the following: BPA can active an innate viral immune response by upregulating unstable interferon-stimulated genes (ISGs), and by binding partner stimulator of interferon genes (STING). It also has additional immune-epigenetic perturbations, suggesting a role for epigenetic inheritance of these immune perturbations.	J Proteome Res. 2020 Feb 7;19(2):644-654.	10.1021/acs.jproteome.9b00548	31816243	動物、in vitro	-	1	1	1	BALB/c	0	20 μg/mL（胚ホモ濃度）	-	-	-	-	不明	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0947	S. Soriano, M. Gil-Rivera, L. Marroqui, P. Alonso-Magdalena, E. Fuentes, I. A. Gustafsson, A. Nadal and I. Martinez-Pinna	2019	Bisphenol A Regulates Sodium Ramp Currents in Mouse Dorsal Root Ganglion Neurons and Increases Nociception	17,β-Estradiol mediates the sensitivity to pain and is involved in sex differences in nociception. This is a widespread environmental disrupting chemical bisphenol A (BPA) has estrogenic activity, but its implications in pain processing are unknown. Here, we investigated the effects of BPA on the excitability of dorsal root ganglion (DRG) neurons from male and female mice. Whole-cell patch-clamp recordings after incubation of dissociated dorsal root ganglia (DRG) nociceptors with 1 nM BPA increased the frequency of action potential firing. SCAM4 encodes the voltage-gated sodium channel Nav1.7, which is present in DRG nociceptors and is essential in pain signaling. Nav1.7 and other voltage-gated sodium channels in mouse DRG are considered threshold channels because they produce ramp currents, amplifying small depolarizations and initiating electrical activity. BPA increased Nav1.7-mediated ramp currents at the cell body with slow depolarizations. Experiments using pharmacological tools as well as DRG from Nav1.7 (−/−) mice indicate that this BPA effect involves ERα and phosphatidylinositol-3 kinase. The mRNA expression and biophysical properties, other than ramp currents of Nav1.7 channels, were unchanged by BPA. Our data suggest that BPA at environmentally relevant doses affects the ability to detect noxious stimuli and therefore should be considered when studying the etiology of pain conditions.	Sci Rep Vol.9 Issue 1 Pages 10306	10.1038/s41598-019-46769-6	31312012	動物	-	1	1	1	不明	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0948	W. Song, M. Puttabyatappa, L. Zeng, D. Vasquez, S. Pennathur and V. Padmanabhan	2020	Developmental programming: Prenatal bisphenol A treatment disrupts mediators of placental function in sheep	Gestational Bisphenol A (BPA) exposure is associated with low birth weight. We hypothesized that the low birth weight is the consequence of reduced placental efficiency and a function of BPA-induced inflammatory, oxidative, lipotoxic, angiogenic, steroidal and fibrotic changes involving epigenetic alterations. Placentomes were collected during early (day 65) and mid (day 90) gestation (term ~147 days) from control and BPA (gestational day 30-90) treated pregnant sheep. BPA treatment reduced placental efficiency (fetal weight/placentome weight) in mid-gestation placentomes. Increased 4, 5(α)-epoxide metabolites, antioxidants, peroxidation, 3β-hydroxysteroid dehydrogenase 1 and nuclear gene Tet-2 suggest that BPA effects on CSA exposure on pregnancy outcome, health status of dams/offspring, levels of circulating inflammatory cytokines in dams/offspring and emotional related behaviors of offspring were evaluated. CSA exposure during pregnancy had no significant effect on pregnancy outcome, liver function, body weight of the dams or body weight and organ weights of offspring at birth. However, CSA exposure during pregnancy, as the name suggests, is the exposure of the mother to CSA during pregnancy. Cesarean section is the surgical delivery of the baby through incisions in the mother's abdomen and uterus. Cesarean section is usually performed when vaginal delivery is risky for the mother or baby. Cesarean section is also known as C-section or C-section. Cesarean section is a surgical procedure to deliver a

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0960	S. Shetty, V. Kumar, V. Ramesh and S. Bharati	2022	Mito-TEMPO protects against bisphenol-A-induced testicular toxicity: an in vivo study	Bisphenol A (BPA) is a common environmental toxin which alters testicular function in both animals and humans. BPA exerts its cytotoxic potential by altering mitochondrial oxidative stress and functioning. Therefore, protecting mitochondria from oxidative stress may prevent BPA-induced testicular damage. In the present study, modulation of BPA toxicity by mitochondria-targeted antioxidant, mito-TEMPO, was studied in male Wistar rats. Experimental animals were divided into four groups (n = 6/group). Group I served as control, group II received BPA (50 mg/kg b.wt.), group III received mito-TEMPO (0.7 mg/kg b.wt.), and group IV received BPA + mito-TEMPO for 35 days. At the end of the treatment, the animals were sacrificed. The mitochondrial oxidative stress, mitochondrial membrane potential (MMP), and enzymatic activity of mitochondrial complex I and IV were estimated in the testicular tissue. Pretreatment of mito-TEMPO protected animals from toxic effects of BPA as indicated by the normalization of sperm parameters and preserved histoarchitecture of testis. BPA treatment in animals significantly increased mitochondria reactive oxygen species (ROS) and lipid peroxidation (LPO). A significant decrease in the activity of mitochondrial complex I was also observed after BPA exposure whereas, mitochondrial complex II activity was increased. In addition, an increase in MMP was also observed in BPA group. Mito-TEMPO successfully normalized mitochondrial ROS and LPO formation. Similar normalization effect was also noted in the activity of mitochondrial complex I, complex IV, and MMP. Results suggested that mito-TEMPO pretreatment significantly protected BPA-induced oxidative stress and thereby mito-TEMPO effectively prevented testicular damage.	Free Radic Res Vol.56 Issue 5-6 Pages 427-435	10.1080/10715762.2022.2133702	36205519	動物	-	1	不明	1	1	0	10 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0961	S. Sharma, S. Ahmad, M. A. Afjal, H. Habib, S. Parvez and S. Raisuddin	2019	Dichotomy of bisphenol A-induced expression of peroxisome proliferator-activated receptors in hepatic and testicular tissues in mice	Environmental and dietary exposure to bisphenol A (BPA) and its toxicological consequences are extensively reported. BPA has multiple cellular targets. One of the mechanisms of action of BPA involves interaction with and activation of nuclear receptors (NRs) including peroxisome proliferator-activated receptors (PPARs). PPARs regulate genes involved in adipogenesis, and lipid and glucose homeostasis. Gestational exposure to BPA has also been specific PPAR expression may decipher the toxicity outcome of BPA response. We studied expression of three forms of PPARs in mouse liver and testes exposed to BPA for 14 days. mRNA and protein expression of PPARα, PPARγ and PPARβ/δ was determined in the liver and testes of male Swiss mice administered BPA (50 mg/kg/day) or equivalent volume of vehicle (olive oil). Histopathological study showed a dose-dependent pattern of changes in liver as well as testes demonstrating xenobiotic effect. These findings imply that while PPAR-independent mechanisms may play a role in BPA-induced pathological changes. The present study warrants exploration of the role of PPARs in BPA-induced effects on male reproductive functions and offers an insight into the peculiar response of BPA on two subchronic levels which may be helpful in designing appropriate risk assessment framework.	Chemosphere. 2019 Dec;236:124264.	10.1016/j.chemosphere.2019.06.234	31319301	動物	肝臓	1	0	単独あり	Swiss mice	1	4,8,16 mg/kg:1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0962	P. Sharma, M. B. Mandal, R. Katiyar, S. P. Singh and H. Bhta	2021	A Comparative Study of Effects of 28-Day Exposure of Bisphenol A and Bisphenol S on Body Weight Changes, Organ Histology, and Relative Organ Weight	CONTEXT: Bisphenol A (BPA), a known endocrine disrupting chemical, is of widespread use in manufacturing of plastic products. Documenting ill health effects of BPA has led the plastic industrialists to replace BPA by its analogues, bisphenol S (BPS) in many products. OBJECTIVE: The present study was undertaken to compare the effects of 28-day exposure of BPA and BPS on body weight changes, organ histology, and relative organ weight in rats. In addition, we detected BPA and BPS in the rat's blood serum. MATERIALS AND METHODS: Adult male albino rats were administered BPA (50 mg/kg/day) or BPS (50 mg/kg/day) or equivalent volume in different groups by oral gavage for 28 days. SUBJECTS AND METHODS: The weight of each rat was noted at the commencement of the study and weekly afterward. On 29th day, the animals were sampled for whole blood and then sacrificed. The dissected out viscera were observed for any significant change in the overall appearance and histological examination. The viscera were preserved and analyzed for the detection of BPA and BPS by high-pressure liquid chromatography. STATISTICAL ANALYSIS USED: Paired and unpaired Student's t test, one-way ANOVA test, and Bonferroni test for multiple comparisons were used as required for statistical analysis, and P < 0.05 was considered statistically significant. RESULTS: Both BPA and BPS produced similar detrimental changes in body weight, histology of stomach, small intestine, lung, and kidney, and relative organ weight of lung and kidney. BPA and BPS detected in the serum of rats were nearly 40 times of the control. CONCLUSIONS: Present data suggests caution about the application of BPS as a substitute of BPA.	Int J Appl Basic Med Res Vol.11 Issue 4 Pages 214-220	10.4103/ijabmr.IJABMR_663_20	34912683	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0963	T. Shalbi, H. N. Balug, M. E. Ben-Othman, A. E. Benjama, M. Elhmshari, B. A. Lwaleed and M. A. Al-Gria	2022	Exposure to low-dose bisphenol A induces spleen damage in a murine model: Potentially through oxidative stress?	BACKGROUND: During early life, exposure to environmental toxicants, including endocrine disruptor bisphenol A (BPA), can be detrimental to the immune system. To our knowledge, a few researches have looked at the effects of developing BPA exposures on the spleen. AIM: The murine model was developed to investigate the underlying molecular mechanisms and mode of BPA action on the spleen subsequent to prolonged early life exposure to BPA. METHODS: Immature (3 week-old) male and female Swiss Albino mice were intraperitoneally injected with 50 µg/kg BPA in corn oil or corn oil alone for 5 weeks. Mouse spleens were harvested and examined histologically at 10 weeks old (adulthood). RESULTS: We observed neurobehavioral impairments and significant increase in peripheral immunocytotoxicity parameters. Furthermore, we found a significant increase in proliferation and necrotic zone were observed in adulthood. BPA-treated mice's histopathological results revealed toxicity in the formof significantly earlier germinal centers of the white pulp and a significant decrease in the red pulp area. Moreover, BPA-treated mice showed significant increase in splenic oxidative stress biomarkers, including a significant increase in the immunohistochemical DNA fragmentation and apoptosis in the splenic tissues of BPA-treated mice compared to controls. In addition, there were increased levels of the lipid peroxidation malondialdehyde end-product, a marker of oxidative lipid damage, in the spleens of BPA-treated mice compared to controls. CONCLUSION: Our study provides evidence that oxidative stress injury induced by early life exposure to BPA could contribute to a range of splenic tissue damages during adulthood.	Open Vet J Vol.12 Issue 1 Pages 23-32	10.5455/OVJ.2022.v12.i1.4	35342727	動物	-	1	0	1	1	0	50 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0964	N. F. S. Shalbi, N. K. Nurul Bashar, N. A. Abul Aziz, R. Dasiman and N. N. Hasbin	2025	Protective role of Cocos nucifera L. water on BPA-mediated oxidative stress and reproductive damage in male rats	Bisphenol A (BPA) may impair male fertility by inducing oxidative stress in the testis, though its effects on spermatogenesis and sperm quality remain unclear. Conversely, Cocos nucifera L. (coconut) water, rich in antioxidants, may counteract BPA's harmful effects. This study investigated the protective role of coconut water against BPA-induced testicular damage in rats. Forty-eight male Sprague-Dawley rats were divided into eight groups (n = 6) and treated daily for 28 days via oral gavage. Groups received distilled water (DW; 10 mL/kg), DW + coconut water (CW; 10 mL/kg), BPA (50 mg/kg), CW + BPA, BPA + vitamin E (100 mg/kg), CW + BPA + vitamin E, vitamin E (100 mg/kg), or coconut water (CW; 10 mL/kg) alone. Body weight was recorded weekly. At the end of the treatment period, animals were euthanized, and testes were collected for histological examination, oxidative stress analysis, and sperm motility assessment. BPA administration reduced glutathione levels, increased malondialdehyde levels, and caused histopathological changes in the testis. Additionally, the group also showed a decrease in sperm motility and viability. Co-administration of CW with BPA significantly decreased malondialdehyde levels and improved glutathione levels in the testis. Furthermore, CW co-administration significantly improved sperm motility, viability, and morphology compared to the BPA group (p < 0.001). However, these parameters were notably impaired by the administration of coconut water to CW+B group (p < 0.001). Conclusively, this study suggests that coconut water influences antioxidant defenses and supports male reproductive health in rats, potentially preventing BPA-induced reproductive damage.	Int J Environ Health Res Pages 1-13	10.1080/09603123.2025.2484782	40152287	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0965	A. C. Sasastre-Bargillan, C. Casandra, D. Ghabaar, D. Ohkaru, M. C. Chimeca Valle Vowod, L. Rogojan, G. A. Filip and I. Bâldea	2022	Neurotoxicity of Bisphenol A and the Impact of Melatonin Administration on Oxidative Stress, ERK/NF-kB Signaling Pathway, and Behavior in Rats	Bisphenol A (BPA) exposure can be associated with neurodevelopmental disorders due to impairment of cell proliferation and synaptic development. Our study evaluated the effects of melatonin (MEL) on antidepressant activity, lipid peroxidation, cytokines, ERK/NF-kB signaling pathway in the hippocampus, and behavioral changes in the neurobehavioral changes in the BPA-treated rats. The animals were divided into 5 groups, control, BPA, BPA + MEL-1 and BPA + MEL-5. MEL (20 mg/kg b.w.) and MEL (5 10 mg/kg b.w.) were orally administered for 28 days. On the 29th day, BPA (5 mg/kg b.w.) was intraperitoneally administered, as well as MEL, 30 min before the behavioral tests. Our results showed that BPA induced depressive-like behavior in the forced swim test and tail suspension test, increased the duration of immobility and decreased the climbing and swimming behavior. Moreover, BPA increased the oxidative stress and apoptosis in the central part of CA1. Malondialdehyde levels were diminished by MEL-5 in the hippocampus and by MEL-1 in the frontal lobe. In the hippocampus, the NAPH level was significantly boosted by both doses of MEL (p < 0.05) while in the frontal lobe, only MEL-5 reduced the NADPH activation. SOD, 1 and 2 significantly decreased the p-ERK and upregulated the NFkB and pNFkB expressions in the hippocampus, while MEL-5 downregulated the NOS1 expression. Both doses of MEL attenuated the BPA-induced histopathological alterations in the hippocampus. These data indicate that MEL can mediate the neuroprotective against BPA-induced neurotoxicity and improves behavioral changes, suggesting a real potential as a protective agent in brain toxicity.	Neurotox Res Vol.40 Issue 6 Pages 1882-1894	10.1007/s12640-022-00618-z	36515867	動物	-	1	0	1	不明	不明	1 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0966	M. A. Selim, S. M. Mosaad and N. M. El-Sayed	2022	Lycopene protects against Bisphenol A induced toxicity on the submandibular salivary glands via the upregulation of PPAR- γ and modulation of Wnt/ β -catenin signaling	BACKGROUND AND AIM: The submandibular salivary glands (SMG) represent a suitable model for studying epithelial cell growth and differentiation. Bisphenol A (BPA) is a xenoestrogen, synthesized to produce polymeric such as polycarbonates and epoxy resins. There are concerns about the occurrence of BPA in food, water as well as its appearance in human tissues and body fluids. Lycopene (LYC) is a carotenoid compound that exerts antioxidant and anti-inflammatory properties. This work was performed to study possible protective effect of LYC against BPA toxicity in SMG. MATERIAL AND METHODS: 40 albino rats were divided into 5 groups. Group I: control group. Group II: received LYC (10 mg/kg b.w.) orally. Group III: received BPA (50 mg/kg b.w.) orally. Group IV: received BPA (50 mg/kg b.w.) orally + LYC (10 mg/kg b.w.) orally. Group V: received BPA (50 mg/kg b.w.) orally + LYC (10 mg/kg b.w.) orally + PPAR-γ antagonist (GW9662) (1 mg/kg b.w.) intraperitoneally. At the end of treatment, the rats were sacrificed. The SMG specimens were taken for histological and biochemical studies. RESULTS: BPA resulted in significant rise in malondialdehyde, nuclear factor κ and interleukin-1β. In contrast, the tissue levels of glutathione and PPAR-γ were significantly decreased. BPA activated Wnt/β-catenin pathway evidenced by upregulating GFA Tie, β-catenin and c-myc expression. Moreover, SMG of BPA showed degenerative changes that affected the parenchyma and stromal elements of the glands. The immunohistochemical localization of cytokeratin 7/8 and 19 of BPA rats revealed weak immunostaining of the serous secretory cells, myoepithelial cells and ductal cells. Upon treatment with LYC, glutathione and PPAR-γ were restored. CONCLUSION: LYC extracts a protective agent against BPA induced pathological changes in SMG.	Int Immunopharmacol Vol.112 Pages 109293	10.1016/j.intimp.2022.109293	36194983	動物	-	1	1	1	1	0	10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0967	S. Sattar, A. Nadeem, W. Shehzad, H. Ur Rehman and M. Jawed	2024	A biochemical and histological evaluation of in vivo exposure of bisphenol P for multi-organ toxicity and pathology in rats	Bisphenol (BPP) is a structural analog of bisphenol A (BPA) and is increasingly used as a substitute of BPA in commercial and household applications. In recent years, BPP has been frequently detected in terrestrial and aquatic ecosystems. Very little epidemiological and experimental information is available on the toxicity potential of BPP in human and animal systems, which is an area of dire necessity to be researched. The current study evaluated the biochemical and histopathological effects of BPP in rats. The seven experimental groups (n = 5 rats/group) included BPA80 (5 mg/kg), BPA160 (160 mg/kg), BPP20 (20 mg/kg), BPP80 (80 mg/kg), and BPP160 (160 mg/kg) orally for remaining one group served as control. The treatment was given for 28 days. At the end of treatment, the rats were sacrificed for collection of blood and tissues for biochemical and histopathological analysis. A significant (p < .05) decrease was observed in the weight of the liver, lungs, and kidneys in the BPP160 group similar to the BPA160 group compared with the control group. Further, a significant (p < .05) decrease was observed in the activities of superoxide dismutase, catalase, and glutathione peroxidase in the liver, lungs, and kidneys in the BPP160 group compared with the control group. A significant (p < .05) increase in the malondialdehyde content in BPP160 group compared with the control group. The histological tissues of BPP-induced histopathological changes in the liver such as nodal alterations, excessive necrosis of hepatocytes, necrotic cholangiocytes, and cytolysis of cells with disrupted cell structure (BPP160), and cellular congestion and degeneration of hepatocytes (BPP80), similar to the two consecutive doses of BPA. The BPP-treated groups also showed varying histopathological changes in kidney tissue, heart tissue, and lung tissue similar to BPA-treated rats. In conclusion, the present study indicated that BPP has the potential to induce oxidative stress and alter the histomorphological architecture of different organs and is as deleterious as BPA.	Toxicol Ind Health. 2024 Apr;40(4):194-205.	10.1177/07482337241233312	38346931	動物	主に肝臓心筋	1	1	1	Wister rat	1	5,50,100 mg/kg:1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_0968	A. Santoro, M. Scafuro, I. Troisi, G. Piegari, P. Di Pietro, E. Melo, D. Coppetta, M. Marino, A. De Angelis, C. Vecchione, G. Paciello, S. Fasano, R. Pierantoni, A. Viggiano and R. Meccariello	2021	Multi-Systemic Alterations by Chronic Exposure to a Low Dose of Bisphenol A in Drinking Water: Effects on Inflammation and NAD(+)-Dependent Deacetylase Sirtuin1 in Lactating and Weaned Rats	Bisphenol A (BPA) is largely used as a monomer in some types of plastics. It accumulates in tissues and fluids and is able to bypass the placental barrier, affecting various organs and systems. Due to huge developmental plasticity, the fetus and newborn are considered the most vulnerable subjects to BPA exposure. Here, we investigated the effects of BPA on lactating rats and their offspring. Female rats were exposed to BPA in drinking water during gestation and lactation. At weaning, newborn rats received the same treatments as dams until six maturation. Five animals/group/BPA dose were euthanized at postnatal days (PND) 21 and 60. Liver, adipose tissue, the size of cerebral cortex/cross-area analyzed in the brain; insulin functional and molecular analyses were carried out in the liver with a focus on the expression of inflammatory cytokines and Sirtuin-1 (Sirt1). Higher BPA levels were found in plasma and adipose tissue from BPA-treated pups (17 PND) but not in weaned animals. Lateral cerebral ventricles were significantly enlarged in lactating and weaned BPA-exposed animals. In addition, apart from microvesicular steatosis, liver morphology did not exhibit any statistically significant difference for morphological signs of inflammation, hypertrophy, or macrovesicular steatosis, but the expression of inflammatory cytokines, Tnfa, Il1b, Il6, and Ccl2, was increased in the liver of BPA-exposed lactating dams and their offspring. Interestingly, Sirt1 was differentially expressed in the liver of PND 60 animals and hormone-dependent in 21 days old rats affected in repeated animals. In conclusion, chronic exposure to a low BPA dose could increase the risk for disease in adult life as a consequence of higher BPA-circulating levels and accumulation in adipose tissue during the neonatal period.	Int J Mol Sci Vol.22 Issue 18	10.3390/ijms22189666	34575829	動物	-	1	1	1	1	0	100 ng/L（耐容平均摂取）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0969	P. Sánchez, B. Castro, S. Martínez-Rodríguez, R. Rico-Palagina, R. G. Del Moral, I. M. Torres and J. E. Ortega	2021	Impact of chronic exposure of rats to bisphenol A from perinatal period to adulthood on intraprostatic levels of 5α -reductase isozymes, aromatase, and genes implicated in prostate cancer development	The synergistic effect of estrogens and androgens is known to play a crucial role in the physiopathology of the prostate gland. Bisphenol A (BPA) is an endocrine-disrupting compound that can interfere with endocrine hormone functioning and thereby influence prostate development. The objective of this study was to examine the impact on prostate expression of aromatase, 5 α -R isozymes, and prostate cancer–related genes of chronic exposure to BPA from perinatal period to adulthood in rats. Wistar rats were exposed to BPA (0.5 mg/kg/day) in drinking water from gestation day 0 to postnatal day 90. Ventral prostate was harvested from perinatal day 1 (PND1) and euthanization on PND90. Their prostate glands were examined by qRT-PCR, Western blot, ICC-IF assay, and morphological study. mRNA and protein levels of 5α -R1 were significantly reduced, and mRNA and protein levels of aromatase were significantly increased in BPA-treated animals, which also showed modifications of 8 out of the 84 key genes implicated in the development of prostate cancer. Because BPA interferes with genes involved in intracrinicity androgen and estrogen production and others implicated in prostate cancer, research is warranted into the prostate disease risk associated with chronic low-dose BPA exposure throughout life.	Environ Res Vol.212 Issue Pt A Pages 113142	10.1016/j.envres.2022.113142	35378123	動物	-	1	1	1	1	0	2.5 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0970	B. Sasanarom, S. Loopreeserikul, S. Kanitpayanuk, N. Kitkumthorn, T. Sanchana and D. Jindatip	2021	Alteration of Extracellular Matrix Components in the Anterior Pituitary Gland of Neonatal Rats Induced by a Maternal Bisphenol A Diet during Pregnancy	The extracellular matrix (ECM) plays crucial roles in the anterior pituitary gland via the mechanism of cell-ECM interaction. Since bisphenol A (BPA), a well-known endocrine disruptor, can cross through the placenta from mother to fetus and bind with estrogen receptors, cell populations in the neonatal anterior pituitary gland could be the target cells affected by this chemical. The present study treated maternal rats with 5000 µg/kg body weight of BPA daily throughout the pregnancy period and then investigated the changes in ECM production by cells, i.e., pericytes and folliculostellate (FS) cells, including their ECM production in the neonatal anterior pituitary at Day 1. We found that pericytes and their collagen synthesis induced, consistent with the increase in the number of FS cells that expressed several ECM regulatory matrix metalloproteinase (MMP)-9 and the ECM degradation product, endostatin, in the BPA-treated group. The immunohistochemical results revealed that BPA exposure significantly induced the number of ECM-producing cells and abnormally altered the ECM composition in the anterior pituitary. Moreover, we observed that BPA exposure also significantly induced the expression of ECM-associated genes, including MMP-9 and ECM-producing cells as well as collagen and the related ECM balancing genes occurred in the neonatal anterior pituitary gland.	Int J Mol Sci Vol.22 Issue 23	10.3390/ijms222312667	34884472	動物	-	1	1	1	1	0	5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0971	S. M. M. Saleh, A. B. Mahmoud, M. B. Al-Salahy and F. A. Mohamed Moustafa	2023	Morphological, immunohistochemical, and biochemical study on the ameliorative effect of gallic acid against bisphenol A-induced nephrotoxicity in male albino rats	This study aimed to determine the effect of gallic acid (GA) on ameliorating bisphenol A (BPA)-nephrotoxicity in male rat kidneys. Forty rats were equipped randomly into four groups: control (rats untreated) and BPA (40 mg/kg b.w.), GA (100 mg/kg b.w.), and BPA + GA (40 mg/kg b.w. + 100 mg/kg b.w.). The experimental period was 30 days. Kidney specimens were collected for histological examination of the renal tissue, immunohistochemical examination of the renal tissue, morphometric measurements, and ultrastructural studies. Kidney function was assessed by determining urea, creatinine, and creatinine clearance. Lipid peroxidation (MDA) in the kidney. The antioxidant enzymes catalase and superoxide dismutase (SOD) were measured in the kidney. Kidney function was assessed by determining urea, uric acid, and creatinine levels. The morphological investigations included hematoxylin and eosin staining for assessing the general histology and determining the glomerular and corpuscular areas, the tubular cell degeneration/necrosis area, and the mean tubulointerstitial area. Also, collagen fiber intensity and polysaccharide content were evaluated. Furthermore, immunohistochemical, morphometric, and ultrastructural studies were carried out. The results revealed morphological, immunohistochemical, and biochemical alterations in the kidney. Most of these changes showed a satisfactory improvement of kidney damage when BPA-administered rats were treated with GA at both doses. In conclusion, GA exhibited a strong protective effect against BPA-induced nephrotoxicity.	Sci Rep Vol.13 Issue 1 Pages 1732	10.1038/s41598-023-28860-1	36720896	動物	-	1	1	1	1	0	40 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0972	M. A. Salfi, H. Khan, M. Jawed, S. Ahmad, Z. Khan, A. Mangla, G. Jindal, S. Panwa, N. Agarwal and S. Raisuddin	2025	Neuroprotective effects of gastrodin against bisphenol A induced-ADHD-like symptoms in rats	Gastrodin (GSD) is a potent pharmaceutical compound extracted from the dried roots of a Chinese medicinal herb, Gastrodia elata Blume. It has been used as a neuroprotective treatment for a range of neurological disorders. OBJECTIVE: This study investigated the neuroprotective effects of GSD against bisphenol A (BPA)-induced attention deficit hyperactivity disorder (ADHD)-like symptoms in the rat model. Weanling male Wistar rats treated with BPA (50 µg/kg b.w., i. M. day one) and co-consistion of treatment were subsequently treated with GSD at two doses (30 and 60 mg/kg b.w., i. p.) daily. After 28 days of completion of the treatment regimen, neurobehavioral parameters such as open field test (OFT), novel object recognition (NOR), and elevated plus maze (EPM) test were evaluated. Lipid peroxidation, reduced glutathione (GSH), monoamine oxidase (MAO) activity, and dopamine (DA) levels were measured in the cerebral cortex (CC) and hippocampus (HC) regions of the brain. Additionally, to assess astrocyte activation the expression of glial fibrillary acidic protein (GFAP) was analyzed by immunostaining. Results show that GSD treatment ameliorated locomotory activity (OFT), memory dysfunction (NOR), and anxiety (EPM) in BPA-exposed rats. Moreover, GSD treatment significantly reduced lipid peroxidation and MAO activity while increasing GSH and DA levels in the CC and HC regions of the brain. Additionally, GSD treatment reduced GFAP expression in the CC and HC. This study provides experimental evidence for a neuroprotective role for GSD against BPA-induced ADHD-like symptoms. GSD demonstrated potential preventive effects against BPA-induced ADHD-like symptoms in rats, which highlights its therapeutic value.	Drug Chem Toxicol Pages 1-14	10.1080/01480545.2025.2473472	40062364	動物	-	1	1	1	1	0	50 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_0973	C. Sahu, S. Singla and G. Jena	2022	Studies on male gonadal toxicity of bisphenol A in diabetic rats: An example of exacerbation effect	Bisphenol A (BPA), a widely used organic synthetic chemical alters spermatogenesis and is a potential risk factor for male infertility. Diabetes-induced hyperglycemia has a negative impact on different vital organs including the testis. However, the effect of BPA on male fertility and gonadal development in diabetic (DM) patients is unknown. This study explores the role of BPA exposure on testicular toxicity in a DM rat. The DM was induced in male Wistar rats (180–200 g) by a single intraperitoneal injection of streptozotocin (STZ) (45 mg/kg b.w.). BPA was administered orally by gavage at 40 mg/kg/day for 5 consecutive weeks. Various endpoints of the toxicity include blood biochemical estimations, histological evaluations, oxidative stress parameters, DNA damage assays (cometa and enterochromin-H), expression of 4-hydroxy-2′-deoxyguanosine (8-OHdG), nuclear factor erythroid 2-related factor 2 (Nrf 2), catalase, superoxide dismutase 1 (SOD-1), a tumor-binding transcription factor 1 (OCT-1), and Ets/ch-1/det homologous protein (CHOP). Results showed that BPA exposure in DM rats significantly altered the testicular histoarchitecture, decreased the sperm count, motility, and sperm viability, and induced testicular DNA damage. Moreover, exposure to BPA in DM rats also increased the expression of the testicular oOH-dG, Nrf2, and SOD-1 proteins. Correlation analysis indicates a positive correlation between apoptosis and 8-OHdG, OCT-1, and DNA damage (nuclear diffusion factor and tail length). The present study confirmed that BPA exposure in DM conditions exacerbated the testicular damages in DM rats. Therefore, the DM condition might have increased male gonadal toxicity due to BPA exposure and requires further attention to maintain their normal reproductive health.	J Biochem Mol Toxicol Vol.36 Issue 4 Pages e22996	10.1002/jbt.22996	35187753	動物	-	1	1	1	1	0	40 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0974	C. Sahu and G. Jena	2024	Combination treatment of zinc and selenium intervention ameliorated BPA-exposed germ cell damage in SD rats: elucidation of molecular mechanisms	Bisphenol A (BPA) is a commonly used environmental toxicant, is easily exposed to the human body and causes testicular damage, sperm abnormalities, DNA damage and apoptosis, and interferes in the process spermatogenesis and steroidal hormone production along with obstruction in testes and epididymis development. Zinc (Zn), a potent regulator of antioxidant balance, is responsible for cellular homeostasis, enzymes and proteins activities during spermatogenesis for cell division and meiotic events. Similarly, selenium (Se) is required in the testes, epididymis and in the activities of different enzymes. Both Zn and Se are essential (simultaneously) for the proper regulation of spermatogenesis and sperm maturation as well as protection against chemical and disease-associated germ cell toxicity. Thus, the study aimed to understand the protective role of Zn and Se against BPA-induced testicular toxicity in male Sprague-Dawley rats. Male rats were divided into four groups (n = 6/group) and treated for 35 days as follows: Group I: Control, Group II: BPA (50 mg/kg b.w.), Group III: BPA + Zn (30 mg/kg b.w.) + Se (0.5 mg/kg b.w.), Group IV: BPA + Zn + Se (same dose level as III) orally by gavage. Results showed that BPA exposure significantly altered the testicular histoarchitecture, sperm parameters, testicular and epididymal thiobarbituric acid reactive substances (TBARS), hydroperoxide (HP), and BPA (72 mg/kg) was administered for 15 weeks. Although BPA exposure did not affect body weight or biochemical parameters, the HCB group exhibited significant histopathological changes in the colon, including inflammation, goblet cell depletion, and crypt damage. Additionally, BPA exposure led to a significant increase in the expression of TLR4, NF-κB, and IL-6 in the colon tissue, indicating activation of inflammatory pathways. Co-exposure with HCB further amplified these effects, suggesting a synergistic interaction between the two compounds. These findings highlight the potential risk of combined exposure to BPA and HCB, which may contribute to colon inflammation and dysfunction. Given the widespread presence of both chemicals in the environment and their ability to accumulate in biological tissues, this study underscores the importance of considering mixture effects in risk assessments. Further research is needed to explore the underlying mechanisms and potential therapeutic interventions to mitigate the adverse effects of these environmental contaminants.	Naunyn Schmiedebergs Arch Pharmacol Vol.397 Issue 9 Pages 6685-6704	10.1007/s00210-024-03044-4	38498059	動物	-	1	1	不明	不明	0	100、200 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0975	C. Sahu and G. Jena	2022	Dietary zinc deficient condition increases the Bisphenol A toxicity in diabetic rat testes	Bisphenol A (BPA) is a widely used endocrine disruptor that causes male reproductive dysfunction in humans and rodents. Diabetes-induced hyperglycemia alters spermatogenesis and antioxidant status, which negatively affects male fertility. Zinc (Zn), a potent regulator of antioxidant balance, is responsible for cellular homeostasis, enzymes and proteins activities during spermatogenesis. Therefore, the present study was designed to investigate the role of Zn deficiency in BPA-induced testicular toxicity in diabetic rats. Male Sprague-Dawley rats were divided into eight different groups: control (normal feed and water), BPA (50 mg/kg b.w.), Zn-deficient diet (ZnD; Zn-free AIN-93G diet), BPA + ZnD, STZ (single dose of 45 mg/kg b.w.), STZ + BPA, STZ + ZnD, and STZ + BPA + ZnD for four weeks. Animals' body and organ weight, sperm count, motility and sperm morphology were examined. Testes and epididymis histopathology were investigated. Testicular DNA damage and sperm apoptosis were evaluated by halo and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assays respectively. Testicular oxidative and nitrosative stress parameters were measured. Testicular steroidogenic acute regulatory protein (StAR), cytochrome P450 family 11 subfamily A member 1 (CYP11A1), 3β-hydroxysteroid dehydrogenase (3β-HSD), 17β-hydroxysteroid dehydrogenase (17β-HSD), and cytochrome P450 family 17 subfamily A member 1 (CYP17A1) expressions were evaluated by western blot analysis. The present results demonstrated that dietary Zn-deficient condition significantly increased the BPA-induced testicular, epididymal and sperm toxicity in diabetic rats due to hyperglycemia. Increased sperm abnormalities, epididymis, testicular structure and DNA damages, sperm apoptosis as well as decreased testicular oxidative and StAR, CYP11A1, 3β-HSD, 17β-HSD, and CYP17A1 expressions. The present results revealed that dietary Zn-deficient condition exacerbated the BPA-induced testicular and epididymal toxicity as well as perturbed the general male reproductive health in diabetic rats.	Mutat Res Genet Toxicol Environ Mutagen Vol.882 Pages 503547	10.1016/j.mrgentox.2022.503547	36155143	動物	-	1	1	1	不明	0	10 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0976	G. P. Sahoo, A. Pattnaik, V. Kumar and G. Jena	2025	Low-dose bisphenol A plus arsenik: Continuous or intermittent exposures in Sprague-Dawley rats; Effects on kidney oxidative stress, DNA damage, ferroptosis, and fibrosis	Arsenic and bisphenol A (BPA) are widespread environmental pollutants. We have studied the nephrotoxicity of arsenite (AS3), (5 mg/L in drinking water, plus BPA, 50 µg/kg oral dose, in juvenile Sprague-Dawley rats, administered continuously (CE) and intermittently (IE) for 90 days. Control (C), AS3, BPA, and AS3 + BPA groups were also studied. Kidney oxidative stress, DNA damage, ferroptosis, inflammation, microscopic and TEM examinations, DNA damage (tail moment), and protein expression. Continuous exposure to AS and BPA significantly increased urinary creatinine, albumin, and total protein, and decreased blood urea nitrogen (BUN). Histopathological and TEM data showed brush border detachment, tuft accumulation, podocyte injury, increased slit diaphragm space, and collagen deposition in both exposure groups. Significantly greater DNA damage was seen in the combined exposure group than in the other experimental groups. Combined exposure in the continuous and intermittent groups showed renal fibrosis and ferroptosis, and gene expression analysis revealed a significant increase in Bax and decrease in GRT 1. Combination exposure was more harmful than the individual exposures in causing kidney injury in these animals.	Mutat Res Genet Toxicol Environ Mutagen Vol.904 Pages 503871	10.1016/j.mrgentox.2025.503871	40382190	動物	-	1	1	不明	1	0	50 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0977	M. F. S. Saad, M. N. H. Abdullah, Y. Lim, H. Bahari, B. Y. Khoo, J. J. Tan and Y. K. Yong	2025	Exploring the role of Bisphenol A in obesity-driven colorectal cancer progression: network toxicology and multi-organ pathology in animal models	Bisphenol A (BPA), an endocrine disruptor, is linked to cancer progression in estrogen-responsive tissues, but its role in promoting colorectal cancer (CRC) progression in the context of obesity remains underexplored. This study examines BPA's influence on CRC in obese Sprague-Dawley rats using network toxicology and experimental models. Computational analysis using the Comparative Toxicogenomics Database, VirtualLinker, and Integrated Discovery Identified pathways such as "CRC" and "chemical carcinogenesis-receptor activation", implicating the PI3K-AKT pathway in IL-1 beta upregulation and BPA's role in CRC during obesity. This study was conducted over 12 weeks, divided into four groups (n = 10): A: Lean, B: Lean + BPA, C: Obese + BPA, D: Obese + CRC + BPA. Lean rats received a standard diet (2.5 kcal/g), while obese rats were fed a 60% high-fat diet (5.56 kcal/g). CRC was induced in rats 1, 2-dimethylhydrazine (40 mg/kg), and BPA (25 mg/kg) was administered for 12 weeks. Although BPA exposure did not affect body weight or biochemical parameters, the HCB group exhibited significant histopathological changes in the colon, including inflammation, goblet cell depletion, and crypt damage. Additionally, BPA exposure led to a significant increase in the expression of TLR4, NF-κB, and IL-6 in the colon tissue, indicating activation of inflammatory pathways. Co-exposure with HCB further amplified these effects, suggesting a synergistic interaction between the two compounds. These findings highlight the potential risk of combined exposure to BPA and HCB, which may contribute to colon inflammation and dysfunction. Given the widespread presence of both chemicals in the environment and their ability to accumulate in biological tissues, this study underscores the importance of considering mixture effects in risk assessments. Further research is needed to explore the underlying mechanisms and potential therapeutic interventions to mitigate the adverse effects of these environmental contaminants.	Toxicol Appl Pharmacol Vol.495 Pages 117227	10.1016/j.taap.2025.117227	39788208	動物	-	1	1	1	1	0	25 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0978	D. Y. Ryu, W. K. Pang, E. O. Adegoke, M. S. Rahman, Y. J. Park and M. G. Pang	2023	Bisphenol-A disturbs hormonal levels and testis mitochondrial activity, reducing male fertility	STUDY QUESTION: How does bisphenol A (BPA) influence male fertility, and which mechanisms are activated following BPA exposure? SUMMARY ANSWER: BPA exposure causes hormonal disruption and alters mitochondrial dynamics and activity, ultimately leading to decreased male fertility. WHAT IS KNOWN ALREADY: As public health concerns following BPA exposure are rising globally, there is a need to understand the exact mechanisms of BPA on various diseases. BPA exposure causes hormonal imbalances and affects male fertility by binding the estrogen receptors (ERs), but the mechanisms of how it mediates the hormonal dysregulation is yet to be studied. STUDY DESIGN SIZE DURATION: This study consisted of a comparative study using mice that were separated into a control group and a group exposed to the lowest observed adverse effect level (LOAEL) of BPA (50 mg/kg) for 5 consecutive weeks. PARTICIPANTS/MATERIALS SETTING METHODS: Male ICR mice (n = 10/group) were used in this study. Mice in the BPA group were orally administered BPA (50 mg/kg) for 5 consecutive weeks, while those in the control group received the same volume of corn oil only. Blood on the daily variations in BW, testis groups, were gauged every day from 8 to 12 weeks. At week exposure, BPA-treated mice were euthanized for a week. Then, the testes and spermatozoa of each mouse were collected to investigate the effects of BPA on male fertility. GP was carried out using the cumulus oocyte complexes, from female hybrid B6D2F1/CrlOri mice (n = 10/group) at 8–12 weeks of age. Then, the COCs were fertilized in vitro with sperm collected from the cauda epididymis of male mice exposed to BPA for 5 weeks. Subsequently, the fertilized oocytes were cultured in vitro. The COCs was performed to determine the levels of sex hormones (T3, T4, and testosterone) in serum. Immunohistochemistry and reactive oxidative stress was used to determine the effects of BPA on the histological morphology and stage VII–VIII testicular seminiferous epithelium. Blastocyst formation and cleavage development rate were evaluated using IVF. MAIN RESULTS AND THE ROLE OF CHANCE: BPA acted by binding to ERs and G protein-coupled receptors and activating the protein kinase A and mitogen-activated protein kinase signaling pathways, leading to aberrant hormone levels and effects on the respiratory chain complex, ATP synthase and protein-related metabolic pathways in testis mitochondria ($P < 0.05$). Subsequently, embryo cleavage and blastocyst formation were reduced after the use of affected sperm, and abnormal morphology of seminiferous tubules and stage VII–VIII seminiferous epithelium in the testis were observed in BPA-exposed mice ($P < 0.05$). LIMITATIONS REASONS FOR CAUTION: Since the protein expression levels in the testes were validated, in vitro studies in each testicular cell type (Leydig cells, Sertoli cells, and spermatogonial stem cells) would be required to shed further light on the exact mechanism resulting from BPA exposure. Furthermore, the BPA doses employed in this study significantly exceed the typical human exposure levels in real-life scenarios. Consequently, it is imperative to conduct experiments focusing on the effects of BPA concentrations, even in low-safe daily human exposures, to comprehensively assess their impact on reproductive health. WIDER IMPLICATIONS OF THE FINDINGS: This study provides evidence that BPA exposure can cause male infertility by altering hormone levels and mitochondrial activity in the testes and provides a solid foundation for subsequent investigations into the effects on male reproductive function and fertility following BPA exposure, and the underlying mechanisms responsible for these effects. In addition, these findings suggest that the LOAEL concentration of BPA demonstrates exceptional toxicity, especially when considering its specific impact on the testes and its adverse consequences for male fertility by impairing mitochondrial activity. Therefore, it is plausible to suggest that BPA elicits distinct toxicological responses and metabolomic endpoints based on the particular concentration levels for each target organ. STUDY FUNDING/COMPETING INTEREST(S): This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2018R1A6A1A06025929). No competing interests are declared.	Hum Reprod Open Vol.2023 Issue 4 Pages hoad044	10.1093/hropen/hoad044	38021376	動物	-	1	1	1	860ZF1/CrlOri	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0979	D. Y. Ryu, W. K. Pang, E. O. Adegoke, M. S. Rahman, Y. J. Park and M. G. Pang	2022	Abnormal histone replacement following BPA exposure affects spermatogenesis and fertility sequentially	Bisphenol A (BPA) is an endocrine-disrupting chemical widely distributed in the environment. Its exposure has been linked to male infertility in animals and humans due to its ability to induce epigenetic modification. Despite extensive research confirming the impact of BPA on epigenetic regulation, fundamental concerns about how BPA causes epigenetic changes and the underlying mechanisms of BPA on the male reproductive system remain unresolved. Therefore, we sought to investigate the effects of BPA on epigenetic regulation and the histone-to-protamine (PRM) transition, which is fundamental process for male fertility in mouse spermatogenesis. Male ICR mice (n = 10/group) at 8–12 weeks of age were orally administered BPA (50 mg/kg) for 5 consecutive weeks. Then, the testes and spermatozoa of each mouse were collected to investigate the effects of BPA on male fertility. GP was carried out using the cumulus oocyte complexes, from female hybrid B6D2F1/CrlOri mice (n = 10/group) at 8–12 weeks of age. Then, the COCs were fertilized in vitro with sperm collected from the cauda epididymis of male mice exposed to BPA for 5 weeks. Subsequently, embryo cleavage and blastocyst formation were reduced after the use of affected sperm, and abnormal morphology of seminiferous tubules and stage VII–VIII seminiferous epithelium in the testis were observed in BPA-exposed mice ($P < 0.05$). Since the protein expression levels in the testes were validated, in vitro studies in each testicular cell type (Leydig cells, Sertoli cells, and spermatogonial stem cells) would be required to shed further light on the exact mechanism resulting from BPA exposure. Furthermore, the BPA doses employed in this study significantly exceed the typical human exposure levels in real-life scenarios. Consequently, it is imperative to conduct experiments focusing on the effects of BPA concentrations, even in low-safe daily human exposures, to comprehensively assess their impact on reproductive health. This study provides evidence that BPA exposure can cause male infertility by altering hormone levels and mitochondrial activity in the testes and provides a solid foundation for subsequent investigations into the effects on male reproductive function and fertility following BPA exposure, and the underlying mechanisms responsible for these effects. In addition, these findings suggest that the LOAEL concentration of BPA demonstrates exceptional toxicity, especially when considering its specific impact on the testes and its adverse consequences for male fertility by impairing mitochondrial activity. Therefore, it is plausible to suggest that BPA elicits distinct toxicological responses and metabolomic endpoints based on the particular concentration levels for each target organ. STUDY FUNDING/COMPETING INTEREST(S): This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2018R1A6A1A06025929). No competing interests are declared.	Environ Int Vol.170 Pages 107617	10.1016/j.envint.2022.107617	36347119	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0980	L. Rytel, L. Könyves and S. Gonkowski	2022	Endocrine Disruptor Bisphenol a Affects the Neurochemical Profile of Nerve Fibers in the Aortic Arch Wall in the Domestic Pig	Bisphenol A (BPA) is a synthetic compound utilized in industry for the production of various plastics. BPA penetrates into the environment and adversely affects living organisms. Therefore, the influence of various BPA doses on the neurochemical characteristics of nerve fibers in the aortic arch wall was investigated in the present study. The experiment was performed on 12 female pigs divided into 3 groups. The animals were orally administered BPA in the following doses: 0.036 mg/kg body weight/day (group 1), 0.36 mg/kg body weight/day (group 2), and 36 mg/kg body weight/day (group 3). The study lasted 90 days. The activity of nerves within the aortic arch wall was measured by the double-labeling immunofluorescence method. It was found that BPA in the lowest dose used in this study (0.036 mg/kg body weight/day) causes a clear increase in the number of nerve fibers containing the activity of enzymes within aortic arch wall. Moreover,

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統合_0998	S. Rajaura, N. Bhardwaj, A. Singh, R. Babu, N. Gupta and M. Z. Ahmed	2024	Bisphenol A-induced oxidative stress increases the production of ovarian cancer stem cells in mice	Bisphenol A (BPA) belongs to the endocrine disruptor chemicals (EDCs) causing various reproductive disorders in females. We analyzed the toxic effects of BPA in the uterus and ovaries. The BPA was administered orally with the repeated low dose (LD, 1 mg/kg) and high dose (HD, 5 mg/kg) of body weight on alternate days for 3 months, via oral gavage to Swiss mice. BPA administration decreases body weight, ovarian weight and size as well as the number of ovarian follicles. The BPA-treated ovaries showed the presence of cystic follicles, hemorrhagic corpus luteum, and hyperplasia in the uterine epithelium and lymphocytic infiltration in the ovary. The BPA-treated uterus shows increased vascularization, atrophied endometrium and myometrium, and endometrial hyperplasia. ER-α with aberrant glandular growth. The ovarian stem cells (CSCs) in the ovaries were identified based on staining with anti-mouse CD44 and anti-mouse CD133 antibodies and analyzed by flow cytometry. Three different populations of ovarian CSCs: CD44+/ CD133-, CD44+/CD133+, and CD44-/CD133+ were recognized based on the intensity of these receptors. CD44+/CD133- and CD44+/CD133+ cell percentages were increased in BPA-treated groups. CD44+/CD133+ cancer-increased in LD but decreased in HD. The BPA administration also reduces ROS production, which decreases the expression of antioxidant genes. Superoxide dismutase-1 (SOD1), Superoxide dismutase-2 (SOD2), Catalase (CAT), Glutathione peroxidase-1 (GPX1), and Peritoxal box (GTF1D1) in ovarian cells. In conclusion, BPA exposure induced an inflammatory response, increased CSC properties, induced ROS, and decreased antioxidant responses in the ovaries.	Reprod Toxicol Vol.130 Pages 108724	10.1016/j.reprotox.2024.108724	39322090	動物	-	1	1	1	1	0	1、5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_0999	G. L. Raja, C. Lite, K. D. Subhashree, W. Santosh and S. Barathi	2020	Prenatal bisphenol-A exposure altered exploratory and anxiety-like behaviour and induced non-monotonic, sex-specific changes in the cortical expression of CYP19A1, BDNF and intracellular signaling proteins in F1 rats	Bisphenol-A (BPA) is one of the extensively studied estrogenic endocrine disrupting chemicals (EDC) with ubiquitous exposure among humans and wildlife. While there are literature reporting the association of bisphenol-A with decreased neurotrophic factor BDNF/expression levels with altered cognitive and emotional behaviour such as anxiety-like and stress-behaviour in animal models, there are no studies in BPA that investigate these altered neurobehavioural outcomes. In parallel with the expression of intracellular proteins involved in BDNF signaling pathway. In this study, pregnant Wistar rats were exposed to BPA through water (0, 0.1, 1, 10 and 100 mg/kg bw) from gestation day (GD) 6 to post-natal day (PND) 21 and the behavioural changes in the offspring were assessed. Our results showed that the altered behaviour in the form of lack of anxiety-like behaviour and CYP19A1 gene were observed in male BPA-exposed offspring, whereas in females, the expression was upregulated. The expression of c-FOS, p-ERK and p-PKA proteins were increased in males, while in females, it decreased. Both the male and the female BPA-exposed offspring exhibited elevated levels of DNMT1 protein. The sex-specific alteration in the expression of CYP19A1 and DNA methyltransferase 1 (DNMT1) suggests that both hormonal and epigenetic dysregulation could underlie the long-term BPA-induced effect on anxiety-like behaviour in the offspring.	Food Chem Toxicol. 2020 Aug;142:111442.	10.1016/j.fct.2020.111442	32450286	動物	神経	1	1 (飲水)	1	1	1	1（0.1ug/kg bw/day）	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1000	S. Rahmani, F. Vakhshiteh, M. Hatjat, P. Sahraeianfard, S. Hassani, E. Ghafour Boujandi, M. Rahimifard, M. Ghobeh, M. Baeeri and M. Abdollahi	2020	Gene-Environmental Interplay in Bisphenol A Subchronic Animal Exposure: New Insights into the Epigenetic Regulation of Pancreatic Islets	Endocrine disrupting chemicals (EDCs) such as bisphenol A (BPA), which is widely used in the plastic industry, have recently been considered to be involved in the pathogenesis of metabolic disorders, including obesity and diabetes. The present study was designed to investigate the effects of BPA exposure on pancreatic β-cell function and the underlying epigenetic mechanisms. Male Wistar rats were exposed to BPA (0, 5, 50, and 500 mg/kg/day) via oral gavage for 90 days. Body weight was recorded weekly, and BPA exposure was continued for 28 days after BPA was ceased. At the end of the treatment, the islets of Langerhans were isolated and purified, and then RNA content was extracted. MicroRNA (miRNA) profiling was evaluated using the real-time polymerase chain reaction (RT-PCR) method. After performing bioinformatics analysis of the RT-PCR data, the gene-ontology and data enrichment in terms of significantly disturbed miRNAs were evaluated through different databases. Our results indicated that BPA (50 and 500 mg/kg/day) significantly increased the body weight gain ($P < 0.05$) and induced glucose intolerance ($P < 0.05$). Moreover, BPA (50 and 500 mg/kg/day) disturbed the blood glucose and lipid profile. During blood glucose and glucose tolerance test (OGTT), BPA (50 and 500 mg/kg/day) disturbed the

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1011	A. R. Pérez, E. G. Parra, S. Mas, J. L. Mosgallo-Pascual, M. Ruiz-Ortega and S. Reyago-Mateos	2021	Bisphenol A Modulates Autophagy and Exacerbates Chronic Kidney Damage in Mice	BACKGROUND: Bisphenol A (BPA) is a ubiquitous environmental toxin that accumulates in chronic kidney disease (CKD). Our aim was to explore the effect of chronic exposition of BPA in healthy and injured kidney investigating potential mechanisms involved. METHODS: In C57BL/6 mice, administration of BPA (120 mg/kg/day, i.p for 5 days/week) was done for 2 and 5 weeks. To study BPA effect on CKD, a model of subtotal nephrectomy (SNX) was performed. Kidney function was assessed by albuminuria and creatinine clearance. Kidney damage was evaluated by histological analysis. Markers of oxidative stress, tissue inflammatory infiltration in the kidney, tubular injury and renal fibrosis, measured by immunohistochemistry and Western blot. BPA was applied subcutaneously by using osmotic pumps. After 12 weeks, the kidneys were analyzed by micro-computed tomography (micro-CT) and a three-point bending test. Comparing the female low- and high-dose groups, a significantly greater marrow area (p < 0.027) was identified in the group exposed to a higher BPA concentration. In addition, the trabecular number tended to be higher in the female high-dose group when compared to the low-dose group (p = 0.06). The cross-sectional thickness tended to be higher in the male high-dose group when compared to the male low-dose group (p = 0.08). Considering our results, BPA-related effects on the bone morphology in female Wistar rats are unbeneficial; after high-dose exposure, while, in male rats, a tendency toward negative effects on the bone morphology in terms of a reduced cross-sectional cortical area and total area could be demonstrated.	Int J Mol Sci Vol.22 Issue 13	10.3390/ijms22137189	34281243	動物	-	1	0	1	1	0	120 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1012	T. Psenas, I. Stratos, A. Nakoff, H. Christ, V. Hauk, C. Meyer and T. Mittlmeier	2022	Bisphenol A-Related Effects on Bone Morphology and Biomechanical Properties in an Animal Model	Bisphenol A (BPA), which is contained in numerous plastic products, is known to act as an endocrine disruptive, toxic, and carcinogenic chemical. This experimental series sought to determine the influence of BPA exposure on the femoral bone architecture and biomechanical properties of male and female Wistar rats. BPA was applied subcutaneously by using osmotic pumps. After 12 weeks, the bones were analyzed by micro-computed tomography (micro-CT) and a three-point bending test. Comparing the female low- and high-dose groups, a significantly greater marrow area (p < 0.027) was identified in the group exposed to a higher BPA concentration. In addition, the trabecular number tended to be higher in the female high-dose group when compared to the low-dose group (p = 0.06). The cross-sectional thickness tended to be higher in the male high-dose group when compared to the male low-dose group (p = 0.08). Considering our results, BPA-related effects on the bone morphology in female Wistar rats are unbeneficial; after high-dose exposure, while, in male rats, a tendency toward negative effects on the bone morphology in terms of a reduced cross-sectional cortical area and total area could be demonstrated.	Toxics Vol.10 Issue 2	10.3390/toxics10020086	35202272	動物	-	1	0	1	1	0	10.2、156 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1013	N. B. Patibha, D. Adiga, S. P. Kabekkodu, S. K. Bhat, K. Satyamoorthy and P. S. Rai	2022	Bisphenol A exposure modulates reproductive and endocrine system, mitochondrial function and cellular senescence in female adult rats: A hallmarks of polycystic ovarian syndrome phenotype	Bisphenol A (BPA) mimics estrogen and consequently suspected to be detrimental to female reproductive system. Biomonitoring confirms the BPA burden is likely leading to a complex condition called polycystic ovarian syndrome (PCOS) which is frequently attributed to female infertility. Due to unclear precise molecular pathomechanisms of BPA in PCOS, we intend to examine the molecular mechanisms of the reproductive, endocrine and metabolic system in female adult rats exposed to BPA. Female Wistar rats were exposed to BPA (0.25 mg/kg/day) by oral gavage for 90 days. Following the exposure, ovaries were harvested for RNA, analyzed RNA-sequencing and gene expression by semi-quantitative RT-PCR, assessed senescence induction by β-galactosidase staining and immunofluorescence in BPA-treated rats. Our data showed hormonal imbalance, impaired folliculogenesis, abnormal expression patterns of target genes, CDKN2A overexpression and enhanced ROS levels in BPA-treated rats. This study provides insights on the effects of BPA exposure on ovulatory hormonal, mitochondrial dysfunction, and senescence that benefit to better understanding of PCOS induced by BPA.	Environ Toxicol Pharmacol. 2022 Nov;96:104010.	10.1016/j.etap.2022.104010	36334871	動物	卵巣	1	1	1	1	0.25 mg/kg/日、150 μg/kg/日	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1014	J. M. Pinska, C. Wormsbaecher, B. M. Cumbia, M. R. Price, M. Cotes-Madina, J. Hotec, S. Agarwal, A. M. Mir, J. W. Sang and C. J. Bard	2025	In utero exposure to estrogenic bisphenol analogues increases mammary tissue stiffness	In utero exposure to estrogenic endocrine disrupting compounds (EDCs) can increase breast cancer risk in adulthood. It has previously been shown that the estrogenic plastic/pen bisphenol A (BPA) alters development of the mammary gland and increases both mammary gland stiffness and tumor susceptibility in rodent models following in utero exposure. Because of its endocrine disrupting properties, BPA has been substituted with structural analogues with varying ability to activate estrogen receptor alpha (ERα). However, the impacts of in utero exposure to many of these analogues is unknown. In this study, we aimed to analyze the impact of bisphenol analogues on collagen deposition and mammary gland stiffness and characterize mammary epithelial development following exposure to these compounds. With the exception of bisphenol S, all bisphenol analogues tested (bisphenol AF, bisphenol B, bisphenol E, bisphenol F, bisphenol S, and bisphenol Z) increased mammary gland stiffness at puberty. Bisphenol S did not increase mammary gland stiffness at puberty, but increased stiffness in the mammary stroma at 3 months of age. Bisphenol S also altered the expression of genes involved in the extracellular matrix and did not follow a clear pattern. These results add to the growing literature on the impact of bisphenol analogues and support the idea that these compounds promote abnormal mammary gland development. Furthermore, these data support a model that bisphenol compounds induce a microenvironment that may promote breast cancer development in an estrogen-dependent manner.	Reprod Toxicol. 2025 Sep;136:108974.	10.1016/j.reprotox.2025.108974	40513842	動物	----------	1	----------	1; CD 1 mice	----------	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_1015	D. Pinci, L. Gidoia, S. Parmigiani and P. Palanza	2020	Effects of Prenatal Exposure to a Low-Dose of Bisphenol A on Sex Differences in Emotional Behavior and Central Alpha(2)-Adrenergic Receptor Binding	Prenatal exposure to bisphenol A (BPA) influences the development of sex differences neurologically and behaviorally across many species of vertebrates. These effects are a consequence of BPA's estrogenic activity and its ability to act as an endocrine disrupter even at very low doses. When exposure to BPA occurs during critical periods of development, it can interfere with the normal activity of sex steroids, impacting the fate of neural circuits and behavioral traits. Here we report the effects of prenatal exposure to BPA on sex differences in emotional behavior and central alpha(2)-adrenergic receptors (α2-ARs), which are involved in many brain and behavioral features, such as the amount of time spent investigating a novel environment. Isometric activity and behavioral lateralism. In some species of rodents, BPA exposure affected many sexual behaviors. Interestingly, these behaviors are at least in part modulated by the catecholaminergic system, which has been reported to be a target of BPA action. In the present study we investigated the influence of prenatal exposure of mice to a very low single dose of BPA on emotional and sexual behaviors and on the density and binding characteristics of alpha(2)-adrenergic receptors. Since α2-adrenergic receptors are widespread in the central nervous system and they can act as autoreceptors, inhibiting the release of noradrenaline and other neurotransmitters from presynaptic terminals, BPA exposure disrupted sex differences in behavioral responses to a novel environment, but did not affect male sexual behavior. Interestingly, BPA induced a change in the binding affinity of alpha(2)-adrenergic receptors in the locus coeruleus and medial preoptic area (mPOA) and it attenuated the sexual dimorphism in the density of the receptors in the mPOA.	Int J Mol Sci Vol.21 Issue 9	10.3390/ijms21093269	32380724	動物	-	1	1	1	1	0	10 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1016	C. Pinzzi, A. Lama, C. Annunziata, G. Cavaliere, C. Ruiz-Fernandez, A. Monnolo, F. Comella, G. Scuotto, M. Sisinnaio, M. P. Mollica, G. M. Rossi, M. C. Ferrante and R. Meli	2020	Oral Bisphenol A Worsens Liver Immune-Metabolic and Mitochondrial Dysfunction Induced by High-Fat Diet in Adult Mice: Cross-Talk between Oxidative Stress and Inflammasome Pathway	Lines of evidence have shown the antiorganistic and transgenerational impact of bisphenol A (BPA), an endocrine disrupting chemical, on immune-metabolic alterations, inflammation, and oxidative stress, while BPA toxic effects in adult mice were are still controlled. Here, we evaluate BPA's worsening effect on several hepatic metabolic processes associated to high-fat diet (HFD)-induced obesity in mice. After 12 weeks HFD feeding, C57BL/6 male mice were exposed daily to BPA (50 μg/kg per os) along with HFD for 3 weeks. Glucose tolerance and lipid metabolism were examined in serum and/or liver. Hepatic oxidative damage (reactive oxygen species (ROS) production, mitochondrial dysfunction, and antioxidant defenses) and inflammation (cytokine production and inflammasome activation) were evaluated by biochemical and molecular analysis. BPA amplified HFD-induced alteration of key factors involved in glucose and lipid metabolism, liver triglycerides accumulation, and worsened mitochondrial dysfunction by increasing oxidative stress, and reducing antioxidant defenses. The exacerbation by BPA of hepatic immune-metabolic dysfunction induced by HFD was shown by increased toll-like receptor-4 and its downstream pathways (i.e., NF-kB and NLRP3 inflammasome) amplifying inflammatory cytokine transcription and promoting fibrosis progression. This study evidences that BPA exposure represents an additional risk factor for the progression of fatty liver diseases, strictly related to the cross-talk between oxidative stress and immune-metabolic impairment due to obesity.	Antioxidants (Basel) Vol.9 Issue 12	10.3390/antiox9121201	33265944	動物	-	1	1	1	1	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1017	C. Pirrone, B. Julian, N. Vega, H. Vidal, D. Naville and B. Le Magueresse-Battistoni	2021	Impact of Estrogen Withdrawal and Replacement in Female Mice along the Intestinal Tract: Comparison of E2 Replacement with the Effect of a Mixture of Low Dose Pollutants	Postmenopausal women represent a vulnerable population towards endocrine disruptors due to hormonal deficit. We previously demonstrated that chronic exposure of ovariectomized C57BL/6 mice fed a high-fat, high-sucrose diet to a low dose mixture of chemicals with one dioxin, one polychlorobiphenyl, one phthalate, and bisphenol A triggered metabolic alterations in the liver but the intestine was not explored. Yet, the intestinal barrier is a key player in the gut-liver axis. Here, we investigated the impact of ovariectomy and chronic exposure to the mixture of chemicals at low doses in mice with/without fat/sugar diet on the intestinal barrier. We characterized genes encoding tight junctions (Ocln1, Zo1a1, Cldn1, Cldn3, Cldn5, Cldn8), and genes related to gut hormones in the jejunum (sg., Cck8, Gcg1, Glp1r1) and to bile acid biosynthesis in the gut (sg., Fgf15, Slc10a2) and liver (sg., Abcb11, Slc10a1) were under estrogen regulation. Exposure to pollutants mimicked some of the effects of E2 replacement, particularly in the lower (sg., Ocln1, Slc1a1) suggesting that the mixture had estrogen-mimetic activities. The present findings have important implications for the understanding of estrogen-dependent metabolic alterations with regards to situations of loss of estrogens as observed after menopause.	Int J Environ Res Public Health Vol.18 Issue 16	10.3390/ijerph18168685	34444432	動物	-	1	1	0	1	0	5 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1018	X. Piao, Z. Liu, Y. Li, D. Yao, L. Sun, B. Wang, Y. Ma, L. Wang and Y. Zhang	2019	Investigation of the effect for bisphenol A on oxidative stress in human hepatocytes and its interaction with catalase	Bisphenol A (BPA) as a chemical raw material, is widely used in the manufacturing process of daily necessities. It was reported that BPA could induce oxidative stress, and catalase (CAT) can protect the body from oxidative stress. In this paper, the effect of BPA on CAT was carried out in vitro and in vivo. Firstly, we studied the effects of BPA on oxidative stress, cell viability and CAT activity in human hepatocytes, and the results of in vitro experiments show that the survival rate of hepatocytes decreased significantly after exposure to BPA, and the increase of BPA concentration can SOD, MDA, GSH-Px

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1037	M. I. Palacios-Arreola, N. A. Morera-Mendoza, K. E. Nava-Castro, M. Segovia-Mendoza, A. Perez-Torres, C. A. Garay-Canales and J. Morales-Montor	2022	The Endocrine Disruptor Compound Bisphenol-A (BPA) Regulates the Intra-Tumoral Immune Microenvironment and Increases Lung Metastasis in an Experimental Model of Breast Cancer	Breast cancer (BC) metastasis represents the main physiopathology leading to poor prognosis and death. Bisphenol A (BPA) is a pollutant, classified as an endocrine disrupting chemical compound with estrogenic activity, which is present in a wide variety of plastic products. Exposure to BPA has been associated with an increased risk of developing BC and metastasis. Nevertheless, the mechanisms by which BPA promotes BC progression remain unclear. Therefore, in this study, we investigated the effect of BPA exposure on the intra-tumoral immune microenvironment and lung metastasis in an experimental model of BC. Female BALB/c mice were exposed orally to a single dose of BPA (50 mg/kg) by oral gavage. Two days later, 4T1 murine breast cancer cells were inoculated into the mammary fat pad. Mice were euthanized 15 days after tumor inoculation, and tumors, spleen, and lungs were collected. Tumor growth was monitored throughout the experiment. Flow cytometry was used to analyze the immune cell populations in the tumor microenvironment, spleen, and lungs. Tumor growth was significantly higher in BPA-exposed mice than in control mice. Moreover, BPA exposure increased the number of lung metastatic nodules and the percentage of metastatic cells in the lungs. Flow cytometry revealed that BPA exposure altered the immune cell composition within tumors, with a notable increase in myeloid-derived suppressor cells (MDSCs) and regulatory T cells (Tregs), both of which are known to promote immune evasion and tumor progression. Additionally, BPA exposure was associated with elevated levels of immunosuppressive cytokines, including IL-10 and TGF-β, within the tumor microenvironment. These findings suggest that BPA exposure may enhance BC metastasis by modulating the immune landscape, thereby facilitating tumor cell dissemination to the lungs. Our results underscore the potential risk posed by environmental exposure to BPA and highlight the importance of considering endocrine disruptors in the context of cancer progression and metastasis. Further studies are warranted to elucidate the precise molecular mechanisms underlying BPA-induced immunosuppression and to explore potential therapeutic interventions to mitigate its adverse effects.	Int J Mol Sci Vol.23 Issue 5	10.3390/ijms23052523	35269666	動物	-	1	0	1	BALB/cAnN (SPF)	0	250 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1038	R. Pagotto, C. G. Santamaria, M. B. Hermegay, J. Abad, M. L. Zanchuraw, L. Kass, M. Crispo, M. M. Muñoz-de-Toro, H. A. Rodriguez and M. Bollati-Fogolin	2020	Perinatal exposure to Bisphenol A disturbs the early differentiation of male germ cells	Understanding the effects of Bisphenol A (BPA) on early germ cell differentiation and their consequences in adult life is an area of growing interest in the field of endocrine disruption. Herein, we investigate whether perinatal exposure to BPA affects the differentiation of gonocytes into spermatogonial stem cells (SSCs) and spermatogonial differentiation. We used Oct4-eGFP transgenic mice to track the expression of the Oct4 gene. This strategy was proved successful to evaluate the spermatogonial stem cells in an undifferentiated stage. Then, BPA treatment was used as a parameter to evaluate the effect of BPA on early germ cell development. Female pregnant transgenic mice were exposed to BPA by oral gavage, from embryonic day 9.5 to postnatal day 7 (PND7). The effects of BPA on male germ cell differentiation were evaluated at PND7, with testicular morphology and proliferation, expression of androgen receptor and the number of undifferentiated spermatogonia as endpoints. We found that perinatal bisphenol A exposure to BPA up-regulates the expression of Oct4 eGFP in testicular cells at PND7. This finding suggests a higher proportion of undifferentiated spermatogonia in BPA-treated animals, compared with non-exposed mice. Moreover, perinatal BPA exposure increased the proliferation of undifferentiated spermatogonia at PND7. Finally, we found that perinatal exposure to BPA disturbed the normal differentiation of male germ cells early in life, mainly by altering the expression of Oct4 and retained long-lasting sequelae at the adult stage, affecting sperm count and testis.	Reprod Toxicol Vol.98 Pages 117-124	10.1016/j.reprotox.2020.09.004	32956838	動物	-	1	1	不明	transgenic	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1039	G. Ozkemakli, A. Batci Ozyurt, P. Ebekoglu, N. D. Zeybek, N. Yersal and B. Kocer-Gumusel	2022	The effects of prenatal and lactational bisphenol A and/or di(2-ethylhexyl) phthalate exposure on female reproductive system	Bisphenol A (BPA) and di(2-ethylhexyl) phthalate (DEHP) are endocrine disrupting chemicals (EDCs) that are abundantly used in polyvinyl chloride plastics, polycarbonates and epoxy resins. Prenatal and early postnatal exposure to EDCs may cause reproductive disorders in females. The present study aimed to investigate the effects of prenatal and lactational exposure to BPA and/or DEHP on female reproductive system. Pregnant rats from various rodent efficacy studies (RED) were randomly assigned to four groups (n = 5/group): Control (received vehicle only), DEHP (20 mg/kg/day), BPA (5 mg/kg/day) and BPA + DEHP (BPA+DEHP; 5 mg/kg/day BPA+20 mg/kg/day DEHP) through 6-13 gestational days and lactation by oral gavage. Female offspring (n = 5/group) were sacrificed at the end of twelfth postnatal week and then euthanized. Reproductive hormones, ovarian follicle numbers and ovarian development were determined. Plasma testosterone and estradiol levels of BPA and BPA + DEHP groups were significantly lower than control. In BPA group, the number of tertiary ovarian follicles decreased significantly compared to control. In the combined exposure group, the number of corpus luteum (CRL), as well as the number of primordial follicles (ORL), showed marked decreases compared to control group. It can be suggested that early life exposure to BPA and DEHP may cause late life adverse effects in female reproductive system, especially after combined exposure.	Toxicol Mech Methods Vol.32 Issue 8 Pages 597-605	10.1080/15376516.2022.2057265	35321620	動物	-	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1040	Ö. Özden Akkaya, A. Yağcı, B. Zik, A. Kibria, S. Güler, S. Çelik and K. Altunbaş	2024	The effect of bisphenol A on the Notch (Notch2 and Jagged2) signaling pathway in the follicular development of the neonatal rat ovary	The formation of primordial follicles determines the pool size of follicles in the ovary, and is crucial for female reproductivity. Oocyte nest breakdown, and the formation of primordial follicles, largely depend upon the communication between oocytes, and the surrounding pregranulosa cells. The neurogenic locus notch homolog protein (Notch) signaling pathway is the key player for this cell-to-cell communication, and is responsible for the maintenance of oocyte nests, primordial follicle formation, and follicular development. Bisphenol A (BPA) is a well-known endocrine disrupting chemical (EDC) that has been shown to affect ovarian development via Notch signaling. Consequently, we investigated the possible influences of BPA treatment on the prepubertal distribution of the follicular stages, follicle numbers, levels of neurogenic locus notch homolog protein 2 (Notch2) and Jagged2 expressions in the ovary. BPA was administered at doses of either 50 μg/kg/day or 50 mg/kg/day at different time intervals, during neonatal and fetal periods in rats. After collecting the ovaries from the various experimental groups, follicular count, cell frequency of apoptosis was determined by TUNEL assay. In addition, Notch2 and Jagged2 expressions were assessed by immunohistochemical staining and qPCR. In summary, BPA treatment affected the follicle numbers and apoptosis level, and Notch2 and Jagged2 expressions varied with follicular stage. It was also observed that these parameters were dose and time dependent with exposure to BPA exposure.	Biotech Histochem Vol.99 Issue 5 Pages 238-259	10.1080/10520295.2024.2361313	39382141	動物	-	1	不明	不明	不明	0	50、50000 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1041	Z. Ouyang, W. Zhu, Y. Xie, W. Yang, J. Liu, Q. Peng and R. Fan	2024	Green Tea Diet Can Effectively Antagonize the Toxicity Induced by Environmental-Related Concentrations of BPA: An Implication from In Vivo and In Silico Studies	The neurotoxicity of bisphenol A (BPA) exposure has been confirmed in vivo and in vitro, and inflammatory response is considered the main pathway. Green tea is a healthy life habit as it is rich in various anti-inflammatory components. To confirm that green tea diet is an effective measure to antagonize BPA-induced neurotoxicity, mice were treated with 0.5 and 5000 μg/kg/day of BPA from postnatal day (PND) 1 to 50 and supplemented with green tea at PND 21. From PND 51, behavioral tests were conducted on mice to assess BPA-induced cognitive, and spatial learning memory capabilities. The open field test and Y-maze test also were conducted to evaluate anxiety-like behavior induced by BPA. Interestingly, green tea diet significantly alleviated BPA-induced anxiety-like behaviors. Meanwhile, the green tea diet effectively reversed BPA-induced microglia activation and neuronal damage in the hippocampus. Moreover, the expression of inflammatory factors (IL-1β, IL-6, and TNF-α) was significantly increased by BPA exposure ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively), and green tea diet significantly reversed the increase of IL-1β, IL-6, and TNF-α induced by BPA ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively). Furthermore, we found that BPA exposure could activate the NF-κB signaling pathway, and green tea diet could significantly inhibit the activation of NF-κB signaling pathway induced by BPA ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively). Molecular docking suggests that various anti-inflammatory components of green tea can competitively bind to the estrogen receptors with BPA. In general, a green tea diet alleviates BPA-induced emotional disorders by inhibiting microglial polarization and hippocampal apoptosis, indicating its effective antagonistic ability against the neurotoxicity induced by environmental BPA exposure.	J Agric Food Chem Vol.72 Issue 37 Pages 20633-20645	10.1021/acs.jafc.4c05627	39230979	動物	-	1	不明	1	不明	0	0.5、5000 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1042	A. P. Ortega-Garcia, V. Diaz-Hernández, P. Cutiaco-Saldaña and H. Merchant-Larios	2021	Bisphenol A alters differentiation of Leydig cells in the rabbit fetal testis	The endocrine disruptor Bisphenol A (BPA) crosses the placental barrier and reaches the fetal organs, including the gonads. In the testis, fetal Leydig cells (FLC) produce testosterone required for the male phenotype and hormonally-cell-cell signaling in the developing testis. Although it is known that BPA affects cell proliferation and differentiation in FLC, studies concerning the mechanism involved are contradictory, mainly due to differences among species. Two developing fetal gonads of rabbits, both ovines and testicles, whereas species with more extended gonadal periods from these two tissue compartments. The rabbit provides a good model to study the effects of BPA in the FLC population in the testis and ovary because the gonads are developed in the same period. We evaluated the effects of BPA on the proliferation and cell population of the developing testis. Using qRT-PCR, we assessed the levels of SF1, CYP11A1, 3,β -HSD, and aromatase transcripts in the gonads of fetal rabbits. Three levels combined with both the mitotic activity and the ultrastructural differentiation of the FLC by nuclear and electron microscopy, respectively. Results indicated that BPA alters the expression levels of essential genes involved in androgen-paracrine signaling, modifies the proliferation and differentiation of the FLCs, and alters the levels of ovine testosterone after birth. Thus, BPA may change the postnatal levels of serum testosterone in male in the impaired FLC population formed by the proliferating ovens and non-proliferating quiescent/resistant FLC.	Int J Dev Biol. 2021;65(4-5-6):403-412.	10.1387/ijdb.200185hm	32930364	動物	精巣	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1	-	胎児対象だがス	-	-	-	-	-	-	-	-	-	-	-	-
統合_1043	O. I. Olunarti, B. A. Alabi, O. S. Michael, A. O. Ojo and B. P. Fatokun	2021	Rutin prevents cardiac oxidative stress and inflammation induced by bisphenol A and dibutyl phthalate exposure via NRF-2/NF-κB pathway	ABA Environmental pollutants such as plastic-component substances (phthalates and bisphenol A) that coexist in natural ecosystems have been linked to an increase in the occurrence of human health hazards, particularly cardiovascular health. This study was designed to investigate single and combined acute toxic effects of dibutyl phthalate and bisphenol A and the possible intervention role of rutin. MATERIALS AND METHODS: Forty two rats were randomized into 7 groups of 6 animals each and were treated as follows for 28 days: Control (0.1% DMSO), Bisphenol A (BPA, 25 mg/kg, p.o), Dibutyl phthalate (DBP, 25 mg/kg, p.o), BPA + DBP, Rutin (100 mg/kg, p.o), BPA + Rutin, DBP + Rutin. Cardiac oxidative stress, inflammation, and histopathological changes were evaluated. RESULTS: Results showed that BPA induced myocardial oxidative stress (OS) marked by elevated malondialdehyde (MDA) increased in DBP + BPA group. Also, DBP increased tissue C-reactive protein (CRP). DBP, DBP + BPA increased tissue nuclear factor kappa B (NF-κB). DBP + BPA increased plasma CRP. BPA increased plasma NF-κB. However, rutin efficiently reduced MDA level. CRP and NF-κB increasing (ICD, ICH and ICC) levels. In DBP and BPA exposed rats. DISCUSSION: These results revealed that bisphenol A and dibutyl phthalate exposure caused oxidative stress and inflammation in the heart through NrF2/NF-κB signaling pathway while oral administration of rutin prevents these effects via upregulation of Nrf2 and suppression of NF-κB signaling pathway.	Life Sci Vol.284 Pages 119878	10.1016/j.lfs.2021.119878	34384828	動物	-	1	1	1	不明	0	25 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1044	S. G. Olukole, E. O. Ola-Davies, D. O. Lanipekun and B. O. Oke	2020	Chronic exposure of adult male Wistar rats to bisphenol A causes testicular oxidative stress: Role of gallic acid	OBJECTIVES: Bisphenol A (BPA) has been reported that among other male reproductive dys functions, it can cause marked estrogenic effects including alteration in serum hormones as well as testicular lesions in exposed animals. This work sought to study the role of gallic acid (GA) in boars embedded on the BPA induced testicular oxidative stress in adult male Wistar rats. MATERIALS AND METHODS: Forty adult male Wistar rats (180-200 g) were randomly assigned into 5 groups of 8 rats each and were treated as follows for 28 days: Control (0.1% DMSO), BPA (25 mg/kg, p.o), GA (50 mg/kg, p.o), BPA + GA (25 mg/kg BPA with concurrent 50 mg/kg GA) and BPA + GA (25 mg/kg BPA with concurrent 100 mg/kg GA). At the end of the experimental period, rats were anesthetized and sacrificed. Blood and organ samples were collected for the assessment of testicular oxidative stress. Testicular oxidative stress was evaluated by measuring the activities of superoxide dismutase (SOD), catalase (CAT), GPx, GST, GR and GSH-Px, and the levels of malondialdehyde (MDA) and nitric oxide (NO). Serum concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH) and testicular PPAR-γ and tissue biochemistry analysis: superoxide dismutase (SOD), catalase (CAT), GSH-Px, glutathione-S-transferase (GST), malondialdehyde (MDA) and nitric oxide (NO) were also evaluated. RESULTS: Findings from the present study showed that BPA significantly ($p < 0.05$) increased testicular MDA and NO levels and decreased the activities of SOD, CAT, GPx, GST, GR and GSH-Px when compared with the control group. However, co-treatment with GA significantly ($p < 0.05$) reversed the BPA induced testicular oxidative stress by decreasing the activities of antioxidant enzymes and increasing the levels of non-enzymatic antioxidants. Furthermore, BPA induced testicular oxidative stress by decreasing the activities of antioxidant enzymes and increasing the levels of non-enzymatic antioxidants. However, co-treatment with GA prevented against these alterations. CONCLUSION: Findings from the present study confirmed the previously reported data and show that the ability of GA as a potent antioxidant, may protect against BPA induced alterations in the male reproductive function. Hence, GA protects against testicular oxidative stress in adult male Wistar rats following chronic exposure to BPA.	Endocr Regul Vol.54 Issue 1 Pages 14-21	10.2478/enr-2020-0003	32597147	動物	-	1	1	1	0	10 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1045	S. G. Olukole, D. O. Lanipekun, E. O. Ola-Davies and B. O. Oke	2019	Maternal exposure to environmentally relevant doses of bisphenol A causes reproductive dysfunction in F1 adult male rats: protective role of melatonin	This study investigated the protective effects of melatonin (Mt), a potent antioxidant, in male Wistar rats exposed to environmentally relevant doses of bisphenol A (BPA) in utero. Pregnant Wistar rats were randomly assigned into 5 groups of 5 rats each and were treated as follows: Control (0.1% DMSO), BPA (0.5 mg/kg bw), BPA + Mt (0.5 mg/kg bw BPA with concurrent 4 mg/kg bw Mt), BPA + Mt (2 mg/kg bw BPA with concurrent 8 mg/kg bw Mt) and BPA + Mt (4 mg/kg bw BPA with concurrent 16 mg/kg bw Mt). Treatments were by gavage from gestational day (GD) 10-21. The BPA treated animals showed dose dependent significant reduction in body weight, gonosomatic index, sperm motility, fertility and count. Also, BPA caused significant reduction in the levels of serum testosterone and luteinizing hormone while it caused significant increase in the levels of follicle stimulating hormone as well as estradiol. Furthermore, BPA induced testicular oxidative stress, including significant decrease in the activities of testicular SOD, GSH and GPx as well as GST, increasing the levels of testicular MDA and H2O2. It further induced interstitial necrosis and germinal cell degeneration in the testis with a subsequent diminution of the tubular and lumina diameter. However, co-treatment with Mt (1) offered tremendous protection against testicular damage induced by BPA. Melatonin is likely to protect against alterations of the male reproductive system caused by BPA through its direct action on the mechanism of anti-oxidants, as well as through the inhibition of necrosis.	Environ Sci Pollut Res Int Vol.26 Issue 28 Pages 28940-28950	10.1007/s11356-019-06153-3	31388950	動物	-	1	1	1	0	25、250 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1046	K. M. Oliveira, L. S. Figueiredo, T. R. Araujo, I. N. Freitas, L. N. Silva, A. C. Boschero and R. A. Ribeiro	2020	Prolonged bisphenol-A exposure decreases endocrine pancreatic proliferation in response to obesogenic diet in ovariectomized mice	Research on the deleterious actions of bisphenol (BPA) have focussed on its effects on insulin secretion during pre/perinatal periods or adulthood. Estrogens also modulate endocrine pancreas physiology in females during aging; however, the effects of BPA on islet morphophysiology after menopause have not been investigated. We evaluated the effects of BPA exposure on glucose homeostasis and islet morphofunction in ovariectomized (OVX) mice fed on a high-fat diet (HFD). Adult Swiss female mice were underwent to bilateral ovariectomy, and with the confirmation of the establishment of surgical menopause, the females were then exposed to BPA (50 μg/kg/day) by gavage for 30 days. Ovariectomy and HFD per se induced glucose intolerance, hyperinsulinemia, and insulin resistance. However, BPA exposure in OVX mice fed on HFD exacerbated hyperglycemia, hyperinsulinemia, glucose intolerance and insulin resistance. BPA did not modulate HFD-induced obesity in ovariectomized mice. Besides, BPA exposure in OVX mice fed on HFD induced body glucose impairments in HFD females, and islets isolated from both HFD and HFD + BPA groups exhibited insulin hypersecretion. The HBPA islets, however, displayed enlarged islet cells and reduced proliferation, in association with the downregulation of mRNAs encoding PCNA (↓ 50%) and CCND2 and upregulation of mRNAs encoding IFN-γ, CHOP, TXP-1, and IL-1β in HBPA islets. BPA consumption in OVX mice impaired the islet cell hyperplasia response to the HFD, partly mediated by increased expression of IFN-γ and CHOP, which impaired the expression of major genes involved in islet cell survival and functionality. Together with higher pro-inflammatory cytokines expression in the islet milieu, these alterations may accelerate β-cell failure in postmenopause.	Steroids Vol.160 Pages 108658	10.1016/j.steroids.2020.108658	32442623	動物	-	1	1	1	Swiss ovariectomized (OVX)	0	50 μg/kg/d（強力半減期）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1047	O. S. Oluh, J. K. Akintunde, A. J. Akamo and U. Akpan	2025	Thymoquinone inhibits Neuroinflammatory mediators and vasoconstriction injury via NF-κB dependent NeuN/GFAP/Ki-67 in hypertensive Dams and F1 male pups on exposure to a mixture of Bisphenol-A analogues	Bisphenol-S (BPS) analogues were inevitable components of numerous domestic products, but these have been identified as agents of teratogenic disorders. This study, therefore, investigated the effect of thymoquinone (TMQ) on the virulence of hypertensive female rats and their F1 male offsprings on exposure to a mixture of Bisphenol-S (BisphenolS® and BisphenolA® 0.5BPS). Female rats were studied into normotensive and hypertensive groups, and both were treated with MilliTonic MBPS (- TMQ, and TMQ only. Exposure to MBPS and on treatment with TMQ lasted at least 63 days. Neurobehavioral assessments were conducted using Open Field (OFT), elevated plus maze and locomotor activity. Immunohistochemistry, dopaminergic and adrenergic receptor assays for Nav1.7 and Nav1.8 ion gene expression, and immunohistochemistry for protein quantification within NAC, renal fast stained, and congo red stains were used for histological assessments. From the results, maternal exposure to MBPS mediated striatal dysfunction via p53 and NF-kB upregulation, decreased BDNF/Ki-67 and NeuN/GFAP ratio, and increased Nav1.7/Nav1.8 ratio in hypertensive dams and F1 male offsprings. Also, MBPS induced vasoconstriction injury via ACE/ET-1/ETAR/ETBR/NO pathway. Hypertensive rats have exacerbated MBPS toxicity. Post-TMQ, increased anxiety and decreased psychomotor activity were associated with MBPS-induced striatal neurotoxicity in F1 male offsprings. However, co-treatment with thymoquinone prevented striatal dysfunction in hypertensive dams and their F1 male offspring. In conclusion, disruption of the delicate balance between apoptotic and cell proliferation culminating in the reduction of mature neurons is responsible for neurodegeneration and neuropathy associated with MBPS exposure. However, these can be prevented through regular consumption of natural products and supplements rich in thymoquinone.	Toxicol Appl Pharmacol Vol.494 Pages 117162	10.1016/j.taap.2024.117162	39577800	動物	-	1	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1048	H. A. Ogwuni, P. M. Aja, E. D. Eze, P. C. Aju, A. A. Mayowa, B. A. Ala, E. U. Ekpono, I. N. Awoke, P. N. Ogbu, U. U. Ukachi, U. U. Orji, P. C. Nweke, C. O. Egbo, E. U. Ekpono, G. O. Ewa, I. O. Iguenyi, E. U. Alum, O. C. Chukwu, L. Aja, G. O. Ani, C. E. Offor, O. E. Yakubu, E. Maduagwuna, J. E. Akobi, S. Nonen and C. G. Awuchi	2024	Cucumeropsis mannii seed oil (CMSO) restores testicular mitochondrial dysfunctions by modulating the activities of dysregulated testicular mitochondrial enzymes in male albino rats exposed to bisphenol A	Bisphenol A, a traditional endocrine disruptor, has been implicated in male infertility. This study investigated the effect of Cucumeropsis mannii seed oil (CMSO) on bisphenol A (BPA)-induced biochemical toxicity to the testes of male albino rats. Twenty-five (25) male albino rats were randomly assigned into five groups (A-E) of five rats each. Group A served as the control and received 1 mL/kg BW of PBS and 1 mL/kg BW CMSO, respectively. Rats in groups B, C, and D received oral administration of 100 mL/kg BW of BPA. Rats in groups C and D received 50 and 100 mL/kg BW of CMSO, respectively, following 14 weeks of exposure to these doses. Some mitochondrial enzymes, mitochondrial membrane potential (MMP), mitochondria testicular protein, and body weight of rats were determined using standard methods. BPA significantly reduced sucrose dehydrogenase, malate dehydrogenase, succinate dehydrogenase, SADH dehydrogenase, and monoamine oxidase activity. Also, BPA prominently decreased the MMP, mitochondrial testicular protein, and body weight of rats. Interestingly, coadministration of BPA and CMSO restored the dysregulated activities of the enzymes and levels of other biomarkers. We postulated that CMSO may be a promising drug for treating systemic toxicity caused by environmental toxicants such as BPA.	Food Sci Nutr Vol.12 Issue 10 Pages 7854-7863	10.1002/fsn3.4379	39479659	動物	-	1	1	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1049	P. Nurlaz, J. Aguelles and C. Perillan	2023	Effects of short-term exposure to low doses of bisphenol A on cellular senescence in the adult rat kidney	Bisphenol A (BPA) is one of the primary chemicals produced by volume worldwide. Extensive literature has raised many concerns about its possible involvement in the pathogenesis of kidney diseases, but its contribution has not been extensively studied. During cellular senescence, the interference of dysfunctional cellular functions promotes further senescence, causing cellular malfunction. Insulin-like growth factor-1 (IGF-1) plays an important protective role in the setting of kidney injury. The goal of the present study was to evaluate the effects of short-term treatment with low doses of BPA on cellular senescence in adult rat kidneys. Male Wistar rats were treated with BPA (0.5 and 50 μg/kg/day) for 15 days. Histological, immunohistochemical, and ultrastructural analyses were performed. Immunohistochemical analysis were performed, and an immunoreactive score (IRS) was calculated. Lipofuscin autofluorescence was used for the study of cellular senescence. The renal cortex showed diffuse autofluorescent lipofuscin signal in the proximal convoluted tubules (PCTs) of males in the BPA50-treated (renal intensity) and BPA50-treated (strong intensity) groups, but not in CONTROL males. Labeling of cortical PCTs with anti-IGF-1 antibodies showed an IRS of 0 in the CONTROL group, two IRSs of 3 and 4 in the BPA50- and BPA500-treated groups, respectively. The present results suggest that low, "safe" doses of BPA induce renal injury, as measured by histological signs of renal changes, increased cellular senescence, and activation of cellular repair systems in PCTs.	Histochem Cell Biol Vol.159 Issue 5 Pages 453-460	10.1007/s00418-022-02178-x	36622388	動物	-	1	0	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

別添-2　統合文献リスト

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1063	K. E. Nava-Castro, R. Ramírez-Nieto, L. A. Mi ichel-García, M. I. Girón-Pérez, M. Segura-Mendoza, M. S. Navidad-Murrieta and J. Morales Montor	2019	Environmental Pollution as a Risk Factor in Testicular Tumour Development: Focus on the Interaction between Bisphenol A and the Associated Immune Response	Bisphenol A (BPA) is an endocrine disruptor to which animals and humans are highly exposed. Many reports have established a relationship between BPA exposure and breast cancer incidence, especially during critical periods of development. However, its effects on the immune response in testicular tumour growth have not yet been described. Thus, we wanted to analyze the effect of perinatal BPA exposure in pregnant female mice on the development of testicular tumours induced by the transplantation of TC1 cancer cells in their male offspring. Female mice were exposed to BPA (50 μg/kg/day) in their drinking water from the 8th day of gestation until the end of lactation. In adulthood, male offspring underwent intratesticular inoculation with 5×10^5 cancer cells. On day 21 after inoculation, mice were euthanized, and cancer was obtained to measure BPA levels using HPLC-coupled to mass spectrometry. The percentages of immune cell populations in peripheral lymph nodes (PLN), the spleen and tumours were evaluated by flow cytometry. In addition, the tumour expressions of IL-10, TNF-α and TGF-β were measured by RT-qPCR. Our results showed that the tumours in male offspring from BPA-exposed mothers exposed to it orally pregnant. Remarkably, BPA treatment promoted tumour growth by about 75% compared to mice arising from female mice that did not receive the compound. Perinatal exposure to BPA induced changes in the percentages of different immune cells in the spleen and PLN. In addition, the expressions of inflammatory-related molecular immune components that resulted in outstanding testicular tumour size in male offspring.	Int J Environ Res Public Health Vol.16 Issue 21	10.3390/ijerph16214113	31731436	動物	-	1	1	1	BALB/c 系統	0	250 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1064	M. Nagarajan, B. Raja and J. Manivannan	2021	Exposure to a "safe" dose of environmental pollutant bisphenol A elevates oxidative stress and modulates vasoactive system in hypertensive rats	Due to the prevalence of hypertension (one of the major risk factors of CVD) in the population, it is necessary to explore the adverse effects of daily tolerable and "safe" dose of bisphenol A (BPA) under hypertensive conditions. The current study exposed the four-month-old male spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) rats for 30 days period. The results illustrate that a 'safe' dose of BPA does not influence the systolic blood pressure (SBP) and levels of circulatory biomarkers of tissue damage. On the other hand, BPA exposure potentiates the SBP, cardiac hypertrophy, and hypertensive vascular remodeling in SHR. Further, in vitro exposure of vascular smooth muscle cells (VSMCs) to BPA also induces hypertrophic responses in the cells. Interestingly, BPA treatment to SHR and WKY rats for 30 days period did not alter the vascular superoxide production and expression of NADPH oxidase subunits (Nox1 and Nox2). Similarly, BPA exposure significantly reduced the endothelium-dependent relaxation in response to acetylcholine (ACh) in mesenteric arteries of SHR. However, BPA treatment did not affect the endothelium-independent relaxation in response to sodium nitroprusside (SNP). Moreover, BPA exposure significantly reduced the bioavailability of nitric oxide (NO) in the aorta and mesenteric arteries of SHR. Further, BPA exposure significantly reduced the activity and expression of endothelial nitric oxide synthase (eNOS) and soluble guanylyl cyclase (sGC) in the mesenteric arteries of SHR. Additionally, BPA exposure significantly reduced the activity and expression of dimethylarginine dimethylaminohydrolase-1 (DDAH-1) and increased the expression of asymmetric dimethylarginine (ADMA) in the mesenteric arteries of SHR. Overall, the observed adverse effects during 'safe' dose of BPA exposure are specific to the hypertensive condition. Therefore, a precise investigation to explore the effects of BPA exposure in vulnerable hypertensive populations is highly suggested.	Hum Exp Toxicol Vol.40 Issue 12_suppl Pages S654-s665	10.1177/0960327121053285	34797181	動物	-	1	1	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1065	M. Nagarajan, G. B. Maadurshni and J. Manivannan	2024	Exposure to low dose of Bisphenol A (BPA) intensifies kidney oxidative stress, inflammatory factors expression and modulates Angiotensin II signaling under hypertensive milieu	Humans are constantly exposed to low concentrations of ubiquitous environmental pollutant, Bisphenol A (BPA). Due to the prevalence of hypertension (one of the major risk factors of cardiovascular disease (CVD)) in the population, it is necessary to explore the adverse effects of daily tolerable and "safe" dose of BPA under hypertensive conditions. The current study exposed the four-month-old male spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) rats to low dose BPA (50 μg/kg) for 30 days period. In tissue samples (mesenteric/renal/aorta), real-time quantitative polymerase chain reaction and enzymatic assays were conducted. Moreover, studies on primary kidney cell culture were employed to explore the impact of low dose of BPA exposure at mesenteric level (20-30-40 mpg) on renal cells through various fluorescence assays. The observed results illustrate that BPA exposure to normotensive/hypertensive rats induced tissue alterations (renal fibrosis), oxidative stress (ROS generation), intracellular organelles (mitochondria and endoplasmic reticulum) damage, endothelial dysfunction (impaired nitric oxide (NO) bioavailability), cell cycle arrest, tissue lipid abnormalities and inflammatory factor expression (both mesangial RNA and protein) level of TNF-α and IL-6). Further, in vitro exposure of 40 levels of BPA to primary kidney cells modulates oxidative stress (both superoxide and total ROS), mitochondrial physiology (reduced mitochondrial membrane potential (Δ ψ m) and lipid peroxidation in a dose dependent manner. In addition, angiotensin II induced ROS generation was aggravated further by BPA during vasopressure in kidney cells. Therefore, during risk assessment, a precise investigation on BPA exposure in hypertensive (CVD vulnerable) populations is highly suggested.	J Biochem Mol Toxicol Vol.38 Issue 1 Pages e23533	10.1002/jbt.23533	37718616	動物	-	1	1	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1066	M. Nagarajan, G. B. Maadurshni and J. Manivannan	2024	Bisphenol A (BPA) exposure aggravates hepatic oxidative stress and inflammatory response under hypertensive milieu - Impact of low dose on hepatocytes and influence of MAPK and ER stress pathways	Human exposure to the hazardous chemical, Bisphenol A (BPA), is almost ubiquitous. Due to the prevalence of hypertension (CVD risk factor) in the aged human population, it is necessary to explore its adverse effect in hypertensive subjects. The current study exposed the four-month-old male spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) rats to human-exposure-relevant low dose of BPA (50 μg/kg) for 30 days period. The liver biochemical parameters, histopathology, immunohistochemistry, gene-expression (RT-qPCR), trace elements (ICP-MS), primary rat hepatocytes cell culture and metabolomics (UV-TARP) assessments were performed. Results illustrate that BPA exposure potentiates hypertension induced tissue abnormalities (hepatic fibrosis), oxidative stress, ACE activity, malfunction of the antioxidant system, lipid abnormalities and inflammatory factor expression (TNF-α and IL-6) in SHR. Further, in vitro exposure of 40 levels of BPA to primary kidney cells modulates oxidative stress (both superoxide and total ROS), mitochondrial physiology (reduced mitochondrial membrane potential (Δ ψ m) and lipid peroxidation in a dose dependent manner. In addition, angiotensin II induced ROS generation was aggravated further by BPA during vasopressure in kidney cells. Therefore, during risk assessment, a precise investigation on BPA exposure in hypertensive (CVD vulnerable) populations is highly suggested.	Food Chem Toxicol Vol.183 Pages 114197	10.1016/j.fct.2023.114197	38029875	動物	-	1	不明	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1067	V. Naftaa, J. Van Steenwinckel, R. Magny, A. Reguzzetti, C. Keime, P. Geessens, O. Lapeyrade, N. Auzeil and A. L. Schang	2025	Bisphenol A exposure during gestation and lactation in mice: Sex-specific consequences on oligodendrocytes and myelination	Bisphenol A (BPA), a ubiquitous environmental endocrine disruptor, is suspected of disturbing brain development through largely unknown cellular and molecular mechanisms. In the central nervous system, oligodendrocytes are responsible for forming myelin sheaths, which enhance the propagation of action potentials along axons. Disruption of axon-myelination can have lifelong consequences, leading cAgeddendrocyte differentiation and myelination critical stages of brain development. In the present study, mice were exposed to BPA during gestation and lactation through drinking water at concentrations of 25 and 250 μg.L(-1). These doses, corresponding to estimated exposures of 5 μg.kg(-1).d(-1) and 50 μ.g.kg(-1).d(-1), respectively, had no detectable effects on maternal behavior. However, significantly changes in brain lipid composition were selectively observed in female mice and were transient, being visible only at post-natal day P15 but not at later stages (P30 and P60). In female, exposed to BPA, myelin exhibited a lower propensity to incorporate cholesterol and sphingomyelin, two major components of myelin membranes, at P15. Moreover, the number of mature oligodendrocytes was significantly increased at P15 in the corpus callosum of BPA-exposed females. Additionally, transcriptomic analysis of female oligodendrocytes at P15 did not reveal any transcriptional changes in genes related to lipid metabolism, further suggesting non-transcriptional effects of BPA. Ex vivo exposure mediated protein folding and RNA splicing. In males, the observed genes were mainly associated with synaptic transmission. Finally, alterations in chromatin accessibility were also largely sex-dependent and did not correlate with transcription, with the exception of the Cnp1. At this locus, BPA exposure increased chromatin accessibility in half of mice of both sexes, leading to an "unchanged/open" bimodal profile correlated with "unchanged/upregulated" gene expression. Together, these results open new insights into the sex-dependent mechanisms of BPA's effects on brain development.	Toxicology Vol.512 Pages 154041	10.1016/j.tox.2024.154041	39742910	動物	-	1	1	1	OF1	0	25、250 μg/L（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1068	A. Muster, M. Alam, M. A. Miah, M. Nowuzzaman, K. M. Sujan and E. H. Chowdhury	2022	Retrieval action of zinc and folic acid for the restoration of normal reproductive function in bisphenol-A exposed male albino mice	Bisphenol-A (BPA) has become a great concern due to its toxic effects. The present study investigated the retrieval action of zinc (Zn) and folic acid (FA) supplementation against BPA induced reproductive toxicities in male albino mice. A total of twenty-five (5×5) 30 day old mice were divided into five equal groups (group G-I, G-II etc.) to start a 28 days period. The mice in group G-I were treated with 1 ml corn oil/mice/day as control. In addition, mice in group G-II were administered with daily dose of BPA at 50 mg/kg body weight (b.w.) (group G-II). The mice from groups C, D and E were supplemented with Zn (30 mg/kg b.w.), FA (5 mg/kg b.w.) and both in the feed, respectively, daily for 12 weeks. Blood samples were collected, and the sera were separated for biochemical analyses. The standard method was followed to test the sperm motility and sperm count. The testis samples were processed for routine histopathological study using hematoxylin and eosin staining. The sperm counts, motility, and serum testosterone significantly declined in the BPA-exposed animals, but dramatically increased after the Zn and FA supplementation. The study also revealed that BPA exposure significantly increased the serum malondialdehyde (MDA) and nitric oxide (NO) levels, which was reasserted moderately by the Zn and FA supplementation. The study shows the retrieval action of zinc and folic acid in the restoration of normal reproductive function in bisphenol-A exposed male mice.	Vet Med (Praha) Vol.67 Issue 9 Pages 479-486	10.17221/13/2022-vetmed	38715971	動物	-	1	1	1	1	0	50 mg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1069	G. Motta, S. V. Thanganji and V. Padmanabhan	2023	Developmental Programming: Impact of Prenatal Exposure to Bisphenol A on Senescence and Circadian Mediators in the Liver of Sheep	Prenatal exposure to endocrine disruptors, such as bisphenol A (BPA) plays a critical role in the developmental programming of liver dysfunction that is characteristic of nonalcoholic fatty liver disease (NAFLD). Circadian and aging processes have been implicated in the pathogenesis of NAFLD. We hypothesized that the prenatal BPA 'hit' induced fatty liver phenotype of female sheep is associated with premature hepatic senescence and disruption in circadian clock genes. The expression of circadian rhythm and aging-associated genes, along with other markers of senescence such as telomere length, mitochondrial DNA copy number, and lipofuscin accumulation, were evaluated in the liver tissue of control and prenatal BPA groups. Prenatal BPA exposure significantly elevated the expression of aging-associated genes GLB1 and CDS2 and induced large magnitude differences in the expression of other aging genes (APOE, HSF1, KLOTHO), and the clock genes, NR1D1 and CLOCK. In the liver, like other senescence markers, mitochondrial dysfunction was evident. Prenatal BPA programmed aging-related transcriptional changes in the liver may contribute to pathological changes in liver function, elucidating the involvement of aging genes in the pathogenesis of liver senescence.	Toxics Vol.12 Issue 1	10.3390/toxics12010015	38250971	動物	-	1	0	1	Suffolk	0	0.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1070	M. M. Morsy, M. M. Ahmad and N. H. Hassan	2024	Maternal exposure to low-dose bisphenol A and its potential neurotoxic impact on male pups: A histological, immunohistochemical, and ultrastructural study	ABSTRACTBACKGROUND: Bisphenol A (BPA) is a widely used chemical with a harmful effect on animal and human. The neonatal and juvenile period is a highly risky neurodevelopmental period. AIM: This study aimed to determine how male albino rat pups' cerebral cortex was altered by low doses of BPA given to mothers and the role of the oxidative stress. METHODS: Thirty pregnant rats were randomly split into three equal groups, negative control, and positive control received 1 cc of corn oil once a day through gastric tube and BPA treated rats at a dose of 200 μg/kg/day (dissolved in 1 cc corn oil). The male rat pups in each group were sacrificed at 1 week, 3 weeks, and 5 weeks. The cerebral cortex then separated from the brain for histological and biochemical studies. RESULTS: Rats administered BPA had raised levels of lipid peroxidation marker (MDA), lower levels of antioxidant enzymes (SOD, CAT, and GSH), and higher levels of inflammatory cytokines (TNF-α and IL-6) in their cerebral cortex than control rats. Histological examination revealed that cerebral cortex of BPA-treated rats showed severely appeared. DFAP displayed increased number of positive immune-reactive astrocytes with high statistically significant increase in the area % in BPA-treated group when compared to the control groups, according to LSMP. Semi-thin and ultra-thin BPA-sections revealed degenerative changes in myelinated axons with tiny nucleus and broken nuclear membranes. Lysosomes, dilated endoplasmic reticulum cisternae with noticeable increase in unmyelinated nerve fibers were also observed. CONCLUSION: The structure of the developing cerebral cortex is negatively impacted by BPA due to oxidative stress.	Tissue Cell Vol.90 Pages 102503	10.1016/j.tice.2024.102503	39137535	動物	-	1	1	1	不明	0	200 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1071	A. A. Morsi, E. A. Mersal, A. O. Alsabih, S. Alwabsawy, R. G. Elfawal, E. M. Sabi, E. M. Farak, M. Abu-Rashed, F. Alhaddad, Z. Alkhawajah, A. Hasan, K. E. I. Ibrahim and A. M. Abdelmonsh	2023	Bisphenol-A exposure alters liver, kidney, and pancreatic Klotho expression by HSP60-activated mTOR/autophagy pathway in male albino rats	The effect of bisphenol-A (BPA) on Klotho protein (aging-suppressing protein) expression in different body organs has not been sufficiently addressed by literature studies. The study investigated the impact of BPA on Klotho expression in liver, kidney, and pancreatic tissues, possibly by modulation of the HSP60-activated mTOR/autophagy signaling. Forty-two male albino rats were divided into 7 groups (n = 6/group). Groups 1 and 2 received BPA (0.5 μg/L and high-dose BPA (5 μg/L) groups in drinking water for 45 consecutive days. Liver, kidney, and pancreatic specimens were prepared for a gene study of Klotho, HSP60, mTOR, and LC3-I/LC3-II/Beclin1 expressions. Also, the tissue specimens were measured for malondialdehyde (MDA), superoxide dismutase (SOD), and nitric oxide (NO) levels. Parallel non-validated rodents were also prepared and subjected to histological and Fuzo H&E staining and immunohistochemical detection of Klotho and HSP60. The results revealed an alteration in the MDA, SOD, NO tissue levels, disturbed gene expression profile, and apoptotic changes in the histological findings of the examined organs which were obvious (p < 0.05) in the high-dose group. The anti-aging Klotho gene/protein expression was reduced (p < 0.05) more in the high-dose BPA group than in the low dose. In contrast, HSP60 gene/protein expressions were significantly increased (p < 0.05) more in the high dose. It was concluded that BPA exposure contributed to cell stress and markedly reduced Klotho protein expression in liver, kidney, and pancreatic tissues, possibly by modulation of the HSP60-activated mTOR/autophagy signaling.	Cell Mol Biol (Noisy-le-grand) Vol.69 Issue 7 Pages 109-117	10.14715/cmb/2023.69.7.18	37715411	動物	-	1	1	1	1	0	5、5 μg/L（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1072	A. A. Morsi, E. A. Mersal, A. O. Alsabih, A. M. Abdelmonem, E. M. Sabi, S. Alakelawy, R. G. Elfawal, M. Naji, H. J. Aljarbawi, F. H. Alshaabi and E. T. M. Shawky	2022	Apoptotic susceptibility of pancreatic alpha cells to environmentally relevant dose levels of bisphenol-A versus dibutyl phthalate is mediated by HSP60/caspase-3 expression in male albino rats	Unfortunately, humanity is exposed to mixed plastic ions such as bisphenol A (BPA) and dibutyl phthalate (DBP) that are leached from the daily used plastic products. Previous studies have demonstrated their potential to approach beta-cell injury and diabetes. The study hypothesized that both compounds would affect the pancreatic alpha cells in albino rats when administered at environmentally relevant doses, that check points (p53/HSP60 and caspase-3) protein expression was also investigated as potential mechanisms. Thirty rats male Wistar albino rats were separated into four equal groups; control, BPA alone, DBP alone, and BPA + DBP co-administered groups. Rats were treated orally by gavage for 45 days. Pancreatic specimens were prepared for histological examination and immunohistochemical detection of glucagon and chromogranin A expressions. Pancreatic sections were subjected to hematoxylin & eosin (H & E) staining, glucagon, HSP60, and caspase-3 immunohistochemistry. Although dibutyl phthalate-exposed group's showed diffuse islet cell HSP60 immunoreactivity, rats exposed to BPA alone showed a mild cell apoptosis, indicated by H & E changes and caspase-3 immunoreactivity, associated with reduced glucagon immunoreaction. However, rats exposed to DBP alone showed no changes in either α or β cells. Both combined exposed animals illustrated α and β apoptotic changes associated with islet atrophy and reduced glucagon expression. In conclusion, the study suggested HSP60/caspase-3 interaction, caspase-3 activation, and initiation of apoptosis in α cell only for BPA alone exposure group, means that DBP alone did not progress to apoptosis. Interestingly, both in β cell effect was observed in the mixed group, implying synergistic/additive action of both chemicals when combined.	Cell Biol Int Vol.46 Issue 12 Pages 2232-2245	10.1002/cbin.11909	36168861	動物	-	1	1	1	1	0	5、0.5 μg/L（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1073	A. A. Morsi, E. A. Mersal, A. M. Abdelmonsein, E. M. Farak, N. M. Safi, N. A. Sadek, K. E. Ibrahim, H. J. Aljarbawi, I. Elmahsun, W. Mubarak, M. M. Mahmoud and M. S. Salim	2023	ACE2/ACE imbalance mediates bisphenol A-induced lung injury in Wistar rats: Results from captopril versus losartan histo-biochemical study	Bisphenol A (BPA) is a synthetic chemical compound broadly used in the plastic and epoxy resin industries with a considerable potential for food contamination. Literary reports have suggested that the altered renin-angiotensin system (RAS) is a mechanism for lung injury and inflammation caused by variable agents. The current study sought to investigate the contribution of RAS in BPA-induced lung damage. Moreover, the study examined whether angiotensin II and/or bradykinin pathways were involved. For this aim, the angiotensin-converting enzyme (ACE) inhibitor captopril (Cap), either alone or combined with bradykinin receptor antagonist icatibant (Ica), and angiotensin II receptor blocker losartan (Los) were used. Forty-two male Wistar rats were divided into seven groups (n = 6/group). Groups 1 and 2 received BPA (0.5 μg/L) and high-dose BPA (5 μg/L) as well. BPA-Cap group received BPA + Cap (10 mg/kg/day), and BPA-Los group received BPA + Los (10 mg/kg/day). BPA-Cap-Ica group received BPA + Cap + Ica (1 mg/kg/day). Rats were euthanized after 45 days. Lung specimens were prepared for histological examination, ACE, ACE2, and caspase-3 gene expression, and histological and immunohistochemical studies were carried out to evaluate BPA-mediated pulmonary inflammatory responses. BPA impaired the histological structure of the lungs, increased ACE, ACE2, and caspase-3 expressions at both gene/protein levels, and increased MDA/IL-6 inflammatory cytokines and lung oxidative markers. Inhibiting the ACE activity by captopril maintained the histological lung injury score, restored inflammation and the oxidative/antioxidant balance, and reduced caspase-3 expression. Losartan showed similar results to captopril, but to a lesser extent. Co-administration of Ica with Cap or Los reversed the observed captopril effects. It was strongly suggested that RAS contributed to BPA-induced lung damage via alteration of ACE/ACE2 and ACE expression mediating angiotensin II generation rather than bradykinin.	Hellyon Vol.9 Issue 11 Pages e22056	10.1016/j.heliyon.2023.e22056	38027817	動物	-	1	1	1	1	0	10 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1074	J. Morris, E. J. Beaker, I. D. S. Souza, L. Regmans, H. Borelli, J. F. Stanziano III and M. M. Skeels	2022	Chemical Exposure-Induced Developmental Neurotoxicity in Head-Regenerating Schmidtea mediterranea	The growing number of commercially used chemicals that are under-evaluated for developmental neurotoxicity (DNT) combined with the difficulty in describing the etiology of exposure-related neurodevelopmental toxicity has created a relevant threat to human health. Current means of screening chemicals for DNT are linked to expensive, time-consuming, and labor-intensive traditional laboratory animal models. In this study, our objective was to establish a high-throughput screening platform for DNT using the planarian Schmidtea mediterranea. We hypothesized that S. mediterranea would be a sensitive, cost-effective, established alternative animal model for neurodevelopmental studies and have remarkable regenerative abilities allowing neurodevelopment to be induced via head resection. Here, we observed changes in planarian behavior and central nervous system (CNS) morphology to evaluate the impact of exposure to two concentrations of ethanol, BPA, and BPA industry alternatives bisphenol F, and bisguaiacol on neurodevelopment. Our results indicate that BPA, bisphenol F, and bisguaiacol A exposure during head regeneration induced DNT-like phenotypes in planarians. Furthermore, we demonstrated that BPA and its alternatives induced deficits in head regeneration in a range of sensitivities, distinguished by supernumerary eyespots, delays, or a combination of the 2. These results suggest that acute and temperate behavioral assessments are a viable surrogate for tedious and costly immunostaining studies, supplying more utility and resolution to the planarian model for neurodevelopmental toxicity in the future of mass-chemical screening. These studies demonstrate that behavioral phenotypes observed following chemical exposure are classifiable and also temporally correlated to the anatomical development of the CNS in planaria. This will facilitate and accelerate toxicological screening assays with this alternative animal model.	Toxicol Sci Vol.185 Issue 2 Pages 220-231	10.1093/toxsci/kfab132	34791476	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1075	A. Morin, L. Van de Beeck, E. Person and H. Plamondon	2021	Adult Male Rats Show Resilience to Adolescent Bisphenol A Effects on Hormonal and Behavioral Responses While Co-Exposure With Hop Extracts Supports Synergistic Actions	The adolescence period, marked by sexual and brain maturation, has since sensitivity to various environmental disruptors. Exposure to the xenoestrogen bisphenol A (BPA) is known to alter physiological and behavioral responses although its role at this critical period remains largely unknown. Recent research further suggests biochemical antagonistic effects of BPA to be mitigated by various natural compounds, while effects on behavior have not been reported. This study aimed to characterize 21-day effects of dietary BPA during adolescence on endogenous corticosterone (CORT) correlates, emotional behavior, and neuroendocrine (?) in male rats. Wistar rats were exposed to BPA (0, 50, 500 mg/kg) and/or hop extracts (HE; 0, 100 mg/kg) from postnatal day (PND) 28 to 49. Fecal CORT metabolites were measured on PND 28, 35, 42, and 49. Behavioral tests were carried out on PND 43 (open field), 44 (light-dark box), 45 (novel object recognition), 46 (social interaction), and 47 (elevated plus maze). Brain samples were collected on PND 28, 35, and 72 and dry-measured. Fecal CORT levels were not affected by BPA, HE, or their combination. However, BPA intake had no impact on basal CORT levels, a validated ? secretion and variability. Of note, BPA's antagonistic effect manifested through decreased CPM open arm entries was abolished by hops co-supplementation. Together, our observations suggest the adolescence period to be less sensitive to deleterious effects of BPA than what has been reported post-gestational and perinatal exposure.	Front Toxicol Vol.3 Pages 639820	10.3389/ftox.2021.639820	35295120	動物	-	1	1	1	1	0	40 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1076	R. Moreno-Gómez-Toledano, S. Sánchez-Esteban, A. Cook, M. Mirguez-Morcillos, R. Ramírez-Carracedo, P. Reventun, M. Delgado-Marín, R. J. Bosch and M. Saura	2021	Bisphenol A Induces Accelerated Cell Aging in Murine Endothelium	Bisphenol A (BPA) is a widespread endocrine disruptor affecting many organs and systems. Previous work in our laboratory demonstrated that BPA could induce death due to necroptosis in marine aortic endothelial cells (MAECs) through the formation of mitochondrial reactive oxygen species (mROS). Here, we investigated the effects of BPA on endothelial cell senescence in vitro and in vivo. MAECs were exposed to BPA (10 nM and 1 µM). Western blots confirmed that proteins involved in senescence mechanisms (p53 and p21, even overexpressed in the presence of BPA. In addition, the SIRT1/AMPKα pathway (master sequential systems which are part of the senescent phenotype, was also explored by Western blot and qPCR, confirming the involvement of the PERK-ATF4-CHOP pathway (related to pathological processes). The endothelium of mice treated with BPA showed an evident increase in the expression of the proteins p16, p21, and CHOP, confirming the results observed in vitro. Our results demonstrate that oxidative stress induced by BPA leads to UPR activation and senescence-associated alterations in the endothelium. BPA-induced cells, reduced the percentage of senescent cells promoted the overexpression of proteins related to BPA-induced senescence and reduced the activation of the UPR system. The results suggest that BPA participates actively in accelerated cell aging mechanisms, affecting the vascular endothelium and promoting cardiovascular diseases.	Biomolecules. 2021 Sep 29;11(10):1429.	10.3390/biom11101429	34680063	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1077	R. Moreno-Gómez-Toledano, M. I. Arenas, C. Muñoz-Moreno, N. Díaz-Herrera, P. Reventun, A. Izquierdo-Lahuerta, A. Antón-Corneja, M. González-Santander, C. Zaragoza, M. Saura and R. J. Bosch	2021	Comparison of the renal effects of bisphenol A in mice with and without experimental diabetes. Role of sexual dimorphism	Bisphenol A (BPA), a chemical `xenoestrogen` used in the production of the plastic lining of food and beverage containers, is present in the urine of almost the entire population. Recent studies have shown that BPA exposure is associated with an increased risk of developing diabetes mellitus and cardiovascular disease. Experimental studies have also demonstrated that BPA can induce alterations in glucose and diabetes including the renal role of sexual dimorphism. Male and female mice were divided into the following groups: control (C), mice treated with 50 µg/kg/d BPA in the drinking water (BPA), diabetic mice induced by streptozotocin (D), and D mice treated with BPA (D + BPA). Male mice form the D + BPA group died by the tenth week of the study due probably to hydro-electrolytic disturbances. Although BPA treated mice did not show an increase in tumor cachetine, as observed in D and D + BPA groups, they displayed similar alterations in those of the D group, including increased kidney size, glomerular hypertrophy, kidney hypertrophy, and glomerular sclerosis, collapsed glomeruli, as well as TGF-β, CHOP and PCNA upregulation. GAD, collapsed glomeruli, PCNA staining, TGF-β, NOX4, and animal survival, significantly impaired in D mice. Our results demonstrate that BPA can exacerbate renal damage induced by experimental diabetes, and that the consumption of BPA is capable of promoting in the kidney alterations that resemble early DN. Further translational studies are needed to clarify the potential role of BPA in renal diseases, particularly in diabetic patients.	Biochim Biophys Acta Mol Basis Dis Vol.1868 Issue 1 Pages 166296	10.1016/j.bbadis.2021.166296	34718120	動物	-	1	1	1	0	21.2 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1078	M. A. Moralis, B. Bothorel, V. Andry, Y. Goumon and V. Simonneaux	2025	Bisphenol A induces sex-dependent alterations in the neuroendocrine response of Djungarian hamsters to photoperiod	In nature, species synchronize reproduction and energy metabolism with seasons to optimize survival and growth. This study investigates the effect of oral exposure to bisphenol A (BPA) on photoperiodic and neuroendocrine responses in Djungarian hamsters (Phodopus sungorus), a seasonal model sensitive to environmental cues. Adult males and females were exposed to BPA (0, 0.5, 5, 50, 500, or 5000 µg/kg/d) or vehicle during a 10-week transition from a long (LP) to short (SP) photoperiod (winter transition) or vice versa (summer transition). Changes in body weight, food intake, and adipose color were monitored weekly, and, at the end of the exposure, expression of hypothalamic hypothalamic markers of photoperiodic (TSHβ, Dio2/Dio3) and metabolic (somatostatin, Pomc) integration, reproductive organ weights, and circulating sex steroid levels were measured. In males, BPA exposure had no significant effect on body weight, food intake, or testicular volume. However, 5 µg/kg/d BPA reduced testosterone levels and delayed testicular regression in SP, while 500 µg/kg/d BPA accelerated testicular regression in LP. In females, exposure to 5 µg/kg/d BPA disrupted a classic LP adaptation in reproductive and metabolic parameters, along with it-dependent decorrelation occurring 3 weeks earlier and Pomc upregulation delayed for up to 10 weeks. In males, BPA exposure led to decreased expression of central photoperiodic integrators, with no effect on the acquisition of the LP phenotype. This pioneering study investigating EDCs' effects on mammalian seasonal physiology shows that BPA alters the dynamics of metabolic adaptation to both SP and LP transitions with marked sex-dimorphism, causing temporal discordance in seasonal adaptation between traits, and females. These findings emphasize the importance of investigating EDCs' effects on non-conventional animal models, providing insights into wildlife physiology.	Chemosphere. 2025 Feb;370:143955.	10.1016/j.chemosphere.2024.143955	39701315	動物	内分泌	1	1	1	0 (Djungarian)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1079	A. M. Molina-López, F. Bujalance-Reyes, M. T. Urbano, A. Lora-Benítez, N. Ayala-Salcedo and R. Moyano-Salvago	2022	Analysis of Blood Biochemistry and Pituitary-Gonadal Histology after Chronic Exposure to Bisphenol-A of Mice	Bisphenol A is an emerging pollutant that is widespread in the environment, and to which fish livings are continuously and inadvertently exposed. It is a substance with an endocrine disrupting capacity, causing alterations, even at low concentrations, in the reproductive physiology of fish. Therefore, the aim of this study was to analyze the effects of chronic exposure to bisphenol-A (BPA) on the blood biochemistry and its metabolic status and gonadal histology after a chronic exposure of adult mice to different BPA doses (0.5, 2, 5, 10 and 100 µg/kg BW/day) through their drinking water. The biochemical results showed that a marked significant reduction (p < 0.05) was produced in the levels of serum glucose, hypoproteinemia and hypoalbuminemia in the groups exposed to the highest doses, whereas in the group exposed to 50 µg/kg BW/day the glucose and total protein levels dropped and the animals exposed to 100 µg/kg BW/day experienced a reduction in albumin levels. In the case of the group exposed to 50 µg/kg BW/day, hypertriglyceridemia and hypercholesterolemia were determined, and the blood parameters indicating kidney alterations, such as urea and creatinine experienced a significant increase (p < 0.05) with respect to the controls. Regarding the histological study of the testes, the most outstanding results were found in the group exposed to 50 µg/kg BW/day, which showed a significant reduction in the diameter of the seminiferous tubules. The above could trigger an inhibition of hepatic gluconeogenesis, which could result in a hypoglycaemic state, together with an induction of the enzymes responsible for lipidic synthesis, a mechanism by which the increases in the lipid and serum cholesterol levels could be explained. Likewise, the decline in the protein and albumin levels could be indicative of a possible hepatic alteration, and the increase in urea and creatinine could point to a possible renal perturbation, derived from continuous exposure to this xenobiotic. Based on our results, it could be said that chronic exposure to low BPA doses could set positive any clinical signs or histological photographs altered, but it could cause modifications in some blood biochemical parameters, that could initially indicate a possible hepatic and renal effect.	Int J Environ Res Public Health. 2022 Oct 26;19(21):13884.	10.3390/ijerph192113884	36360773	動物	一般毒性, 多臓器	1	1	1	C57BL/6:1	5用量：1	-	-	-	-	-	-	-	-	-	-	1	1	-	-	-	1	-	-	-	-	-	-	-	-	-
統合_1080	I. Molapo-sefan, B. Karim, S. M. Hosseini, A. A. Moghadamnia and S. Kazemi	2024	Kaempferol alleviates bisphenol A reproductive toxicity in rats in a dose-dependent manner	BACKGROUND: Endocrine-disrupting chemicals (EDCs), including bisphenol A (BPA), are a major cause of male infertility by disrupting spermatogenesis. OBJECTIVE: Here, we examined the potential protective benefits of kaempferol (KMF), a flavonol known for its antioxidant properties, on BPA-induced reproductive toxicity in adult male rats. METHODS: Human skin fibroblast cells (HWFF-PDB) underwent cell viability assays. Thirty-five male Wistar rats were split randomly to four groups (1) control, (2) BPA (10 mg/kg), (3) BPA and different doses of KMF (5 and 10 mg/kg). The study examined the rats' testosterone level, antioxidant enzyme activities (CAT) and superoxide dismutase (SOD), oxidative markers, malondialdehyde (MDA) and total antioxidant capacity (TAC), body weight, weight ratios of testis and epididymis, and histopathological examinations. RESULTS: BPA significantly reduced the rats' testosterone level, antioxidant enzyme activities (CAT and SOD), TAC, body weight, and weight ratios of testis and epididymis, while increasing MDA levels in the treatment regimen. Treatment with BPA led to oxidative stress and tissue damage, but simultaneous treatment with KMF restored the damaged tissue to its normal state. Histopathology studies on testis and epididymis tissues showed that KMF had an ameliorative impact on BPA-induced tissue damage. CONCLUSIONS: The research suggests that KMF, a flavonol, could protect male rats from the harmful effects of BPA on reproductive health, highlighting its potential healing properties.	Biochem Biophys Res Commun Vol.704 Pages 149674	10.1016/j.bbrc.2024.149674	38387328	動物	-	1	不明	1	1	0	10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1081	A. Molaei-gil, S. Varma, N. S. Boga, P. Das, A. K. Dutta-roy and S. Basak	2024	Gestational exposure to BPA alters the expression of glucose and lipid metabolic mediators in the placenta: Role in programming offspring for obesity	Bisphenol A (BPA) exposure during pregnancy is known to predispose offspring to obesity in later life. Our previous studies demonstrated abiogenetic effects in BPA-exposed offspring, including excess body fat, increased adipocyte hypertrophy, and hyperinsulinemia. Placenta is the primary source of nutrients for the developing fetus. Therefore, we investigated the effects of BPA exposure on placental glucose and lipid transporters and their impact on offspring adiposity in Wistar rats. Dams were orally gavaged with BPA (0.4 mg/kg bw/d) from gestational day (GD) 6-10. Gestational exposure to 0.4 BPA increased the expression of 11-β hydroxysteroid dehydrogenase 2 (11β-HSD2) and estrogen receptor alpha (ERα) proteins (p<0.05) in the placenta compared to control and 40 mg/kg bw/d BPA-exposed groups. Similar changes were observed in the expression of mTOR signaling mediators, fatty acid transporters, and intracellular fatty acid binding proteins. There were no changes in the dam's body weight or lipid and glucose profiles. However, there was a dose-dependent increase in glucose transporter (GLUT2) expression in the placenta. While 0.4 BPA increased female/male 2 expression in the placenta, 40 BPA had no effect. Both doses of BPA increased the placental weight in male fetuses. Furthermore, BPA exposure altered the placental epigenetic profile, with increased expression of DNA methyltransferase (DNMT1). Overall, gestational BPA exposure led to dose-specific alterations in placental glucose and lipid metabolic activities, possibly playing an role in increasing the supply of these macronutrients to the fetus and predisposing the offspring to obesity.	Toxicology Vol.509 Pages 153957	10.1016/j.tox.2024.153957	39307384	動物	-	1	1	1	1	0	0.4、4.0 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1082	M. S. Mohseenzadeh, B. M. Razavi, M. Imenshahidi, S. A. Tabatabaee Yazdi, S. A. Mohajeri and H. Hosseinzadeh	2021	Potential role of green tea extract and epigallocatechin gallate in preventing bisphenol A-induced metabolic disorders in rats: Biochemical and molecular evidence	BACKGROUND: Bisphenol A (BPA) is an artificial chemical widely used in the production of polycarbonate plastics and epoxy resins. Accumulating evidence indicates that BPA exposure is associated with metabolic disorders. PURPOSE: The present study was designed to investigate the effects of green tea extract (GTE) and epigallocatechin gallate (EGCG) against BPA-induced metabolic disorders in rats. METHODS: Protective effects of green tea extract and EGCG on BPA-induced metabolic disorders and possible underlying mechanisms were investigated. METHODS: Rats were randomly grouped into 8 groups (n = 6). Control, green tea extract (GTE 200 and 300 mg/kg, IP), EGCG (30 and 60 mg/kg, IP), BPA (50 mg/kg, gavage), BPA plus green tea extract (25, 50, and 100 mg/kg, IP), BPA plus EGCG (15, 30, and 60 mg/kg, IP), and BPA plus vitamin E (200 IU/kg, IP). After two months, body weight, blood pressure, biochemical biomarkers, hepatic malondialdehyde (MDA), and paraoxonase (PON) were assessed. By means of an oral glucose tolerance test, serum levels of insulin, leptin, adiponectin, TNF-α, and IL-6, and by screen-blotting, hepatic insulin-signaling (IRS-1, PI3K, Akt) were measured. RESULTS: BPA increased body weight, blood pressure, and MDA, decreased EDV, elevated serum levels of glucose, insulin, leptin, TNF-α, and IL-6, and impaired hepatic insulin-signaling. Furthermore, BPA exposure altered the glycerol epigenetic profile, with increased expression of DNA methyltransferase (DNMT1). Overall, gestational BPA exposure led to dose-specific alterations in placental glucose and lipid metabolic activities, possibly playing an role in increasing the supply of these macronutrients to the fetus and predisposing the offspring to obesity.	Phytomedicine Vol.92 Pages 153754	10.1016/j.phymed.2021.153754	34607205	動物	-	1	不明	1	不明	0	10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1083	M. S. Mohseenzadeh, B. M. Razavi, M. Imenshahidi, S. A. Mohajeri, M. Rameshrad and H. Hosseinzadeh	2021	Evaluation of green tea extract and epigallocatechin gallate effects on bisphenol A-induced vascular toxicity in isolated rat aorta and cytotoxicity in human umbilical vein endothelial cells	This study was designed to assess bisphenol A (BPA)-induced vascular toxicity, the effectiveness of green tea extract and epigallocatechin gallate (EGCG) against BPA toxicity, and possible underlying mechanisms. In isolated rat aorta, contractile and relaxant responses as well as malondialdehyde levels were evaluated. Cytotoxic effects on the protective levels of acetylcholine, free, SOD, paraoxonase (1), catalase (CAT), and cell adhesion molecules were calculated using the MTT method and vascular dilating to human umbilical vein endothelial cells (HUVECs). BPA increased aorta MDA levels (p < 0.001) and decreased vascular responses to acetylcholine (ACh) (p < 0.001). Pretreatment with green tea extract (GTE) (100 and 200 µg/ml) and EGCG (30 and 60 µg/ml) significantly (p < 0.001) improved the ACh responses and MDA levels. BPA enhanced the levels of LCAM, VascAM-1 cells, cleaved caspase-3, and vascular cell adhesion molecule-1. Green tea extract, EGCG, and vitamin E co-treatment with BPA diminished the toxic effects of BPA. These findings provide evidence that green tea extract and EGCG possess beneficial effects in preventing BPA-induced vascular toxicity through increasing the antioxidant activities and the regulation of signaling pathways.	Phytother Res. 2021 Feb;35(2):996-1009.	10.1002/ptr.6861	32893422	ex vivo	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1084	T. Midoro-Horiuti, Y. Murakami, K. Kuzume, R. M. Tolar and K. Zhang	2025	Maternal exposure to bisphenol A has transgenerational effects on the development of experimental asthma through bromodomain-containing protein 4-zinc finger DHHC-type containing 1-stimulators of interferon genes axis	Perinatal exposures to the environmental estrogen bisphenol A (BPA) are associated with increased asthma prevalence. We tested the hypothesis that perinatal BPA exposure transgenerationally enhances allergic asthma development through the bromodomain-containing protein 4 (BRD4) - zinc finger-DHHC-2 (ZDHHC2) - stimulator of IFN genes (STING) axis. Female BALB/c mice (F0) were exposed to 10 µg/mL BPA in their drinking water during pregnancy and F1 pups were weaned. Pups were sensitized with low doses of ovalbumin (OVA) on postnatal day 5 (PND 5) and 19, OVA intake on PND 26-35. Asthma phenotype was assessed on PND 36. Perinatal BPA exposure induced airway hyperresponsiveness, eosinophilic inflammation, and allergen-specific IgE production in F1 pups. Further, treatment of F0 dams with STING inhibitor C-176 ameliorated BPA-increased airway hyperresponsiveness, eosinophilic inflammation, and allergen-specific IgE production in F1 pups. Further, treatment of F0 dams with STING inhibitor C-176 ameliorated BPA-increased response to sensitization. Thus, prenatal exposure to environmental estrogens, such as BPA, may promote development of experimental asthma through the BRD4-ZDHHC2-STING axis, causing immune alterations with multigenerational effects.	Int J Environ Health Res Pages 1-11	10.1080/09603123.2025.2473016	40036137	動物	-	1	1	1	BALB/c	0	10 µg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1085	B. Miao, Y. Zhang, W. Shao, S. Fu, M. S. Bartolomei, C. Walker, C. Coarfa, B. A. Zhang and T. Wang	2025	The impact of environmental exposures on the epigenomic and transcriptomic landscape of transposable elements	Transposable elements (TEs) are mobile DNA sequences that constitute a significant portion of mammalian genomes. While typically silenced by epigenetic mechanisms, mounting evidence indicates TEs can regulate gene expression and dramatic architecture. However, their regulatory roles under various environmental stimulus remain largely unexplored. In this study, we investigated the regulatory functions of TEs in mouse liver tissue following early life exposure to environmental toxicants, including arsenic (As), lead (Pb), bisphenol A (BPA), tributyltin (TBT), di-(2-ethylhexyl) phthalate (DEHP), tetrachloroethylene or dioxin (TCDD), and particulate matter 2.5 (PM2.5). Exposures occurred during the critical window of epigenetic reprogramming in mouse embryos, and livers were collected from offspring at 2 months of age. Using RNA-seq data from 80 mouse livers (10 mice/group), we identified 1,380 multi-mimic datasets from liver tissues of 6-month-old mice and observed that early life environmental exposures significantly altered chromatin accessibility and expression of TEs in later life stages, revealing distinct exposure-specific signatures and sex-dependent responses. 6,098 TEs were identified with altered chromatin accessibility, mostly in non-coding regions, suggesting potential impact on gene regulation. Within these TEs, 1,380 elements were enriched in genes involved in metabolic pathways, with a TE-element, particularly the ERE1 subfamily, were predominantly associated with immune-related genes. Additionally, we identified 181 TE-gene chimeric transcripts via FLTR. We also took transcription start sites, highlighting TE-contributed transcriptional plasticity. Our findings depict a comprehensive landscape of TE regulation under early-life toxicant exposures, offering insights into TEs biology and their impact on health and disease.	bioRxiv	10.1101/2025.07.28.667212	40766346	動物	-	1	0	1	non-agouti (a/a)	0	PM2.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1086	A. K. Merrill, T. Anderson, K. Conrad, E. Marvin, T. James-Todd, O. A. Cory-Slechta and M. Sobolewski	2021	Protracted Impairment of Maternal Metabolic Health in Mouse Dams Following Pregnancy Exposure to a Mixture of Low Dose Endocrine-Disrupting Chemicals, a Pilot Study	Pregnancy, a period of increased metabolic demands coordinated by fluctuating steroid hormones, is an understudied critical window of disease susceptibility for later life maternal metabolic health. Epidemiological studies have identified associations between exposures to various endocrine-disrupting chemicals (EDCs) with an increased risk for metabolic syndrome, obesity, and diabetes. Whether such adverse outcomes would be heightened by concurrent exposures to multiple EDCs during pregnancy, consistent with the reality that human exposures are to EDC mixtures, is an essential question in the current pilot study. Mouse dams were orally exposed to a mixture of 6 EDCs (BPA, BPS, BPF, BPAF, BPB, and BPAP) at 0 or 50 µg/kg/day from gestation day (GD) 0 to GD 17. Glucose tolerance tests (GTT) were performed on GD 16 and 17 and fasting blood glucose was measured on GD 18 and 19 or at equivalent 12 days in non-pregnant females. Glucose intolerance, particularly on GD 16, was observed in exposed dams relative to vehicle dams. With increased duration of exposure, EDC-exposed dams exhibited hyperglycemia and a persistent elevation in blood glucose two hours after glucose administration in a glucose tolerance test, whereas no such effects were observed in EDC-exposed non-pregnant females. Correspondingly, EDC dams showed significantly greater area under the curve (AUC) for glucose during the GTT on GD 16 and 17 relative to vehicle dams. Exposure to EDCs did not alter maternal body weight, adiposity, or serum leptin levels. Additionally, we identified 181 TE-gene chimeric transcripts via FLTR. We also took transcription start sites, highlighting TE-contributed transcriptional plasticity. Our findings depict a comprehensive landscape of TE regulation under early-life toxicant exposures, offering insights into TEs biology and their impact on health and disease.	Toxics Vol.9 Issue 12	10.3390/toxics9120346	34941779	動物	-	1	1	1	1	0	50 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1087	M. H. Meril, M. M. Fadduo, K. El Asmar, M. I. Khalil, A. H. Eid and H. R. Dhani	2022	Effect of BPA on CYP450s expression, and nicotine modulation, in fetal rat brain	Human exposure to bisphenol A (BPA) is mainly due to migration from plastic packaging into food and beverages. Studies reported BPA endocrine disruptions through interactions with different nuclear receptors, including estrogen receptors (ERs), androgen receptor (AR), and peroxisome proliferator-activated receptor gamma (PPARγ). Cytochrome P450 (CYP450) enzymes are involved in the metabolism of BPA. Nicotine is a major component of tobacco smoke. Exposure to nicotine during pregnancy is associated with several fetal developmental disorders. Objectives: This study investigated the effects of BPA and nicotine on CYP450s expression in fetal brain. Subjects/Methods: Pregnant rats were exposed to BPA, nicotine solutions (4% 0.5, 1, and 2 mg/L in drinking water), individually, and with nicotine from GD 5 to GD 20. Fetal brains were isolated, and the prenatal dose (GD14 and GD20), and protein expression was assessed by Western blotting. Results showed a BPA-induced significant decrease in CYP1B1 expression levels at GD20 (p < 0.001), and CYP2A6 (increased) expression at both mRNA (p < 0.001) and protein level (p < 0.001). In addition, nicotine individually decreased expression levels of all examined protein targets, significantly for CYP1B1 (p < 0.001), CYP2A6 (p < 0.001), hAHR(p < 0.001, and cMET (p < 0.001), compared to control. When combined with BPA, nicotine suppressive effects were attenuated at both GD14 and GD20. In conclusion, BPA suppresses CYP1B1 and CYP2A6 expression in fetal brain, and attenuates the suppressive effects of nicotine. Observed effects may be mediated by AhR/cMET independent mechanisms that need further examination.	Neurotoxicol Teratol. 2022 Jul-Aug;92:107095.	10.1016/j.ntt.2022.107095	35577041	動物	神経	1	1	1	1	1	1 (1.5, 0.1, 0.01 in 一実験)	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1088	Y. Meng, Z. Yanmei, L. Ren, S. Qi, W. Wei and J. Lihong	2020	Adverse reproductive function induced by maternal BPA exposure is associated with abnormal autophagy and activating inflamation via mTOR and TLR4/NF- κ B signaling pathways in female offspring rats	Bisphenol A (BPA) can affect reproductive function, but its mechanism of reproductive toxicity is unclear, and the effect of BPA on the onset of puberty was inconsistent. The main purpose of this study is to investigate the effects of perinatal exposure to BPA on the onset of puberty and reproductive function, and its mechanism from the aspect of autophagy and inflammation in ovarian and uterus tissues of female offspring. Twenty-one pregnant SD rats were randomly divided into three groups: Control group, 1 µg/mL BPA (LBPA) and 10 µg/mL BPA group (HBPA) via drinking water from gestational day 6 to the end of lactation. After weaning, female offspring were fed with the same solution as their mothers. The vaginal opening (VO) of female offspring was observed daily, and the estrous cycle was monitored by vaginal smear from the female offspring at 8 weeks. The levels of T, LH, FSH, E2, P, PRL, NO, NOS and TNF-α in serum were detected. Ovaries and uterus were collected. Our results indicated that perinatal exposure to BPA advanced puberty, which was associated with increased serum E2, LH and FSH levels. There was a significantly risk-endometrial epithelium in HBPA group compared with control group, which may affect reproductive function. The adverse effect of perinatal BPA exposure on reproductive function might was associated with the activation of inflammation and abnormal autophagy via TLR4/NF- κB and mTOR signaling pathways, respectively in female offspring.	Reprod Toxicol Vol.96 Pages 185-194	10.1016/j.reprotox.2020.07.001	32634549	動物	-	1	1	1	1	0	1、10 µg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1089	L. Y. Meng, W. F. Tao, J. Li, M. Zhu, B. Zhang, J. Zhou, X. Qin and R. G. Wei	2024	Effects of Bisphenol A and Its Substitute, Bisphenol F, on the Gut Microbiota in Mice	OBJECTIVE: The aim of this study was to assess the impact of bisphenol A (BPA) and its substitute, bisphenol F (BPF), on the caloric food commonly intake and function of mice. METHODS: We exposed 8-week-old female C57BL/6J mice to BPA or BPF at 0.5 mg/kg/day for 4 weeks. RESULTS: Compared with the control group, BPA and BPF exposure significantly increased the body weight, obesity, calorie consumption, and inflammation rate significantly altered in mice exposed to BPA or BPF. This change was characterized by elevated bacterial 16 rRNA sequencing levels of Bacteroidetes/Firmicutes (G/F) and Escherichia/Shigella and decreased levels of Prevotella 9 and Streptococcus. Additionally, pathways related to carbohydrate and amino acid metabolism showed substantial enrichment. CONCLUSIONS: Mice exposed to different BP analogs exhibited distinct gut microbial community richness, composition, and related metabolic pathways. Considering the essential role of gut bacteria in maintaining intestinal homeostasis, our study highlights the intestinal toxicity of BPs in vertebrates.	Biomed Environ Sci Vol.37 Issue 1 Pages 19-30	10.3967/bes2024.003	38326718	動物	-	1	1	1	1	0	0.5 mg/kg、50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1090	L. Meng, Z. Ouyang, Y. Chen, C. Huang, Y. Yu and K. Fan	2024	Low-dose BPA-induced neuronal energy metabolism dysfunction and apoptosis mediated by PINK1/parkin mitophagy pathway in juvenile rats	Bisphenol A (BPA) is related to neurological disorders involving mitochondrial dysfunction, while the mechanism remains elusive. Therefore, we explored it through in vitro and in vivo experiments. In vitro, Hippocampal neurons derived from neonatal rats of different genders were exposed to 0-100 nM and 100 μM BPA, autophagy activator Rapa and inhibitor 3-MA for 7 d. The results suggested that even neurotoxic BPA (1-100 nM) diminished Ca2+ homeostasis and damaged the mitochondria in female gene. In contrast, 100 μM BPA increased the number of autophagic lysosomes, LC3-II/LC3-I ratio and Beclin1 expression, and decreased puncta expression (p < 0.05), suggesting that the entry of damaged mitochondria into autophagic pathway was promoted, while the autophagic degradation pathway was blocked. This further disrupts neuronal energy metabolism, as evidenced by reduced ATP production and ATP/ADP ratio. Rapa and 3-MA could not reverse the damage caused by 100 μM BPA. In vivo, SD rats were exposed to 0, 0.5, 5, and 50 mg/kg BPA during PND 7-21 to identify impaired the structure of hippocampal mitochondria, increased the number of autophagic vacuoles, the ratio of neuronal apoptosis, and the expression levels of pro-apoptotic proteins Cyt C, Bax, Bad, and Caspase3, and decreased the expression of anti-apoptotic protein Bcl2 (p < 0.05). Particularly, male rats are more sensitive to low-dose BPA than females. Overall, environmental doses BPA can induce the imbalance of energy metabolism in hippocampal neurons via PINK1/parkin mitophagy, thereby inducing their apoptosis. Importantly, this study provides a theoretical basis for attenuating BPA-related neurological diseases.	Sci Total Environ. 2024 Jun 15:929:172655.	10.1016/j.scitotenv.2024.172655	38653419	動物	神経	1	0（腹腔内）	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1091	L. Meng, S. Gui, Z. Ouyang, Y. Wu, Y. Zhuang, Q. Pang and R. Fan	2023	Low-dose bisphenols exposure sex-specifically induces neurodevelopmental toxicity in juvenile rats and the antagonism of EGCG	Bisphenols (BPs) can negatively affect neurobehaviors in rats, whereas the mechanism remains unclear. Here, the mechanism of BPs-induced neurodevelopmental toxicity and its effective detoxification measures were investigated in vitro and in vivo. In vitro experiments, primary hippocampal neurons from neonatal rats of different genders were treated with bisphenol A (BPA), bisphenol F (BPF) and bisphenol AF (BPAF) at 1-100 nM (i.e., BE-adaptive) and low-golden (EGCG) and ES, an antagonist of ß-protein-coupled estrogen receptor (GPER) for 7 d. Results indicated that BPs affected neuronal morphogenesis, impaired GABA synthesis and Glu/GABA homeostasis. Neuronal morphogenetic damage induced by low-dose BPA may be mediated by GPER. Sexuality-related BPs toxicity was found, and the female rats were more sensitive to BPA and BPB. In in vivo studies, exposure to BPA (0.5 μg/kg/day) and PND 21-63 caused oxidative stress and inflammation in rat hippocampus, disrupted neuronal morphogenesis and neurotransmitter homeostasis, ultimately impaired spatial memory of rats. Males are more sensitive to BPA exposure than females. Both in vivo and in vitro studies indicated that EGCG, a polyneuroglen, can alleviate BPA-induced neurotoxicity. Taken together, low-dose BPA exposure can sex-specifically disrupted neurodevelopment and further impaired learning and memory ability in rats, which may be mediated by GPER. Promisingly, EGCG effectively mitigated the BPA-induced neurodevelopmental toxicity.	J Hazard Mater Vol.459 Pages 132074	10.1016/j.jhazmat.2023.132074	37473573	動物	-	1	不明	1	不明	0	0.5 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1092	S. J. Mekbaey, M. S. AlGhamdi, M. E. A. Elhalwagy, S. A. Alkolmy and A. I. A. Bin Dohaish	2022	Disturbance in Some Fertility Biomarkers Induced and Changes in Testis Architecture by Chronic Exposure to Various Dosages of Each of Nonylphenol or Bisphenol A and Their Mix	This investigation was conducted to demonstrate the potential impacts of different doses of Bisphenol A (BPA) or Nonylphenol (NP) and their mixtures on some biological activities in male albino rats. Seventy male albino rats were allocated to the control group (G1) and were given 1 mL of ethanol. G 2 and G 3 were given 100 mg/kg of each of BPA and NP. G 4 and G 5 were given 25 mg/kg of each of BPA and NP. G 6 was given a high dose mixture (HDM) of 100 mg/kg of BPA + 100 mg/kg of NP. G 7 was given a low dose mixture (LDM) of 25 mg/kg of BPA + 25 mg/kg of NP. Sperm motility, sperm count, and sperm morphology were determined, as well as a histopathological examination of the testis, at the end of the experimental period. The results indicated a pronounced decrease in sperm motility, sperm count, and sperm morphology. A hyperexpression (3 HSD), concomitant with a significant reduction in serum Superoxide dismutase (SOD), catalase enzyme (CAT), and total antioxidant capacity (TAC) in all treated groups. A significant elevation in TNF-alpha, TAP, Beta, and Caspase 3 serum was recorded individually and in the groups treated with high doses. The disturbance is represented by histological damage in the testis in the germinal epithelium and a decrease in spermatozoa inside the lumen of seminiferous tubules. The effects on testis tissues were dose-dependent, pronounced in mixture doses, and remarkable in higher doses. In conclusion, exposure to BPA and NP strongly impairs antioxidants, inherent inflammatory mediators, and testis tissue architecture. Furthermore, the data from this investigation support the idea that exposure to BPA and NP in reality fits the multiple damages.	Life (Basel) Vol.12 Issue 10	10.3390/life12101555	36294990	動物	-	1	1	1	1	0	25、100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1093	K. Machay Al-Anazi, M. Jabr Aljuaid, M. Abul Farah , A. Hossam Mahmoud, A. I. Algaban, M. Ayad Ali and F. M. Abou-Tarboush	2022	Maternal and developmental toxicity of Bisphenol-A in SWR/J mice	Bisphenol-A (BPA), an organic compound with two phenol functional groups, is a widely used industrial plasticizer with known estrogenic properties. It is used in the manufacture of epoxy resins and polycarbonate plastics. This study was designed to evaluate and assess the possible toxicity arising from the oral administration of BPA to pregnant mice. Sixteen SWR/J mice (10 mice per treatment and dosage of BPA: 0.24, 240 and 360 mg/kg/day) were the source of five day intervals during gestation (D1-5, D6-10 and D11-15), while control groups received only corn oil. The results indicated that BPA was associated with a reduction in the number of implantation sites, fetal body weight, and fetal crown-rump length in the 360 mg/kg/day BPA group. Placental weight was significantly reduced in the 240 and 360 mg/kg/day BPA groups. Fetal resorptions were higher in the 360 mg/kg/day BPA group than in the control group. They also showed marked reduction in fetal body weight, fetal crown-rump length, and placental weight. Maternal and fetal mortality rates, abortion and foetal resorption rates were not affected by BPA administration, however. The above findings were concluded by discussing the possible mechanisms involved in producing these effects.	Saudi J Biol Sci Vol.29 Issue 3 Pages 1543-1549	10.1016/j.sjbs.2021.11.014	35280563	動物	-	1	1	1	SWR/J	1	0.24、240、360 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1094	A. A. Martínez-Peña, A. Peña-Castillo, L. Y. Parra-Forero, I. Hernández-Ochoa, L. R. Hernández-Barrientos, S. Macíntosh and C. A. Mendoza-Rodríguez	2019	Parental perinatal exposure to bisphenol A reduces the threshold to disrupt blastocyst implantation via decreasing talin, occudin and E-cadherin levels	The aim was to evaluate the effect of perinatal BPA exposure of one or both parents on the implantation rates and expression of talin, occludin and E-cadherin in the uterine epithelial cells (UEC) of the offspring. Pregnant Wistar dams (F0) received BPA or vehicle from gestational day (GD) 0 to lactation day (T). T animals were reared forming four groups: Control dam-Control son (C-C; F1), BPA dam-Control son (BP-C; F1), Control dam-BPA son (C-B; F1), BPA dam-BPA son (BP-B; F1). F1 dams were sacrificed at GD 8. Significantly decreased number of implantation sites was observed in the BP-C group as compared to the C-C group, which correlated with decreased talin apical/basal expression ratio, occludin apical expression, and E-cadherin apical/lateral expression ratio in the UEC. Furthermore, decreased E-cadherin expression in the blastocyst was observed. Our data suggest that reduced protein expression in F1 BPA-offspring could result from decreased progesterone concentrations.	Reprod Toxicol. 2019 Jun;86:86-97.	10.1016/j.reprotox.2019.04.005	31028817	動物	子宮	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1095	A. Manona, A. De Bartolo, V. Rago, F. Conforti, L. Urbančič, T. Angelone, R. Mazza, M. Mandalà and C. Rocca	2025	Prenatal Bisphenol A Exposure Impairs Fetal Heart Development: Molecular and Structural Alterations with Sex-Specific Differences	Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, with increasing evidence suggesting that their origins may be in prenatal life. Endocrine-disrupting chemicals (EDCs), such as bisphenol A (BPA), have been implicated in the alterations of fetal programming mechanisms that cause a predisposition to long-term cardiovascular vulnerability. However, the impact of prenatal endocrine disruption on fetal heart development and its sex-specific nature remains incompletely understood. This study investigates the molecular and structural effects of low-dose prenatal BPA exposure on fetal rat hearts. Our results reveal that BPA disrupts estrogen receptor (ER) signaling in a sex-dependent manner, with distinct alterations in ERα, ERβ, and GPER1 expression. BPA exposure also triggers significant inflammation, oxidative stress, and cell death, as evidenced by increased TNF-α, IL-1β, and caspase-3 activity, particularly in female hearts. Structural analysis further demonstrates that BPA impairs cardiac development, leading to reduced ventricular wall thickness and protein accumulation, decreased CM1 and increased HCN1 levels. These alterations are accompanied by increased markers of cardiac dysfunction (BNP, MMP), which are more pronounced in females, and sex-specific regulatory (Cx43, Cx40, TBX1, TBX20, JP, and TGFβ1), while more pronounced response in males. Histological analysis corroborated these molecular findings, revealing structural alterations as well as glycogen depletion in male fetal hearts, consistent with altered cardiac morphogenesis and metabolic stress. These effects were milder in females, reinforcing the notion of sex-specific vulnerability. Moreover, prenatal BPA exposure affected myocardial fiber architecture and vascular remodeling in a sex-dependent manner, as evidenced by reduced expression of desmin alongside increased levels of CD31 and KI67. Overall, our findings provide novel insights into the sex-dependent mechanisms of prenatal endocrine disruption during fetal heart development and its contribution to the early origins of CVD, underscoring the urgent need for targeted preventive strategies and further research into the functional impact of BPA-induced alterations on postnatal cardiac function and long-term disease susceptibility.	Antioxidants (Basel) Vol.14 Issue 7	10.3390/antiox14070863	40722967	動物	-	1	1	1	1	0	2.5 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1096	M. Marmudino, E. Bo, E. Carlini, A. Farinetti, G. Ponti, I. Zanella, D. Di Lorenzo, G. C. Panzica and S. Gotti	2021	Hypothalamic Expression of Neuropeptide Y (NPY) and Pro-OpioMelanoCortin (POMC) in Adult Male Mice Is Affected by Chronic Exposure to Endocrine Disruptors	In the arcuate nucleus, neuropeptide Y (NPY) neurons increase food intake and decrease energy expenditure, and control the activity of pro-opiomelanocortin (POMC) neurons, that decrease food intake and increase energy expenditure. Considering the role of the hypothalamic arcuate nucleus in the control of energy homeostasis and its sensitivity to circulating hormones, we investigated whether chronic exposure to endocrine disruptors (EDCs), which can interfere with the endocrine system causing adverse health effects, is an important organism-environment risk factor. We investigated the effects of long-term exposure to some EDCs, at environmentally relevant doses, on NPY and POMC systems of adult male mice that had been previously demonstrated to be a target of some of these EDCs, after short-term exposure. Animals were chronically fed for four months with a phytoestrogen-free diet containing two different concentrations of bisphenol A, diethylhexanoic, trioctyltin, or DDE. At the end, brains were processed for NPY and POMC immunohistochemistry and quantitatively analyzed. In the arcuate and dorsomedian nucleus, both NPY and POMC immunoreactivity showed a statistically significant decrease in the paraventricular nucleus, only the NPY system was affected, while the POMC system was not affected. Finally, in the VMH the NPY system also affected whereas no POMC immunoreactive material was observed. These results indicate that adult exposure to different EDCs may alter the hypothalamic circuits that control food intake and energy metabolism.	Metabolites Vol.11 Issue 6	10.3390/metabo11060368	34207679	動物	-	1	1	0	1	0	0.15～15 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1097	E. Marchlewicz, C. McCabe, Z. Djuric, M. Hoerhoff, J. Berko, L. Tang, P. K. Song, K. Peterson , V. Padmanabhan and D. C. Dolinoy	2022	Gestational exposure to high fat diets and bisphenol A alters metabolic outcomes in dams and offspring, but produces hepatic steatosis only in dams	The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide. Perinatal development is a critical window for ailment. Using health trajectory, and evidence supports the role of perinatal programming in chronic metabolic diseases. To examine the impact of diet and bisphenol A (BPA) on the developmental trajectory of NAFLD in offspring, we exposed dams from pre-gestation through lactation to a human-relevant dose of oral BPA coupled with diets of high fat Western or Mediterranean-style diets. We assessed hepatic steatosis by quantifying hepatic triglycerides (TGs) and metabolic health by measuring body weight, relative organ weights, and serum hormone levels in dams and offspring at postnatal day (D) PND20 and D3 months of age. In dams, consumption of the Western or Mediterranean diet increased hepatic TGs 1.7-2.1-fold, and exposure to BPA further increased TGs 1.3-fold in females exposed to the Western diet. Hepatic steatosis was not observed in offspring. Offspring exposed to the Western diet had increased body weight at PND20 and D3 months, and exposure to the Mediterranean diet only in males. Offspring exposed to the Mediterranean diet only in males had organ weights. At 3 months, sex-specific, however, in organ weight and hormone levels were observed in males perinatally exposed to Western + BPA or Mediterranean + BPA. These findings suggest lifestage-specific interactions of perinatal exposures to experimental diets, and BPA on offspring metabolic health without effects on NAFLD later in life. Importantly, alterations in beta-phenotype by diet and BPA exposure appear to impact offspring health trajectory, emphasizing the need to define later diet in assessing effects of environmental exposures on offspring health.	Chemosphere. 2022 Jan;286(Pt 2):131645.	10.1016/j.chemosphere.2021.131645	34426127	動物	代謝	1	1	1	0	0	1	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1098	Y. Mao, D. Li, Q. Yang, X. Pei, Z. Duan and M. Ma	2023	Prenatal BPA exposure disrupts male reproductive functions by interfering with DNA methylation and GDNF expression in the testes of male offspring rats	BPA is a ubiquitous environmental endocrine-disrupting chemical, and maternal exposure to BPA is associated with impaired male reproductive functions; however, the mechanisms remain to be elucidated. Glial cell line-derived neurotrophic factor (GDNF) plays an important role in maintaining normal spermatogenesis and fertility. However, the effect of prenatal BPA exposure on GDNF expression and its mechanism in the testis has not been reported. In this study, pregnant Sprague-Dawley rats were exposed orally respectively to 0.05, 0.5, 5, and 50 mg/kg/day BPA via oral gavage from gestational day (GD) 9 to GD 21, and 8 pregnant rats in each group. In GD21 testes, histochemistry, real-time PCR, western blot, and methylation-specific PCR (MSP) were used to detect the rat hormone levels, testicular histopathology, mRNA and protein expression of DNA methyltransferases (DNMTs), and the methylation level of the GDNF promoter, respectively. The results showed that BPA exposure significantly increased the serum testosterone (T) and luteinizing hormone (LH) and testosterone/estradiol (T/E2) ratio and reduced testicular histopathological changes, which indicated the damage of male reproductive function. Prenatal BPA exposure also upregulated Dnmt3a 1 in 5 mg/kg group and Dnmt3b in 0.5 mg/kg group, but down-regulated Dnmt1 in 50 mg/kg group at PND 21. As PND 56, Dnmt1 was significantly increased in 0.05 mg/kg group but decreased in 0.5, 5, and 50 mg/kg groups. Dnmt3a was significantly increased in 0.05 and 0.5 mg/kg groups but decreased in 5 and 50 mg/kg groups. The mRNA and protein expression levels of Gdnf were decreased in 5 and 50 mg/kg groups at PND 21, but the methylation level of Gdnf promoter was significantly increased in 0.5 mg/kg group, but decreased in 5 and 50 mg/kg groups at PND 21. In conclusion, our study indicates that prenatal BPA exposure disrupts male reproductive functions, interferes with the expression of GDNF/Gdnf, and decreases Gdnf expression in the testes of male offspring. Gdnf expression may be regulated by DNA methylation; however, the detailed mechanism needs to be further investigated.	Environ Sci Pollut Res Int. 2023 Apr;30(18):53741-53753.	10.1007/s11356-023-26154-7	36864339	動物	内分泌/精子/精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1099	W. Mao, L. Mao, F. Zhou, J. Shen, N. Zhao, H. Shi, J. Ma and Z. Hu	2023	Influence of Gut Microbiota on Metabolism of Bisphenol A, a Major Component of Polycarbonate Plastics	Bisphenol A (BPA) is a major component of polycarbonate plastics and epoxy resins. While many studies have investigated the effect BPA exposure has upon changes in gut microbial communities, the influence of gut microbiota on an organism's ability to metabolize BPA remains comparatively unexplored. To remedy this, in this study, Sprague Dawley rats were intermittently (i.e., at a 7-day interval) or continuously dosed with 500 μg BPA/kg body weight (bw) via oral gavage. Urine, feces, and blood samples were collected at 0, 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79,

別添-2 統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性評価基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群との間隔以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1102	J. Mao, J. A. Kinkade, N. J. Rivera and C. S. Rosenfeld	2021	miRNA changes in the mouse placenta due to bisphenol A exposure	Aim: To determine small RNA expression changes in mouse placenta induced by bisphenol B (BPB) exposure. Methods: Exposing female mice to BPB two weeks prior to conception through gestational day (GD) 18, whereupon placentas were collected, frozen in liquid nitrogen and stored at -80° C. Small RNA libraries were isolated and used for small RNA sequencing. Results: 10 small RNAs were differentially expressed. Target miRNAs were closely aligned to those expressed by thymus and brain, and pathway enrichment analyses indicated that each target miRNAs regulate neurogenesis and associated neurodevelopment processes. Conclusions: BPB induces current small RNAs in mouse placentas that might provide biomarkers for BPB exposure. Further, the placenta might affect fetal brain development through the secretion of miRNAs.	Epigenomics Vol.13 Issue 24 Pages 1909-1919	10.2217/epi-2021-0339	34841895	動物	-	1	1	1	1	0	<200 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1103	J. Mao, A. Jain, N. D. Denslow, M. Z. Nouri, S. Chen, T. Wang, N. Zha, J. Kuh, S. J. Sarma, B. W. Surowiz, Z. Lei, L. W. Sumner, N. J. Rivera, R. M. Roberts, G. Tuteja and C. S. Rosenfeld	2020	Bisphenol A and bisphenol S disruptions of the mouse placenta and potential effects on the placenta–brain axis	Placental trophoblast cells are potentially at risk from circulating endocrine disrupting chemicals, such as bisphenol A (BPA). To understand how BPA and the reputedly more inert bisphenol S (BPS) affect the placenta, CD1® ICR mouse dams were fed 250 μg/kg body weight BPA or BPS daily for 2 wk and then bred. They continued to receive these chemicals until embryonic day 12.5, whereupon placental samples were collected and compared with treatment and control. BPA and BPS altered the expression of an identical set of 12 genes. Both exposures led to a decrease in the area occupied by cytokeratin-immunoreactive giant cells (GCs) within the junctional zone, markedly reduced placental serotonin (5-HT) concentrations, and lowered 5-HT GC immunoreactivity. Concentrations of dopamine and 5-hydroxyindoleacetic acid, the main metabolite of dopamine, were also reduced by BPA and BPS exposures. Placentas from male fetuses were more sensitive to BPA and BPS than placentas from female fetuses. These findings suggest that this neurosteroidogenic tissue could be a metabolically active, direct target of endocrine disruption. Moreover, a negative correlation existed between dopamine's GC area and its fetal sex. These outcomes lead to the following conclusions. First, BPA exposure causes almost identical placental effects as BPA. Second, a major target of BPA/BPS is either syncytiotrophoblast or GCs within the junctional zone. Third, imbalances in neurotransmitter-positive GCs, and an observed decrease in docosahexaenoic acid and estradiol, also occurring in response to BPA/BPS exposure, likely affect the placental basis also of the developing mouse fetus.	Proc Natl Acad Sci U S A Vol.117 Issue 9 Pages 4642-4652	10.1073/pnas.1919563117	32071231	動物	-	1	1	1	1	0	200 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1104	S. Z. Mansour, F. S. M. Moawed, M. M. M. Badawy and H. E. Mohamed	2020	Boswellic Acid Synergizes With Low-Level Ionizing Radiation to Modulate Bisphenol Induced-Lung Toxicity in Rats by Inhibiting JNK/ERK/c-Fos Pathway	Bisphenol A (BPA) is a low molecular weight chemical compound that has a deleterious effect on the endocrine system. It was used in plastics manufacturing with injurious effects on different body systems. Occupational exposure to low-level ionizing radiation (<2 Gy) is shown to attenuate an established inflammatory process and therefore enhance cell protection. Therefore, the objective of this study was to investigate the protective effect of boswellic acid (BA) accompanied by whole-body low-dose gamma radiation (~75 cGy) against BPA-induced lung toxicity in male albino rats. BPA intoxication induced a rat dose of 500 mg/kg/BW. Rats received 50 mg BA/kg BW by gastric gavage concomitant with BPA (5 d/wk, 4 consecutive weeks). Rats were exposed to whole-body gamma irradiation at a dose rate of 0.5 Gy/min, and the rats received BA and/or γ- R individual BPA-treated rats. Results revealed that BPA induced lung injury indicating oxidative damage biomolecules, (MDA and NADPH oxidase gene expression), inflammatory indices (NFR, TNF-α, IL-6, and gene expression of CCR-10. Moreover, BA and or γ- R ameliorated the lung inflammation via regulation of the JNK/ERK/c-Fos and NLRP3 / IL-1 signaling pathways. Interestingly, our data demonstrated that BA is synergistic interaction with γ- R to influences control against BPA-induced lung injury via anti-oxidant mediated and inflammatory activities.	Dose Response Vol.18 Issue 4 Pages 15593258209069597	10.1177/15593258209069597	33192203	動物	-	1	1	1	1	0	500 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1105	M. Manikandan, N. Sivagurunathan, A. K. Uma Maheshwari, V. S. Anilkish and L. Calivarathan	2024	Selenium ameliorates oxidized phospholipid-mediated testicular dysfunction and epididymal sperm abnormalities following Bisphenol A exposure in adult Wistar rats	Bisphenol A (BPA) is an endocrine-disrupting compound extensively utilized in the production of polycarbonate polymers and epoxy resins that, upon exposure, pose a significant threat to male reproductive health because of its oxidogenic properties. Accumulating evidence suggests that BPA exposure disrupts the normal process of spermatogenesis, alters testicular morphology and functions, and induces testicular steroidogenesis and hormonal signaling. However, the precise mechanism by which BPA affects testicular function remains unclear. In this study, we explored the mechanism underlying BPA-induced testicular abnormalities and evaluated the potential effects of Selenium (Se). Thirty-two adult male albino Wistar rats were divided into four groups, each containing eight rats. The control group received normal saline, and BPA was administered at 50 mg/kg body weight, with or without Se supplementation, for 30 days. Se supplementation (2.5 mg/kg body weight) was initiated 1 week before BPA administration. BPA administration resulted in alterations in testicular architecture, characterized by basement membrane disintegration and degeneration of seminiferous tubules, leading to a significant reduction in sperm count, motility, and viability. Additionally, BPA exposure led to a substantial decrease in testosterone levels and testicular steroidogenic enzyme activities, including 3β-HSD and 17β-HSD. Furthermore, BPA induced oxidative stress in the testes, as indicated by elevated levels of thiobarbituric acid reactive substances (TBARS) and decreased the activities of the antioxidant enzymes superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase. In addition, BPA significantly reduced the activities of Ca2+ and Mg2+ ATPases and hydroxyacid dehydrogenases, interfering with testicular steroidogenesis. In rats, supplementation of Se and BPA reduced the levels of oxidized phospholipids and increased the activities of antioxidant enzymes, leading to improved testicular function and epididymal sperm parameters, suggesting that Se plays a critical role in alleviating endocrine disruptor-induced testicular dysfunctions in rats.	Reprod Toxicol Vol.130 Pages 108751	10.1016/j.reprotox.2024.108751	39549767	動物	-	1	不明	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1106	A. Mangla, P. Goswami, B. Sharma, S. Suramya, G. Jindal, M. Javed, M. A. Salfi, S. Pawar, T. C. Nag and S. Rakshit	2024	Obesity aggravates neuroinflammatory and neurodegenerative effects of bisphenol A in female rats	Bisphenol A (BPA), a common plastic ion, is categorized as a xenobiotic compound. Its impact on individuals exhibits sex-linked variations. Several biological and environmental factors impact the degree of toxicity. However, nutritional factors have profound influence on toxicity outcome. BPA has been demonstrated to be an obesogen. However, research on the potential role of obesity as a confounding factor in BPA toxicity is limited. This study investigated the impact of obesity on BPA-induced neurotoxicity in female rats. Female Wistar rats were divided into four groups, each containing six rats: control, BPA (50 mg/kg), HFD, and HFD + BPA. Cognitive functions were evaluated through novel object recognition (NOR) tests and Morris water maze (MWM) tests. Biochemical changes in hormonal level, lipid profile, oxidative stress, and antioxidants were also determined. HFD + BPA group rats showed a significant decline in memory function in NOR test. The cerebral cortex (CC) of the brain showed increased neurodegenerative changes, as measured by intracellular vacuolated protein 3 (VAP-1) accompanied by histopathological confirmation. The increased level of neuroinflammation was demonstrated by microglial activation (Iba-1) and protein expression of nuclear factor- kappa B (NF-κ) in the brain. Obesity also caused significant (p < 0.05) increase in lipid peroxidation accompanied by reduced activities of antioxidant enzymes (glutathione-S-transferase, catalase and glutathione peroxidase) and decrease in reduced glutathione (p < 0.05) when compared to non-obese rats with BPA treatment. Overall, study revealed that obesity serves as a risk factor in the toxicity of BPA which may exacerbate the progression of neurological diseases.	Toxicol Mech Methods Vol.34 Issue 7 Pages 781-794	10.1080/15376516.2024.2349538	38699799	動物	-	1	1	1	不明	0	10 mg/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1107	W. K. Mandler, W. McKinney, T. A. Skaudis, A. K. Knepp, S. E. Anderson, L. G. Jackson, S. Keeley, K. Krajnak, A. P. Shinault, M. T. Farcas, L. Battelli, S. A. Friend, A. B. Stefaniak, T. A. Thomas, J. Mathieson and Y. Qian	2025	Assessment of pulmonary toxicity of inhaled polycarbonate 3D printer emissions in rats	This study investigated the potential pulmonary toxicity of polycarbonate (PC) emissions from fused filament fabrication (FFF) three-dimensional printing (3DP) during inhalation in Sprague Dawley rats. Previously, our research team characterized PC emissions generated from a commercial FFF 3DP and identified bisphenol A (BPA) as the primary chemical of concern. Male rats were exposed to BPA (0.5 mg/m3) or underwent sham control (filtered air) and exposure groups (n=5–10/group). Each group was further divided into two subgroups: (n = 5/subgroup) with exposure durations of 1, 4, 8, 16, or 30 days (5 hr/day, 5 days/week). Following a 28-hr post-exposure period, body weight was measured, and blood samples were collected for hematological and biochemical analysis. Bronchoalveolar lavage fluid (BALF) was obtained from the right lung's cardiac. The left lung and head/nasal tissues were preserved for histopathological evaluation. Lung deposition was estimated using the Multiple-Path Particle Dosimetry model, electron microscopy, and enhanced darkfield microscopy. In addition, filter samples were collected to measure bisphenol A. Exposure resulted in an estimated deposition of 0.26 μg/day within the alveoli and small airways. Microscopy indicated limited particle deposition in the lung, primarily consisting of micron-sized debris. Exposure to PC emissions caused minimal pulmonary inflammation, as evidenced by a slight increase in neutrophils in BALF. Lung protein were elevated in the 30-day exposure group, although histopathology revealed no exposure-related changes in the lungs. In conclusion, this study found no marked pulmonary inflammation or toxicity in rats exposed to 3 mg/m3 of PC 3D printing emissions for up to 30 days (5 hr/day).	J Toxicol Environ Health A Vol.88 Issue 16 Pages 627-646	10.1080/15287394.2025.2473559	40071543	動物	-	1	0	不明	1	0	2.5 mg/m³	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1108	M. A. Malloy, J. J. Kochmanski, T. R. Jones, J. A. Colacino, J. M. Goodrich, D. C. Dolinoy and L. K. Svoboda	2019	Perinatal Bisphenol A Exposure and Reprogramming of Imprinted Gene Expression in the Adult Mouse Brain	Genomic imprinting, a phenomenon by which genes are expressed in a monoallelic, parent-of-origin dependent fashion, is critical for normal brain development. Expression of imprinted genes is regulated via epigenetic mechanisms, including DNA methylation (5-methylcytosine; 5mC), and disruptions in imprinting can lead to disease. Early life exposure to the endocrine disrupting chemical bisphenol A (BPA) is associated with abnormalities in brain development and behavior, as well as with disruptions in epigenetic patterning, including 5mC and DNA hydroxymethylation (5-hydroxymethylcytosine; 5hmC). Using an established mouse model of perinatal environmental exposure, the objective of this study was to examine the effects of perinatal BPA exposure on epigenetic regulation of imprinted gene expression in adult mice. Two weeks prior to mating, dams were randomized to receive one of three treatments: 0 (Control), 4 (Low BPA), or 40,000 (High BPA) μg BPA/kg diet. Exposure was maintained throughout mating, gestation, and lactation. Offspring were sacrificed at 6 months of age. Expression of three imprinted genes (Peg3/Igf2r/Kcnq1ot1), as well as three genes encoding proteins critical for regulation of 5mC and 5hmC (Tet1, Tet2, and Tet3), were evaluated in the right cerebral midbrain using qRT-PCR. Perinatal BPA exposure was associated with a significant increase in male Kcnq1ot1 (p = 0.028) and Dnmt1 (p = 0.021) expression in the right cortex, as well as increased expression of Tet3 in the midbrain (p = 0.021). Expression of Tet2 and Kcnq1 were positively correlated in the midbrain. Analysis of Tet1, Tet2 and Dnmt1 at the 5mC locus was conducted in parallel samples using standard and oxidative bisulfite conversion followed by pyrosequencing. This analysis revealed enrichment of both 5mC and 5hmC at this locus in both brain regions. No significant changes in 5mC and 5hmC at Kcnq1 were observed with perinatal BPA treatment. Together, these data suggest that perinatal BPA exposure results in altered expression of Kcnq1, Dnmt1, and Tet3 in the adult mouse brain. Further studies with larger sample sizes are necessary to understand the mechanistic basis for these changes, as well as to determine the implications they have for brain development and function.	Front Genet Vol.10 Pages 951	10.3389/fgene.2019.00951	31649729	動物	-	1	1	1	Avy/a	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1109	Y. Malaisé, C. Lencina, C. Cartier, M. Olier, S. Menanteau and L. Guzylack-Piriou	2021	Bisphenol A, S or F mother's dermal impregnation impairs offspring immune responses in a dose and sex-specific manner in mice	Bisphenol (BPA) is an endocrine disruptor (ED) widely used in thermal papers. Regulatory restrictions have been established to prevent risks for human health, leading to BPS substitution by structural analogues, like BPS and BPF. We previously demonstrated that oral perinatal exposure of BPA had long-term immune responses later in life. It appears now essential to reinforce our understanding on immune impact of different routes of BP exposure. In this study, we aimed at comparing the impact of mother dermal exposure to BPs on offspring immune system at adulthood. Dorsal mice were dermally exposed to BPA, BPS or BPF at 0.5 mg/kg/d from 2 weeks before mating to weaning. Offspring were sacrificed at 8 weeks old. Immune cell populations were characterized in the ileum, spleen and blood by flow cytometry. Systemic levels of cytokines were quantified by Luminex assay. Results: Dermal exposure to BPs altered offspring immune systems levels that was dependent on the BP, the dose and offspring sex. These findings provide, for the first time, results on long-term consequences of dermal perinatal BPs exposure on immune responses in offspring. This work warns that it is mandatory to consider immune markers, dose-response as well as sex in risk assessment associated with new BPA's alternatives.	Sci Rep Vol.11 Issue 1 Pages 1650	10.1038/s41598-021-81231-6	33462300	動物	-	1	0	1	C3H/HeN	0	5 、 50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1110	K. Makowska, K. Szymańska, J. Calka and S. Gonkowski	2021	The Influence of Bisphenol A (BPA) on the Occurrence of Selected Active Substances in Neuroglia 1 (NRG1)-Positive Enteric Neurons in the Porcine Large Intestine	Bisphenol A (BPA) is a substance used in the manufacture of plastics which shows multidirectional adverse effects on living organisms. Since the main path of intoxication with BPA is via the gastrointestinal (GI) tract, the stomach and intestine are especially vulnerable to the impact of this substance. One of the main factors participating in the regulation of intestinal functions is the enteric nervous system (ENS), which is characterized by high neurochemical diversity. Neuregulin 1 (NRG1) is one of the tissue-known active substances. In the ENS, During the present study (performed using the double immunofluorescence method), the co-localization of NRG1 with other neuronal substances in the ENS of the cranial and the ascending and descending colon has been investigated under physiological conditions and after the administration of BPA. The obtained results indicate that NRG1-positive neurons also contain substance P, vasoactive intestinal polypeptide, a neuronal isoform of nitric oxide synthase and galanin and the degree of each co-localization depend on the type of enteric plexus and the particular fragment of the intestine. Moreover, it has been shown that BPA generally increases the degree of co-localization of NRG1 with other substances.	Int J Mol Sci Vol.22 Issue 19	10.3390/ijms221910308	34638647	動物	-	1	1	1	Pietrain × Duroc	0	0.05 、 0.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1111	K. Makowska, E. Lepiarczyk and S. Gonkowski	2022	The Comparison of the Influence of Bisphenol A (BPA) and Its Analogue Bisphenol S (BPS) on the Enteric Nervous System of the Distal Colon in Mice	Bisphenol A (BPA), commonly used as a plasticizer in various branches of industry has a strong negative effect on living organisms. Therefore, more and more often it is replaced in production of plastics by other substances. One of them is bisphenol S (BPS). This study for the first time compares the impact of BPS and BPA on the enteric neurons using double immunofluorescence technique. It has been shown that both BPS and BPA cause changes in the neurochemical coding of the enteric neurons in the distal colon. Both substances increase the number of neurons containing nitric oxide synthase (nNOS) and vasoactive intestinal polypeptide (VIP). A smaller number of substances was observed in the case of BPS. The changes noted under the impact of both bisphenols are similar and concern the same neuronal populations. However, the immunoreactivity of all neuronal factors studied. The impact of BPS on some populations of neurons was stronger than that noted under the influence of BPA. The obtained results clearly show that BPS (similarly to BPA) administered for long time is not neutral for the enteric neurons, even in relatively low doses and may be more potent than BPA for certain neuronal populations.	Nutrients Vol.15 Issue 1	10.3390/nu15010200	36615857	動物	-	1	1	1	1	0	5 、 50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1112	K. Makowska, P. Lech, M. Majewski, A. Rychlik and S. Gonkowski	2021	Bisphenol A affects vipergic nervous structures in the porcine urinary bladder trigone	Bisphenol A (BPA) is used in the production of plastics approved for contact with food and tool. Upon entering living organisms, BPA, as a potent endocrine disruptor, negatively affects various internal organs and systems. Considering the above, the present study aimed to determine the impact of BPA on the urinary bladder trigone in pigs. The research material was collected from 30 female crossbred pigs. The chemical architecture of the urinary bladder intrinsic innervation has not yet been studied. Due to the important neurochemical factors involved in the regulation of urinary bladder functions, a vasoactive intestinal polypeptide (VIP), which primarily participates in the regulation of muscular activity and blood flow. Therefore, this study aimed to determine the influence of various doses of BPA on the distribution pattern of VIP-positive neural structures, located in the wall of the porcine urinary bladder trigone using the double immunofluorescence method. The obtained results show that BPA influences both, an increase in the number of both neurons and nerve fibres containing VIP in the porcine urinary bladder trigone. This may indicate that VIP participates in adaptive processes of the urinary bladder evoked by BPA.	Sci Rep Vol.11 Issue 1 Pages 12147	10.1038/s41598-021-91529-0	34108533	動物	-	1	1	1	Pietrain × Duroc	0	0.05、0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1113	K. Makowska, P. Lech and S. Gonkowski	2023	Bisphenol A Effects on Neurons' Neurochemical Character in the Urinary Bladder Intramural Ganglia of Domestic Pigs	Bisphenol A (BPA), a substance globally used to produce plastics, is part of many everyday items, including bottles, food containers, electronic elements, and others. It may penetrate the environment and living organisms, causing many disorders in the functioning of various internal organs and systems. Considering the above, the present study aimed to determine the impact of BPA on the neurochemical coding of the intramural ganglia in the urinary bladder body in pigs and the role of vagal nerve in these changes. The material was collected from 30 female crossbred pigs. The urinary bladder body is located in the ganglia located in the urinary bladder wall, and changes in the neurochemical characterization of these neurons may be the first signs of BPA-induced pathological processes in this organ.	Int J Mol Sci Vol.24 Issue 23	10.3390/ijms242316792	38069115	動物	-	1	1	1	Pietrain × Duroc	0	0.05、0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1114	K. Makowska and S. Gonkowski	2024	Comparison of the Influence of Bisphenol A and Bisphenol S on the Enteric Nervous System of the Mouse Jejunum	Bisphenols are dangerous endocrine disruptors that pollute the environment. Due to their chemical properties, they are globally used to produce plastics. Structural similarities to oestrogen allow bisphenols to bind to oestrogen receptors and affect internal body systems. Most commonly used is the plastic industry is bisphenol A (BPA), which also has negative effects on the nervous, immune, endocrine, and cardiovascular systems. Therefore, more and more often it is replaced in the production of plastics by other substances. One of them is bisphenol S (BPS). This study for the first time compares the impact of BPS and BPA on the enteric nervous system (ENS) in mouse jejunum. The study showed that both studied toxins impact the number of nerve cells immunoreactive to substance P (SP), galanin (GAL), vasoactive intestinal polypeptide (VIP), the neuronal isoform of nitric oxide synthase (nNOS), and vesicular acetylcholine transporter (VAChT). The observed changes were similar in the case of both tested bisphenols. However, the influence of BPS showed stronger changes in neurochemical coding. The results also showed that long-term exposure to BPS significantly affects the ENS.	Int J Mol Sci Vol.25 Issue 13	10.3390/ijms25136941	39000048	動物	-	1	1	1	1	0	5 、 50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成根拠評価への進め、当該時点評価段階で原則として解説。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1115	K. Makowska and S. Gonkowski	2023	Changes Caused by Bisphenols in the Chemical Coding of Neurons of the Enteric Nervous System of Mouse Stomach	Bisphenol A (BPA), an organic chemical compound which is widely used in the production of plastics, can severely damage live organisms. Due to these findings, the plastic industry has started to replace it with other substances, including bisphenol S (BPS). The aim of the present study was to investigate the effects of BPA and BPS on the chemical coding of the enteric neurons in the mouse stomach. The obtained results show that both substances have a similar impact. Enhancement of nerve cells immunoreactive to substance P (SP), galanin (GAL), and nitric oxide synthase (nNOS) could become an marker of cholinergic neurons) and vasoactive intestinal polypeptide (VIP). Changes observed under the impact of both bisphenols depended on the neuronal factor, the type of the enteric ganglion and the doses of bisphenols studied. Generally, the increase in the percentage of neurons immunoreactive to SP, GAL, and/or VIP, and the decrease in the percentage of nNOS+ positive neurons, was noted. Severity of changes was more visible after BPA administration. However, the study has shown that long-time exposure to BPS also significantly affects the ENS.	Int J Environ Res Public Health Vol.20 Issue 6	10.3390/ijerph20065125	36982030	動物	-	1	1	1	1	0	5 、50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1116	K. Makowska and S. Gonkowski	2022	Changes in the Enteric Neurons Containing Selected Active Substances in the Porcine Descending Colon after the Administration of Bisphenol A (BPA)	Bisphenol A (BPA) is an endocrine disruptor widely distributed in the environment due to its common use in the plastics industry. It is known that it has a strong negative effect on human and animal organisms, but a lot of data concerning the influence of BPA on the enteric nervous system (ENS) is still lacking. Therefore, the aim of the present study was to investigate the impact of BPA on the neurochemical coding of the enteric neurons in the descending colon of the domestic pig, which can be considered to be a suitable model for the human digestive system. Detailed analysis of the obtained results showed that the examined BPA dose, which is considered safe for living organisms, has a significant effect on the neurochemical characterization of the enteric neurons located in the descending colon. The administration of BPA caused an increase in the number of enteric neurons containing substance P (SP) and vasoactive intestinal polypeptide (VIP) with a simultaneous decrease in the number of neurons positive for galanin (GAL) and vesicular acetylcholine transporter (VAChT) used as a marker of cholinergic neurons). Changes were noted in all types of the enteric plexuses, i.e., the myenteric, submucous, and intramural plexuses. Moreover, the changes were dependent on the part of the descending colon in which the enteric neurons studied. The results have shown that BPA may affect the descending colon through the changes in neurochemical characterization of the enteric neurons located in this segment of the gastrointestinal tract.	Int J Environ Res Public Health Vol.19 Issue 23	10.3390/ijerph192316187	36498260	動物	-	1	1	1	Pietrain × Duroc	0	0.05、0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1117	K. Makowska and S. Gonkowski	2021	Changes Caused by Low Doses of Bisphenol A (BPA) in the Neuro-Chemistry of Nerves Located in the Porcine Heart	Bisphenol A (BPA) contained in plastics used in the production of various everyday objects may leach from these items and contaminate food, water and air. As an endocrine disruptor, BPA negatively affects many internal organs and systems. Exposure to BPA also contributes to heart and cardiovascular system dysfunction, but many aspects connected with this activity remain unknown. Therefore, this study aimed to investigate the impact of BPA in a dose of 0.05 mg/kg body weight/day for many months, such a dose is regarded as a tolerable daily intake TDI dose of BPA—completely safe for living organisms) on the neurochemical characterization of the enteric neurons located in the heart wall using the immunofluorescence technique. The obtained results indicated that BPA caused in such a relatively low dose fragmentary changes, i.e., it increased the number of cholinergic neurons (visualized by vesicular acetylcholine transporter (VAChT), a marker of cholinergic neurons), substance P and tyrosine hydroxylase (used here as a marker of sympathetic innervation). However, BPA did not change the number of nerves immunoreactive to vesicular acetylcholine transporter (used here as a marker of cholinergic structures). These observations suggest that changes in the heart innervation may be at the root of BPA-induced circulatory disturbances, as sufficient sympathogenic and/or parasympathetic effects of the endocrine disruptor. Moreover, changes in the neurochemical characterization of nerves in the heart wall may be the first sign of exposure to BPA.	Animals (Basel) Vol.11 Issue 3	10.3390/ani11030780	33799766	動物	-	1	1	1	Pietrain × Duroc	0	0.05 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1118	K. Makowska and S. Gonkowski	2020	Bisphenol A (BPA) Affects the Enteric Nervous System in the Porcine Stomach	Bisphenol A (BPA) is widely utilized in plastic production process all over the world. Previous studies have shown that BPA, with its similarity to estrogen, may negatively affect living organisms. It is acknowledged that BPA disturbs the activity of multiple internal systems, including the nervous, reproductive, urinary, and endocrine systems. BPA also affects the gastrointestinal tract and enteric nervous system (ENS), which is placed in the wall of the gastrointestinal tract from the esophagus to the rectum. The aim of the study was to investigate the impact of BPA on the neurochemical coding of the enteric neurons in the porcine stomach. The obtained results showed that BPA affects the number of nervous structures in the porcine gastric wall immunoreactive to vesicular acetylcholine transporter (VAChT, a marker of cholinergic neurons), substance P (SP), vasoactive intestinal polypeptide (VIP), galanin (GAL), and cocaine- and amphetamine-regulated transcript peptide (CART). The character and severity of noted alterations depended on the part of the ENS, the BPA dose, and the type of neuronal substance. Manifestation of BPA-evoked is an increase in the number of nervous structures containing SP, GAL, and/or CART, and a decrease in the number of cholinergic neurons, in all parts of the gastric wall. The number of VIP-positive nervous structures increased in the enteric myenteric ganglia, along with the muscular and mucosal layers, while it decreased in the submucous ganglia. The exact mechanism of noted changes was not absolutely obvious, but they were probably related to the neuroprotective and adaptive processes constituting the response to the impact of BPA.	Animals (Basel) Vol.10 Issue 12	10.3390/ani10122445	33419365	動物	-	1	1	1	Pietrain × Duroc	0	0.05、0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1119	K. Makowska, K. R. C. Fagundes and S. Gonkowski	2023	Influence of bisphenol A and its analog bisphenol S on cocaine- and amphetamine-regulated transcript peptide-positive enteric neurons in the mouse gastrointestinal tract	INTRODUCTION: Bisphenol A (BPA) is used in large quantities for the production of plastics and is present in various everyday objects. It penetrates living organisms and shows multidirectional adverse influence on many internal organs. For this reason, BPA is often replaced in plastic production by other substances. One of them is bisphenol S (BPS), whose effects on the enteric nervous system (ENS) have not been explained. METHODS: Therefore, the present study compares the influence of BPA and BPS on the number of enteric neurons containing cocaine- and amphetamine-regulated transcript (CART) peptide located in the ENS of the stomach, jejunum and colon with the use of double immunofluorescence method. RESULTS: The obtained results have shown that both bisphenols studied induced an increase in the number of CART-positive enteric neurons in the stomach and jejunum. However, in the colon, the number of CART-positive neurons was reduced by BPA and BPS. Moreover, the number of CART-positive nerve fibers increased in the stomach and jejunum and decreased in the colon. The changes caused by BPS are more noticeable than those observed after BPA administration. In the stomach and jejunum, bisphenol induces changes, even in low doses, and changes caused by BPS were similar or less pronounced than those noted under the impact of BPA, depending on the segment of the gastrointestinal tract and ganglion type studied. DISCUSSION: The results show that BPS affects the enteric neurons containing CART in a similar way to BPA, and the BPS impact is even stronger in the colon. Therefore, BPS is not neutral for the gastrointestinal tract and ENS.	Front Mol Neurosci Vol.16 Pages 1234841	10.3389/fnmol.2023.1234841	37675141	動物	-	1	1	1	1	0	5 、50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1120	K. Makowska, J. Calka and S. Gonkowski	2023	Effects of the long-term influence of bisphenol A and bisphenol S on the population of nitrergic neurons in the enteric nervous system of the mouse stomach	Bisphenol A (BPA) is an endocrine disruptor commonly used in the production of plastics. Due to its relatively well-known harmful effects on living organisms, BPA is often replaced by its various analogues. One of them is bisphenol S (BPS), widely used in the plastics industry. Until recently, BPS was considered completely safe, but currently, it is known that it is not safe for various internal organs. However, knowledge about the influence of BPS on the nervous system is scarce. Therefore, the aim of this study was to investigate the influence of two doses of BPS and BPA on the enteric nitrergic neurons in the ICC circumference located using the double immunofluorescence technique. The study found that both substances studied increased the number of nitrergic neurons, although changes under the impact of BPS were less, visible than those induced by BPA. Therefore, the obtained results, for the first time, clearly indicate that BPS is not safe for the innervation of the gastrointestinal tract.	Sci Rep Vol.13 Issue 1 Pages 331	10.1038/s41598-023-27511-9	36609592	動物	-	1	1	1	1	0	5 、50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1121	M. Majid, A. Farhan, M. W. Baig, M. T. Khan, Y. Kamal, S. S. U. Hassan, S. Bungau and I. U. Haq	2022	Ameliorative Effect of Structurally Divergent Oleanane Triterpenoid, 3-Epihederiinol from Ipomoea batatas against BPA-Induced Gonadotoxicity by Targeting PARP and NF- κ B Signaling in Rats	The aerosa-ric triterpenoids (PTIs) of plant origin are reported to restrain prostate cancer (PCa) cell proliferation. This study aims to assess 3-epihederiinol (EPIH) isolated from aerial part of Ipomoea batatas against PCa in bisphenol A (BPA)-induced rats. Rats were divided into 5 groups (= 6) and treated for 28 days as follows: Group I (control) received 1 mL/kg of 1% DMSO, Group II (BPA) received BPA (~20 mg/kg bw) + 0.5 mL/kg of 1% DMSO, and Group III (BPA + EPIH) received BPA (~20 mg/kg bw) + EPIH (5 mg/kg bw). BPA treatment (< 0.05 and < 0.01) data were also observed a drastic rise in prostate gland wet (10.416 and 14.7%) and PCa cell co-cultured with BPA (~20 mg/kg bw) + EPIH (5 mg/kg bw) showed significant (< 0.05 and < 0.01) data and dose-dependent drastic rise in prostate gland wet (10.416 and 14.7%) and PCa cell co-culture in apoptotic cell population (FITC-Annexin V+/PI-) (5.138 ± 1.72 cells) and PCC (76.23 ± 3.67 cells). According to Western blots, EPIH administration significantly enhanced the cleavage of caspases and PARP, elevated BAX and P53 and decreased BCL-2 and NF- κ B expression, thereby triggering apoptosis in PCa cells. When male Sprague Dawley rats were intoxicated with Bisphenol A (BPA), an apparent increase in prostate mass (0.478 ± 0.04 g) in comparison to control (0.380 ± 0.02 g) indicates prostatitis. Multilinear treatment of EPIH (10 mg/kg) significantly reduced prostate size (0.368 ± 0.04 g). EPIH treatment also significantly (< 0.05) reduced the elevated levels of prostatic acid phosphatase (PAP), prostate-specific antigen (PSA), and testosterone in BPA-induced rats. Histological studies (H&E, E, and TUP +, caspase-colocalized antiinflammatory potential of the compound. Overall, EPIH has shown better binding affinity with target molecules, acceptable ADMET profile, potent antiproliferative and apoptotic nature and significant reduction in inflamed prostate mass of rats. The present study demonstrates acceptable physicochemical and pharmacokinetic properties of the compound with excellent druglikeness nature. Hence EPIH in the form of standardized formulation can be developed as primary or adjuvant therapy against PCa and toxic-induced prostatotoxicity.	Molecules Vol.28 Issue 1	10.3390/molecules28010290	36615482	動物	-	1	不明	1	1	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1122	A. Mahmoudi, F. Hedrich, Z. Boudiaguiı, I. Faki, H. Gtobel, L. Ayadi, M. Chamkha and S. Sayadi	2023	Comparative study of the effect of oleuropein and hydroxytyrosol rich extracts on the reproductive toxicity induced by bisphenol A in male rats: biochemical, histopathological, and molecular analyses	Bisphenol A, or BPA, gives rise to the composition of a large number of products including sunglasses, sturdy building bodies, receipts, or food packaging. Nowadays, there is a growing tendency that BPA may be at the origin of reproductive dysfunctions. Olive oil is considered a source of bioactive compounds, such as oleuropein and hydroxytyrosol, which have been shown to exhibit several biological properties. The present study aimed to evaluate the potential protective role of olive leaf extracts against BPA-induced testicular damage in Wistar rats. The animals were randomly divided into 4 groups: control, BPA treated (10 mg/kg bw), BPA and oleuropein rich extract (10 mg/kg) treatment, and the last group treated with BPA and hydroxytyrosol rich extract (10 mg/kg). Biochemical parameters and histological and molecular analysis were evaluated. Our data demonstrated that BPA treatment caused significant alterations in biochemical parameters, disorganization of germinal epithelium, and an regulation of p53 and Bax, and a reduction of Bcl-2 protein levels. The ingestion of oleuropein- and hydroxytyrosol- rich extracts attenuated BPA-induced biochemical and histological changes. In fact, olive leaf extracts enhanced the enzymatic antioxidant system and the level of Bcl-2, and reduced the expression of p53 and Bax. Fairly, our findings propose that olive leaf extracts may counteract with BPA-induced nephrotoxicity in rats.	Environ Sci Pollut Res Int Vol.30 Issue 32 Pages 78735-78749	10.1007/s11356-023-27836-y	37273043	動物	-	1	不明	1	1	0	10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1123	M. Mahdavinia, L. Khorsandi, S. Alizadi-davish, A. Samimi, M. A. Dehghani and L. Zeidooni	2021	Liver histopathological alteration and dysfunction after bisphenol A administration in male rats and protective effects of naringin	OBJECTIVE: Bisphenol A (BPA) is an organic synthetic compound, often used in manufacturing polycarbonate plastics. Researches have shown the role of BPA as an endocrine disruptor. The present study intended to evaluate the hepatoprotective properties of naringin, an active flavanone glycoside present in many citrus fruit, against hepatotoxicity induced by BPA. MATERIALS AND METHODS: Male Wistar rats were orally treated with 50 mg/kg BPA for 30 consecutive days for induction of toxicity and 50, 80 and 100 mg/kg naringin for the same period along with BPA or alone. RESULTS: The results revealed that BPA significantly increased serum levels of triglyceride, lactate dehydrogenase (LDH), alkaline phosphatase (ALP), lipid peroxidation, and aspartate aminotransferase (AST) and significantly reduced catalase, glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities in liver tissue homogenate. Histopathological examination revealed that BPA induced hepatocellular damage, including congestion, vacuolization, and necrosis. Naringin (50, 80, 100 mg/kg) significantly reduced BPA-induced elevation of serum levels of triglyceride, LDH, ALP, AST, alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT). Furthermore, the results displayed that administration of 80 and 100 mg/kg naringin improved hepatotoxicity and altered lipid peroxidation level, serum values of triglyceride and liver enzymes, and oxidative stress factors that were induced by BPA. The effect of loss doses of 80 and 100 mg/kg naringin was more noticeable than that of dose 50 mg/kg. CONCLUSION: The findings suggested the protective effects of naringin against BPA -induced hepatotoxicity via ameliorating liver histopathological alteration, suppressing oxidative stress and lipid-lowering properties.	Avicanna J Phytomed Vol.11 Issue 4 Pages 394-406	10.22038/ajp.2021.17649	34290970	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1124	W. A. H. Madurange Karu-ranatthe, Y. H. Choi, S. R. Park, C. M. Lee and G. Y. Kim	2022	Bisphenol A inhibits osteogenic activity and causes bone resorption via the activation of retinoic acid-related orphan receptor α	Bisphenol A (BPA) has deleterious effects on bone metabolism; however, its underlying mechanism has not yet been comprehensively understood. Here, we investigated whether ROR α plays an important role in BPA-induced bone resorption both in vitro and in vivo. We found that BPA (0.1–1 μM) inhibited osteogenic activity (including ALP activity and mineralization), decreased the expression levels of osteoblast markers (such as RUNX2, OSX, and ALP) in human MG-63 osteoblast-like osteosarcoma cells, and inhibited osteoblastic zebrafish formation in zebrafish larvae. Additionally, BPA diminished JC (glycerophospholipid-induced osteoblast differentiation and bone formation in vivo. Moreover, BPA (1 μM) increased the activity of osteoclastogenesis (including TRAP activity and mineralization), the expression levels of osteoclast markers (such as the NFATc1/c-fos and/or M-CSF/RANKL/OPG signaling pathway), and ROS production in RAW 264.7 cells. Additionally, BPA diminished the cell height of RAW264.7 cells, respectively, which another marked symptom of BPA-like stem cells, and BPA elements with non-osseous interactions, resulting in the activation of ROR α. However, an ROR α inverse agonist potently inhibited BPA-induced anti-osteogenic activity and vertebral formation in zebrafish larvae, concomitant with inhibition of osteogenic gene expression. Overall, our findings reveal that BPA inhibits osteoblast differentiation and bone formation by activating ROR α. These results suggest that BPA exposure (0.1–1 μM) can cause various bone-resorptive diseases, such as osteoporosis.	J Hazard Mater. 2022 Sep 15:438:129458.	10.1016/j.jhazmat.2022.129458	35780740	in vitro	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1125	Z. Ma, A. B. Parris, E. W. Howard, M. Davis, X. Cao, C. Woods and X. Yang	2020	In Utero Exposure to Bisphenol a Promotes Mammary Tumor Risk in MMTV-Erbb2 Transgenic Mice Through the Induction of ER-erbB2 Crosstalk	Bisphenol A (BPA) is the most common environmental endocrine disrupting chemical. Studies suggest a link between perinatal BPA exposure and increased breast cancer risk, but the underlying mechanisms remain unclear. This study aims to investigate the effects of in utero BPA exposure on mammary tumorigenesis in MMTV-erbB2 transgenic mice. Pregnant mice were subcutaneously injected with BPA (5, 50, 500 ng/kg and 25, 250, 2500 μg/kg) or vehicle control (sesame oil) from gestation day 10 to 17. Female offspring were palpated for mammary tumors weekly from 20 weeks of age. Mammary tumor incidence was 83% (10/12) in the 2500 μg/kg BPA-treated group, but only 8% (1/12) in the vehicle control. Increased luminal hyperplasia, early neoplastic lesions, and preneoplastic foci were also observed in the BPA-treated mammary glands, which was accompanied by elevated mammary tumorigenesis. CD31-IHC-based FACS analysis revealed that in utero exposure to 500 ng/kg BPA induced expansion of luminal and basal/myoepithelial cell subpopulations at PND 35. Molecular analysis of mammary tissues at PND 70 showed that in utero exposure to low doses of BPA induced upregulation of ERα, p-ERα, cyclin D1, and c-myc, concomitant activation of erbB2-EGFR, erbB2-STAT3, and Akt, and upregulation of growth factors/ligands. Our results demonstrate that in utero exposure to low dose BPA promotes mammary tumorigenesis in MMTV-erbB2 mice through induction of ER-erbB2 crosstalk and mammary epithelial reprogramming, which advance our understanding of the mechanisms associated with in utero exposure to BPA-induced breast cancer risk. The models also support using MMTV-erbB2 mouse model for relevant studies.	Int J Mol Sci Vol.21 Issue 9	10.3390/ijms21093095	32353937	動物	-	1	0	1	0	1	ex. 500 ng/kg、250 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1126	X. Ma, Y. Wang, W. Li, K. Wang and S. Zhang	2024	Bisphenol A Disrupts Ribosome Function during Ovarian Development of Mice	This study examines the impact of Bisphenol A (BPA), a prevalent environmental microgenic toxicant, on the ovarian development of mice. Mice were exposed to varying BPA doses from in utero to prenatal stages, up to 8 weeks of age. Ovarian tissues were analyzed using RNA-seq, revealing significant BPA-induced changes in gene expression. Notably, BPA exposure led to a dose-dependent increase in PND21 ovary significantly increased, and the number of corpus luteum in ova, damaged ovarian BPA. In contrast, the mice with PND 56 did not show apparent ovarian injuries. On the other hand, ribosome-related genes were detected in both PND21 and PND 56 mice ovaries, and EIF4 was increased under the influence of BPA. Transcriptomic analysis revealed BPA's significant impact on ribosomal gene expression, marked downregulation of Rpl13 and Rpsa, and upregulation of Rpl13 in both age groups. These transcriptomic alterations were further corroborated by real-time PCR, highlighting a dose-dependent effect of BPA on Rpsa. Our findings confirm BPA's detrimental effects on ovarian health, with more pronounced damage in younger mice, suggesting heightened vulnerability in this group. The study underscores ribosomes as critical targets in BPA-induced ovarian developmental disruptions.	Toxics. 2024 Aug 26;12(9):627.	10.3390/toxics12090627	39330555	動物	卵巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-
統合_1127	Q. Ma, P. Deng, M. Lin, L. Yang, L. Li, L. Guo, L. Zhang, M. He, Y. Lu, H. Pi, Y. Zhang, Z. Yu, C. Chen and Z. Zhou	2021	Long-term bisphenol A exposure exacerbates diet-induced prediabetes via TLR4-dependent hypothalamic inflammation	Bisphenol A (BPA), an environmental endocrine-disrupting compound, has been revealed associated with metabolic disorders such as obesity, prediabetes, and type 2 diabetes (T2D). However, its underlying mechanisms are still not fully understood. Here, we provide new evidence that BPA is a risk factor for T2D from a case-control study. To explore the detailed mechanisms, we used two types of diet models, standard diet (SD) and high-fat diet (HFD), to study the effects of long-term BPA exposure on prediabetes. In 8-week-old mice, We found that BPA exposure for 12 weeks exacerbated HFD-induced prediabetic symptoms. Female mice showed increased body mass, serum insulin level, and impaired glucose tolerance, while male mice only exhibited impaired glucose tolerance. No change was found in SD-fed mice. Besides, BPA exposure enhanced astrocyte-dependent hypothalamic inflammation in both male and female mice, which impaired proopiomelanocortin (POMC) neuron functions. Moreover, eliminating inflammation by full-like receptor 4 (TLR4) knockout significantly ameliorated the adverse effects of BPA on the hypothalamus and diet-induced prediabetes. Taken together, our data revealed a key role for TLR4-dependent hypothalamic inflammation in regulating the effects of BPA on prediabetes.	J Hazard Mater. 2021 Jan 15:402:123926.	10.1016/j.jhazmat.2020.123926	33254826	動物	代謝	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない　　通格性評価（疫学）1：該当、0：該当しない　　通格性評価（in vitro）1：該当、0：該当しない　　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階評価への進め、当該時評価段階で除害に基づき除害。　　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1128	L. Ma, H. Yu, X. Wang, D. Li, Y. Zhang, X. Pei, Z. Duan and M. Ma	2020	The effects of maternal exposure to BPA during pregnancy on the male reproductive system and the testicular microRNA expression profile	The effect of prenatal bisphenol A (BPA) exposure is increasingly concerned. We investigated the effect of maternal BPA exposure during pregnancy on male offspring and its potential mechanism. Thirty pregnant Sprague Dawley (SD) rats were randomly divided into exposed and control groups. At PND30, the number of sperms, testicular hormones, and testicular tissue of the BPA-exposed group decreased, and testicular tissue structure damaged in offsprings. At GD20, the mRNA profile in the testis of male offspring was examined and the express ion levels of 26 deregulated mRNAs were validated by qRT-PCR. We found that miR-361-5p, miR-350a-3p, and miR-29b-2-5p had significantly different expression levels in the testis. These results suggest that maternal exposure to BPA can lead to differential changes in progeny mRNAs, which will provide direction for future in-depth mechanisms of reproductive injury.	Environ Sci Pollut Res Int. 2020 May;27(14):17290-17302.	10.1007/s11356-020-08156-x	32157532	動物	内分泌/精子/精巣	1	1	1	1	0	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1129	M. Luo, L. Li, M. Ding, Y. Niu, X. Xu, X. Shi, N. Shan, Z. Qiu, F. Fiao and C. Zhang	2023	Long-term potentiation and depression regulatory microRNAs were highlighted in Bisphenol A induced learning and memory impairment by microRNA sequencing and bioinformatics analysis	The mechanisms of Bisphenol A (BPA) induced learning and memory impairment have still not been fully elucidated. MicroRNAs (miRNAs) are endogenous, non-coding small RNA molecules involved in the process of transient historical neuroplasticity. To investigate the role of miRNAs in BPA-induced learning and memory impairment, we analyzed the impacts of BPA on miRNA expression profile by high-throughput sequencing in mice hippocampus. Results showed that mice treated with BPA displayed impairments of spatial learning and memory and changes in the expression of miRNAs in the hippocampus. Numerous miRNAs were significantly differentially expressed after BPA exposure, of these, 13 and 5 miRNAs were up- and downregulated, respectively. Bioinformatic analysis of Gene Ontology (GO) and pathway suggests that BPA exposure significantly influenced long-term potentiation (LTP) and long-term depression (LTD) related genes and pathways, including glutamatergic synapse, calcium signaling pathway, cAMP signaling pathway, GABAergic synapse, LTP signaling pathway, LTD signaling pathway, G protein-coupled receptor, Eight BPA-responsive differentially expressed miRNAs targeting LTP and LTD were further screened to validate the miRNA sequencing data using Real-Time PCR. The deregulation expression levels of proteins of five target genes (CaMKII, MAPK1/3, PTEN, AMPAR, and PLC-β3) were investigated via western blot, for further verifying the results of gene target analysis. Our results revealed that LTP and LTD related miRNAs and their targets could contribute to BPA-induced impairment of learning and memory. This study provides valuable information for novel miRNA biomarkers to detect changes in impairment of learning and memory induced by BPA exposure.	PLoS One. 2023 Jan 19;18(1):e0279029.	10.1371/journal.pone.0279029	36656826	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-
統合_1130	L. Luo, Y. Chen, Q. Ma, Y. Huang, L. Xu, K. Shu, Z. Zhang and Z. Liu	2024	Ginger volatile oil inhibits the growth of MDA-MB-231 in the bisphenol A environment by altering gut microbial diversity	To examine the impact of ginger volatile oil (GVO) on the growth of MDA-MB-231 breast cancer cells in the presence of bisphenol A (BPA) by modulating the diversity of gut microbiota. METHODS: MDA-MB-231 breast cancer cells were injected subcutaneously into the right armpit of female BALB/c Nude (nu/nu) mice to create a triple-negative breast cancer model. Thirty nude mice were randomly divided into 5 groups: control group, BPA group, BPA + GVO (0.1 g/kg) group, BPA + GVO (0.2 g/kg) group, and BPA + GVO (0.4 g/kg) group. The mice were gavaged with BPA (50 mg/kg/day) and/or GVO (0.1, 0.2, 0.4 mg/kg/day) or given by gastric once a day for 3 weeks. At the end of the experiment, the changes of tumor mass and tumor volume were observed and compared in 5 groups of nude mice bearing mice. High-throughput sequencing (16S rRNA) was used to detect the changes of gut microflora in each group. RESULTS: The volume and weight of breast cancer decreased in the low, medium and high dose groups of GVO. Among them, the difference between the high dose group and the BPA group reached a significant level (P < 0.05). The success and abundance of gut flora decreased following BPA treatment, but increased after combined treatment of BPA and GVO. In the tumor control group, the ratio of Firmicutes/F) and Bacteroidetes/B) increased by over 0.3362 That the phylum level, while the ratio of BPA group further decreased 0.5363.80. After feeding GVO, the number of Lactobacillus, Ruminococcus, Bacteroides increased. the F/B ratio increased, and the level of Lactobacillus and Ruminococcus increased. In the BPA and GVO treatment group, the intestinal microbiota structure was still membrane fragments, multicellular transport and metabolism. This is followed by some work changes and interaction, and immunization function. After GVO administration the Even positive bacteria (G+) cells had an increasing trend and the Even negative bacteria (G-) tests had a decreasing trend. CONCLUSION: The species and abundance of gut flora decreased following BPA treatment, but increased after combined treatment of BPA and GVO.	Heliyon Vol.10 Issue 2 Pages e24388	10.1016/j.heliyon.2024.e24388	38298688	動物	-	1	1	1	Malls/Sr-mal/mu　NOG	0	0.2 mg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1131	D. Luo, X. Tang, Y. Wang, S. Ying, Y. Hu, H. Liu, P. A. Khosa and S. Li	2024	Selenium deficiency exacerbated Bisphenol A-induced intestinal toxicity in chickens: Apoptosis and cell cycle arrest mediated by ROS/P53	Bisphenol A (BPA) is a phenolic organic synthetic compound that is used as the raw material of polycarbonate plastics, and its safety issues have recently attracted wide attention. Selenium (Se) deficiency has gradually developed into a global disease affecting intestinal function via oxidative stress and apoptosis. However, the toxic effects and potential mechanisms of BPA exposure and Se deficiency in the chicken intestines have not been reported. In this study, 1-day-old male broilers were randomly divided into four groups: control group, Se deficiency group, BPA group, and Se deficiency + BPA group. The results showed that Se deficiency aggravated BPA-induced intestinal damage, as evidenced by the disturbed tissue morphological structure, serum D-lactic acid, diamine oxidase activities, and DNA damage, activated PI3K pathway, and Caspase-dependent apoptosis, and induced apoptosis and cell cycle arrest. Using protein-protein molecular docking, we found a strong binding ability between P53 and peroxiredoxin proliferation-activated receptor γ coactivator 1, thereby regulating mitochondrial dysfunctional apoptosis. In addition, we used Se and/or L-cysteine and ebselen + Se in vitro intervention and found that Se and/or L-cysteine and ebselen + Se intervention reversed the aforementioned adverse effects. This study clarified the potential mechanisms by which Se deficiency exacerbates BPA-induced intestinal injury in chickens through reactive oxygen species/P53, which provides a new idea for the study of environmental combined toxicity of Se deficiency, and insights into animal intestinal health from a new perspective.	Sci Total Environ. 2024 Feb 25:913:169730.	10.1016/j.scitotenv.2023.169730	38160834	動物、in vitro	-	0	不明	不明	不明	0	0.05 g/kg	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1132	L. Lu, L. Shen, S. Cui, Y. Huang, Y. Gao, X. Zhu, G. Lu, C. Zhang and S. Zhuang	2023	Angiogenic Activity and Mechanism for Bisphenols on Endothelial Cell and Mouse: Evidence of a Structural-Selective Effect	Increased epidemiological evidence indicates the association of bisphenol exposure with human vascular disorders, while the underlying mechanism has not been clarified. Here, we sought to unveil the potential angiogenic activity and mechanism for bisphenols (BPs) with different structures. Bisphenol A (BPA) and bisphenol S (BPS) at a concentration of 1 nM to 10 μM significantly increased the migration of EA.hy926 cells and CTCW. Bisphenol AF (BPAF) at 1 nM to 10 μM significantly increased the migration of EA.hy926 cells and CTCW. Bisphenol AF (BPAF) at 1 nM to 10 μM significantly increased the migration of EA.hy926 cells and CTCW. At doses of 0.002, 0.2, and 20 μg/kg/day for the 5 weeks, Bisphenol A (BPA) and bisphenol S (BPS) at 0.2 and 20 μg/kg/day significantly increased both the number and length of blood vessels in the mesenteral spreading, while later length and increased spreading were significantly inhibited by 17.2 and 65.7% after exposure to tetrabromobisphenol S (TBBPS) at 1 μg/kg/day, respectively. Mechanistically, TBBPS and BPAF significantly inhibited the interaction between thyroid hormone receptor β (TRβ) and thyroid receptor (TR), while BPA and BPS exhibited the reversed interaction. TRβ, while BPA and BPS exhibited the reversed interaction. TRβ, while BPA and BPS exhibited the reversed interaction between TRβ and thyroid receptor (TR), resulting in abnormal PI3K signaling with consequent distinct angiogenic activity. BPA- and BPS-induced pan-angiogenic effects and TBBPS-induced anti-angiogenic effects due to their distinct disruption on the TRβ/β-PI3K pathway. Our work provided new evidence and mechanistic insight on the angiogenic activity of bisphenols and expanded the scope of endocrine disruptors with interference in vascular homeostasis.	Environ Sci Technol. 2023 Aug 15;57(32):11803-11813.	10.1021/acs.est.3c03883	37505069	動物	血管障害	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1133	D. López-Rodríguez, D. Franssen, E. Sawin, A. Gérard, C. Balcat, S. Blacher, A. Noël and A. S. Parent	2019	Persistent vs Transient Alteration of Folliculogenesis and Estrous Cycle After Neonatal vs Adult Exposure to Bisphenol A	Exposure to bisphenol A (BPA), a ubiquitous endocrine-disrupting chemical (EDC), is known to produce variable effects on female puberty and ovulation. This variability of effects is possibly due to differences in dose and period of exposure. Little is known about the effects of adult exposure to environmentally relevant doses of this EDC and the differences in effect after neonatal exposure. This study sought to compare the effects of neonatal vs adult exposure to a very low dose or a high dose of BPA to 2 weeks on ovulation and folliculogenesis, and to explore the hypothalamic mechanisms involved in such disruption by BPA. One-day-old and 90-day-old female rats received daily subcutaneous injections of corn oil (vehicle) or BPA (10 μg/kg/d or 50 mg/kg/d) for 15 days. Neonatal exposure to both BPA doses significantly disrupted the estrous cycle and induced a decrease in primordial follicles. Effects on estrous cyclicity and folliculogenesis persisted into adulthood, consistent with a disruption of organizational mechanisms. During adult exposure, both doses caused a reversible disruption of the estrous cycle and a decrease in the number of corpora lutea, without affecting folliculogenesis. Only the high dose of BPA increased the number of antral follicles. No effect was also observed. Alterations of the hypothalamic expression of the clock gene Per1 and the reproductive peptide phoenixin indicated a disruption of the hypothalamic control of the periodicity (1/4 days) by BPA.	Endocrinology Vol.160 Issue 11 Pages 2558-2572	10.1210/en.2019-00505	31503316	動物	-	1	0	1	不明	0	25 mg/kg/31　5 mg/kg/31	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1134	D. López-Rodríguez, C. F. Ayhan, V. Delli, E. Sawin, M. Campanile, M. Mahfi, D. Franssen, A. Gérard, S. Blacher, E. Tirelli, A. Noël, A. Lumeij and A. S. Parent	2021	Multi- and Transgenerational Outcomes of an Exposure to a Mixture of Endocrine-Disrupting Chemicals (EDCs) on Puberty and Maternal Behavior in the Female Rat	BACKGROUND: The effects of endocrine-disrupting chemicals (EDCs) on fertility and reproductive development represent a rising concern in modern societies. Although the neuroendocrine control of sexual maturation is a major target of EDCs, little is known about the potential role of the hypothalamus in puberty and ovulation disruption transmitted across generations. OBJECTIVES: We hypothesized that developmental exposure to an environmentally relevant mixture of EDCs would induce transgenerational disruptions of the hypothalamic mechanisms involved in female puberty and maternal behavior. METHODS: We investigated the transmission of a disrupted reproductive phenotype via the maternal germline or via epigenomic mechanisms, involving maternal care. METHODS: Adult female Wistar rats were exposed prior to and during gestation and until the end of lactation to a mixture of the following: DEHP, di-n-butyl phthalate (DnBP), di(2-ethylhexyl) phthalate (DEHP), bisphenol A (BPA), vinclozolin, prochloraz, procymidone, linuron, iprodione, 4,4'-dichlorodiphenyldichloroethylene, and methoxychlor. F1 (embryo/fetus exposed), F2 (germline exposed), and F3 (second-generation) females were studied across generations. RESULTS: Early exposure to EDCs induced a decrease in primordial follicles. Effects on estrous cyclicity and folliculogenesis persisted into adulthood, consistent with a disruption of organizational mechanisms. During adult exposure, both doses caused a reversible disruption of the estrous cycle and a decrease in the number of corpora lutea, without affecting folliculogenesis. Only the high dose of BPA increased the number of antral follicles. No effect was also observed. Alterations of the hypothalamic expression of the clock gene Per1 and the reproductive peptide phoenixin indicated a disruption of the hypothalamic control of the periodicity (~4 days) by BPA.	Environ Health Perspect Vol.129 Issue 8 Pages 87003	10.1289/ehp8795	34383603	動物	-	1	1	0	1	0	1.5 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1135	A. López-Moreno, A. Torres-Sánchez, A. Suárez, A. Ruiz-Rodríguez and M. Aguilera	2025	Perinatal bisphenol A exposure impairs gut microbial colonization: Implications for offspring obesity and neurodevelopment	Exposure to plasticizer xenobiotics such as BPA has emerged as a significant health challenge due to globalized and industrial packaged food production. Toxicological approaches in animal models have revealed complex effects, using variable doses of BPA, on reproduction, development, obesity, immune function, metabolic and systemic toxicity. Recently, gut microbiota has emerged as a key player in regulating the impact of xenobiotic exposure on host metabolism. The effect that BPA may exert on the gut microbiota and its consequences for the host's health remains unclear. Exposure to BPA during the perinatal period requires special attention and characterization, as it is a critical window for microbiota establishment and host development. Therefore, this study aimed to evaluate the impact of BPA exposure during the perinatal period on the establishment of the gut microbiota and its relationship with the offspring's metabolic and neurobehavioral phenotype. Female Wistar rats were exposed to BPA (50 mg/kg/day) via drinking water during the perinatal period (preconception, gestation, and lactation). Offspring were analyzed at postnatal day 21 (PND21, weaning) and PND70 (adulthood), after administered BPA, and the increase in weight and fat accumulation, the gut microbiota composition, and the cognitive development of the offspring were analyzed. In addition, a high-fat diet (HFD) was given to the mice two to the synergistic obesogenic effect of BPA. Our results demonstrated that BPA exposure impaired the natural remodeling of the gut microbiota during pregnancy. For instance, Ruminococcus and Prevotellaceae decreased during natural remodeling of the gut microbiota during pregnancy, but they did not change in the BPA-exposed pregnant mice. Conversely, several members of the Eubacteriaceae genus increased during normal pregnancy, but BPA exposure prevented this increase. Moreover, BPA exposure altered the microbiota composition of the offspring, with significant changes observed in the abundance of Lactobacillus in the offspring. Perinatal BPA exposure impaired changes during colonization and maturation process of the offspring gut microbiota. Identifying Lactobacillus, Eubacterium and Escherichia-Shigella as signature genera enriched in BPA and BPA-exposed mice fed with HFD, was involved in a more efficient at energy harvesting from the diet. Moreover, perinatal BPA exposure seemed to alter fat and lean percentages and triggered Escherichia-Shigella overgrowth. Escherichia-Shigella overgrowth was associated with increased activity, spatial learning, and memory, mimicking impulsivity and hyperactivity-like behavior in the offspring. In conclusion, BPA exposure and HFD exert an influence on the vertical transfer of gut microbiota from mothers to offspring and drive towards an altered establishment of gut microbiota-brain in early life, contributing to enhancing susceptibility to obesity and behavioral disorders.	Ecotoxicol Environ Saf Vol.298 Pages 118295	10.1016/j.ecoenv.2025.118295	40349470	動物	-	1	1	1	1	0	100 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1136	A. López-Montoya, A. Sosa-Aristizi, M. Colorado-Zuñiga, E. Méndez-Bolaina, I. Torres-Montero and A. Ramos-Ligonio	2025	Exposure to Bisphenol-A increases susceptibility to Trypanosoma cruzi infection	Bisphenol-A (BPA), an endocrine disruptor, disrupts hormonal and chemical signaling within the body, negatively impacting health. One target of this disruption is the immune system. While BPA has been implicated in increased susceptibility to some pathogen infections, its effects on protozoan parasite infections remain understudied. This work evaluated the effect of BPA exposure on experimental Trypanosoma cruzi parasitemia in BALB/c mice. Female mice were exposed to BPA (50 mg/kg/day) via drinking water for 21 days before infection with T. cruzi. Parasitemia was monitored by microscopy and confirmed by RT-PCR, and liver tissue was examined using histomorphometric methods. Body-wet- and spleen weights in BPA-treated parasitemia during T. cruzi infection and decreased levels of IgG2a, IgG1a, and IgG2b isotypes. Furthermore, BPA modulated the expression of pro-inflammatory cytokines in response to infection. In addition, all mice exposed to BPA showed alterations in liver enzymes compared to the control group. These results demonstrated that the immune system during critical periods of T. cruzi infection is highly sensitive to BPA exposure, increasing susceptibility to the parasite.	Exp Parasitol. 2025 Aug:275:108990.	10.1016/j.exppara.2025.108990	40714029	動物	免疫	1	1	1	1	0	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1137	Z. Long, J. Fan, G. Wu, X. Liu, H. Wu, J. Liu, Y. Chen, S. Su, X. Cheng, Z. Xu, H. Su, M. Cao, C. Zhang, C. Hei and X. Wang	2021	Gestational bisphenol A exposure induces fatty liver development in male offspring mice through the inhibition of HNF1b and upregulation of PPARγ	Bisphenol A (BPA) is an endocrine-disrupting chemical (EDC) associated with non-alcoholic fatty liver disease (NAFLD). The effects of gestational BPA exposure on hepatic lipid accumulation in offspring are not fully understood. Here, we investigated the sex-dependent effects of gestational BPA exposure on hepatic lipid and glucose metabolism in the offspring of mice to reveal the mechanisms underlying gestational BPA exposure-associated NAFLD. Pregnant mice were administered gavage with or without 1 μg kg(-1) day(-1) BPA at embryonic day 7.5 (E7.5)-E18.5. Hepatic glucose and lipid metabolism were evaluated in these models. Both male and female offspring mice exhibited hepatic fatty liver after BPA treatment. Lipid accumulation and glucose metabolism were observed in male offspring. We then observed aberrant activation of lipid regulators in the liver and bad inhibition of peroxisome proliferator-activated receptor γ (PPARγ) repressed hepatic lipid accumulation induced by gestational BPA exposure. We also found a sex-dependent decrease of hepatocyte nuclear factor 1 homeobox B (HNF1b) in male offspring mice after BPA exposure. Moreover, HNF1b knockdown in HepG2 cells and primary hepatocytes from male offspring mice aggravated BPA-induced hepatic lipid accumulation and glucose metabolism. Mechanistically, HNF1b deficiency promoted PPARγ transcription by increasing the binding of hepatocyte nuclear factor 4 alpha (HNF4α) to the PPARγ promoter. Gestational BPA exposure induced NAFLD in male offspring. These data provide new insights into the mechanism of gestational BPA exposure-associated sex-dependent glucose and lipid metabolic dysfunction. Graphical abstract Schematic of the mechanism of gestational BPA exposure-induced glucose and lipid metabolic dysfunction.	Cell Biol Toxicol. 2021 Feb;37(1):65-84.	10.1007/s10565-020-09535-3	32623698	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-
統合_1138	Z. Liu, M. Liu, H. Wang, P. Qin, Y. Di, S. Jiang, Y. Li, L. Huang, N. Jiao and W. Yang	2024	Glutamine attenuates bisphenol A-induced intestinal inflammation by regulating gut microbiota and TLR4-p38/MAPK-NF-κ B pathway in piglets	Bisphenol A (BPA), as a kind of widely exerted environmental hazardous material, brings toxicity to both humans and animals. This study aimed to investigate the role of glutamine (Gln) in intestinal inflammation and microbiota in BPA-challenged piglets. Thirty two piglets were randomly divided into two groups according to 2 factors including BPA (0 or, 0.1%) and Gln (0 or, 1%) supplemented in basal diet for a 21-day feeding experiment. The results showed BPA exposure impaired piglets' growth performance and disrupted intestinal morphology. Dietary Gln supplementation alleviated the above BPA-induced intestinal dysfunction, while decreasing serum pro-inflammatory cytokine levels in BPA-challenged piglets. In addition, Gln attenuated intestinal mucosal damage and inflammation by remodeling the activation of toll-like receptor 4 (TLR4)-p38/mitogen-activated protein kinase (MAPK)-nuclear factor kappa-B (NF-κB) signaling pathway. Moreover, Gln supplementation altered the composition of gut microbiota, characterized by increased abundances of Bacteroidetes, Prevotella, Ruminococcus and Prevotellaceae and the content of short-chain fatty acids in cecum contents caused by BPA exposure. Moreover, there existed potential relevance between the gut microbiota and pro-inflammatory cytokines and cecal short-chain fatty acids. In conclusion, Gln is critical nutrition for attenuating BPA-induced intestinal inflammation, which is partially mediated by regulating microbial balance and suppressing the TLR4/p38/MAPK/NF-κ B signaling.	Ecotoxicol Environ Saf Vol.270 Pages 115836	10.1016/j.ecoenv.2023.115836	38154151	動物	-	1	1	0	Gram + cocci/rods + Trichoma	0	500 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1139	X. Liu, L. Zeng, X. Liu, Y. Zhou, G. Rang and M. Wang	2025	Targeted Metabolomics and Widely Targeted Quantitative Lipidomics Reveal Synergistic Metabolic Interference in Adipose Tissue After the Combined Chronic Exposure to Bisphenol A Substitutes, Bisphenol S and Bisphenol F, and Fructose in Male Rats	The combined effect of environmental exposure and dietary behavior plays a vital role in the occurrence of diseases. Bisphenol S (BPS) and bisphenol F (BPF) are the most commonly used substitutes for bisphenol A (BPA). Previous studies have demonstrated the combined exposure to BPS and fructose caused significant disorders of glycolipid metabolism in adipose tissue. However, the interference caused by the combined exposure to BPS and fructose or BPF and fructose on adipose tissue is still unclear. In the present study, we performed a integrated analysis of targeted energy metabolomics and widely targeted quantitative lipidomics to investigate the effects of BPS combined with fructose and BPF combined with fructose on the adipose tissue of male rats. The results showed that the body weight gain and the adipose coefficient of rats exposed to BPS combined with fructose or BPF combined with fructose increased significantly, while higher dose BPS or lower dose BPF combined with fructose also caused severe injuries significantly. Additionally, the levels of BPS combined with fructose might lead to polyunsaturated lipid depletion, while higher dose BPS combined with fructose might lead to choline and carnitine depletion. Lower dose BPF combined with fructose might inhibit fatty acid oxidation, while higher dose BPF combined with fructose might cause accumulation of free fatty acids. These results indicated the response patterns of adipose tissue to different doses of BPS or BPF combined with fructose were significantly different, and the adipocyte sucrose signaling pathway might be the important target for metabolic remodeling in adipose tissue.	J Biochem Mol Toxicol Vol.39 Issue 8 Pages e70440	10.1002/jbt.70440	40787705	動物	-	1	1	1	1	0	0.25、25 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1140	X. Liu, Z. Wang and F. Liu	2021	Chronic exposure of BPA impairs male germ cell proliferation and induces lower sperm quality in male mice	BACKGROUND: Bisphenol A (BPA) is a well-known endocrine disruptor that affects male fertility. However, the main biological events through which BPA affects spermatogenesis remain to be identified. METHODS: Adult male mice were treated by feeding with drinking water containing BPA (0.2 μg/ml, 20 μg/ml, 200 μg/ml, respectively) for two months. Testes were collected for detection of testosterone levels. Proteins associated with germ cell proliferation were detected by immunohistochemistry and western blot analysis. Epididymal spermatozoa were collected for sperm quality evaluation and male fertility assay by in vivo fertility. RESULTS: Serum testosterone levels and cauda epididymal sperm counts were significantly decreased in BPA-treated mice. Cell proliferation was decreased in BPA-treated testes, as evidenced by the decreased PCNA and Ki-67 expression in SC-1 cells. TM3 cells. The BPA-treated mice were characterized by decreased sperm quality, serum testosterone levels and, cauda epididymal phenotype characterizing with low pregnancy rates, and reduced fertilization efficiency. In term BPA (0.2 μg/ml) treatment, PCNA and PLZF were down-expressed that indicated impaired germ cell proliferation. STAT3 was down-expressed in BPA-treated mice, but expressions of other proteins associated with meiosis and blood-testis barrier were not significantly altered. CYP11A1 and HSD3B1 were down-expressed in BPA-treated mice that demonstrated reduced steroidogenesis activity. BPA has a concentration-dependent inhibition effect on the proliferation of SC-1 and SC-2 cells. Conclusively, low doses BPA exposure reduced mice sperm quality mainly by impacting germ cell proliferation, leading to reduced male fertility. The study could provide relevant information for investigation on molecular mechanisms and potential therapy on male reproduction.	Chemosphere. 2021 Jan:262:127880.	10.1016/j.chemosphere.2020.127880	32777607	動物	内分泌/精子/精巣	1	1	1	1	1	----------	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1141	X. Liu, G. Li, J. Zhong, G. Rong, G. Ou, X. Qin, Y. Tang and M. Wang	2023	Impact of combined chronic exposure to low-dose bisphenol A and fructose on serum adipocytokines and the energy target metabolome in white adipose tissue	Background: Adipose tissue is a dynamic endocrine organ that plays a key role in regulating metabolic homeostasis. Previous studies confirmed that bisphenol A (BPA) or fructose can interfere with the function of adipose tissue. Nonetheless, knowledge on how exposure to BPA and fructose impacts energy metabolism in adipose tissue remains limited.Purpose: To determine impact of combined chronic exposure to low-dose bisphenol A and fructose on serum adipocytokines and the energy target metabolome in white adipose tissue.Method: 67 energy metabolic intermediates in adipose tissue and 7 adipocytokines in serum from Sprague Dawley rats exposed to environmentally relevant doses of BPA (0, 0.5, 5, and 50 μg/kg/day) and/or 10% fructose in drinking water for 90 days were analyzed by a targeted metabolomics approach. Results: Exposure to BPA significantly increased ceramide-1-phosphate, sphingosine-1-phosphate, succinic acid, adenosine triphosphate (ATP), adenosine monophosphate (AMP), leucine, and isoleucine. However, these parameters were not significantly affected by higher dose BPA combined with fructose. Interestingly, the level of succinate (an intermediate of the citric acid cycle) increased dose-dependently in adipose tissue, and the level of apelin-13 (a versatile adipocytokine) decreased dose-dependently in serum after combined exposure to BPA and fructose. The mechanistic analysis revealed that succinate, and apelin-13 were significantly correlated with apoptosis, ceramide-1-apelin-13, and adiponectin, while tyrosine was significantly correlated with citric acid.FINDP under combined exposure to BPA and fructose.Conclusions: these findings indicated that lower dose BPA combined with fructose could exacerbate the impact on glycolysis, energy storage, and some nucleotide biosynthesis. In adipose tissue, and adipokines/cytokines, such as ceramide-1-and apelin-13, may be related to metabolic interference induced by BPA and fructose exposure.	Hum Exp Toxicol Vol.42 Pages 9603271231271992	10.1177/09603271231271992	37990541	動物	-	1	不明	不明	1	0	0.25、25 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1142	R. Liu, B. Liu, L. Tian, X. Wu, X. Li, D. Cai, X. Jiang, J. Sun, Y. Jin and W. Bai	2023	Induction of reproductive injury by bisphenol A and the protective effects of cyanidin-3-O-glucoside and protocatechuic acid in rats	Bisphenol A (BPA) has attracted growing attention as a well-known environmental pollutant due to its high risk of male reproductive toxicity. In this study, transcriptomics profiling combined with metabolomic techniques was applied to explore the intervention effects of BPA-induced male reproductive toxicity. We demonstrated that cyanidin-3-O-glucoside (C3G) and its main metabolite protocatechuic acid (PCA) significantly increased testosterone and luteinizing hormone (LH) levels in the serum of rats, and improved spermatozoa quality. Furthermore, we identified and screened differentially expressed genes (DEGs) and metabolites (DMs) that functionally enriched in steroid hormone biosynthesis, PPAR signaling pathway, and fatty acid metabolism. Among them, Cyp11a1, Cyp17a1, Hsd3b1, Hsd3b6, Hsd17b3, Scarb1, and Acsl 1 were key DEGs, while C20:4 and PC18:4 dramatically elevated and were key DMs in the metabolic network. Moreover, BPA exposure induced oxidative stress, and cell cycle arrest caused by BPA. In addition, molecular docking and correlation results implied that C3G and PCA competitively acted on BPA binding to the estrogen receptors α and β. ERα and ERβ and shared common key amino acids. The main interaction modes between small molecules and estrogen receptors included π–π stacking, salt bridges, hydrogen bonds, and hydrophobic interactions. Therefore, our study sheds light on C3G and PCA supplementation can protect male reproduction from BPA-induced injury.	Sci Total Environ. 2023 Jul 20:883:163615.	10.1016/j.scitotenv.2023.163615	37105472	動物	生殖ホルモン	1	1	1	1	0	0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1143	R. Liu, B. Liu, L. Tian, X. Jiang, X. Li, D. Cai, J. Sun, W. Bai and Y. Jin	2022	Exposure to Bisphenol A Caused Hepatotoxicity and Intestinal Flora Disorder in Rats	Bisphenol A (BPA) is a globally utilized industrial chemical and is commonly used as a monomer of polycarbonate plastics and epoxy resins. Recent research reveals that BPA could cause potential adverse biological effects and liver dysfunction. However, the underlying mechanisms of BPA-induced hepatotoxicity and gut dysbiosis remain unclear and deserve further study. In this study, male Sprague Dawley rats were exposed to BPA (0, 10, 50, and 270 mg/kg) for 90 days. Our results showed that BPA significantly increased the serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) levels. Moreover, a high dose of BPA caused significant increases in serum alanine aminotransferase (ALT), total cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-C), while high-density lipoprotein-cholesterol (HDL-C) was significantly decreased in BPA-treated rats. The gene expression of PXR (i.e. Nr1i2) and Nr1i3 were decreased in the liver of high doses of BPA-administrated rats, as well as the protein levels of SIRT1, PXR (i.e. Nr1i2), and TP-53B. However, the protein expression of IL-1β and TNF-α was significantly increased in BPA-treated rats. In addition, BPA exposure altered the intestinal microbiota in hepatocytes and promoted cell apoptosis. In the liver by up-regulating the protein levels of Bax, cleaved Caspase3, and cleaved PARP1, while down-regulating the Bcl-2 in the liver. More importantly, a high dose of BPA significantly altered the composition of the intestinal microbiota. BPA at high doses led to increases in the relative abundance of Firmicutes to Bacteroidetes (F/B), and the relative abundance of Proteobacteria, while decreased the relative abundance of Prevotella. 9 and Ruminococcus_1 at the genus level by increasing the abundance of Escherichia-Shigella. Our results suggest that C3G has an effective regulatory effect on BPA-induced disorder of lipid metabolism.	Int J Mol Sci Vol.23 Issue 14	10.3390/ijms23148042	35887390	動物	-	1	1	1	1	1	10、 90、 270 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1144	R. Liu, Y. Jin, B. Liu, Q. Zhang, X. Li, D. Cai, L. Tian, X. Jiang, W. Zhang, J. Sun and W. Bai	2023	Untargeted Lipidomics Revealed the Protective Effects of Cyanidin-3-O-glucoside on Bisphenol A-Induced Liver Lipid Metabolism Disorder in Rats	Bisphenol A (BPA) is an estrogenic endocrine disruptor that induces metabolic disorders. Cyanidin-3-O-glucoside (C3G) has multiple functional activities and is the most abundant anthocyanin belonging to the flavonoid family. Protocatechuic acid (PCA) is the primary metabolite of C3G. This study aimed to explore the protective effects of C3G and PCA on BPA-induced liver lipid metabolism disorder. The results showed that C3G significantly ameliorated the serum levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total cholesterol, triacylglycerol, and glucose and serum enzymes (ALT and AST). Furthermore, liver lipidomics indicated that C3G effectively facilitated the recovery of differential lipid metabolites, including TGs, phosphatidylethanolamines, phosphatidylcholines, lysophosphatidylcholines, phosphatidylinositol, cholesterol esters, and phosphatidylserines, and reversed the levels of hepatic lipid synthesis-related genes. Our results suggest that C3G has an effective regulatory effect on BPA-induced disorder of lipid metabolism.	J Agric Food Chem. 2023 Jan 18;71(2):1077-1090.	10.1021/acs.jafc.2c06849	36597173	動物	代謝	1	1	1	1	0	0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1145	L. Liu, H. Cui, Y. Huang, Y. Zhou, J. Hu and Y. Wan	2022	Enzyme-Mediated Reactions of Phenolic Pollutants and Endogenous Metabolites as an Overlooked Metabolic Disruption Pathway	It is generally recognized that phenol-containing molecules rapidly undergo phase II metabolic reactions, whereas glucuronide and sulfate are conjugated to form water-soluble products. Here, we report direct reactions of bisphenol A (BPA) and its halogenated analogs (BPC, BPF, BPS, and TBBPA) with endogenous metabolites catalyzed by human peroxidases. Using BPA as a model, the oxidation of bisphenol A catalyzed by a model peroxidase, horseradish peroxidase, was used to identify the products. Human liver microsomes incubations, and the newly elucidated enzyme, MPO-5-OH, was found in in vivo exposure to mice. MPO-5-OS were frequently detected in urine from the general population at levels comparable to those of glucuronide/sulfate conjugated BPA. Recombinant human cytochrome P450s were applied to find that CYP1A2 catalyzed the formation of three newly discovered nitro-metabolites by binding the NO2 hydroxyl group to the BPA phenolic ring, leading to the significantly retained endocrine-disrupting activities of BPA (0.1%–1%) compared to ERα. The effects of the reaction on the homeostasis of reactive/antioxidants were finally assessed by in vitro assay and in vivo mice exposure. The generation of BPA-O-10% decreased the GT concentrations and increased the reactive oxygen species generation after exposure to BPA at environmentally relevant concentrations. The identified reactions provided an overlooked metabolic disruption pathway for phenolic pollutants.	Environ Sci Technol. 2022 Mar 15;56(6):3634-3644.	10.1021/acs.est.1c08141	35235842	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1146	K. Liu, S. Kadarmagati, J. Danzler, S. Pathak, K. L. Abbott, J. M. Sabatini, S. B. Pondugula, B. T. Akingbemi and M. Dhanasekaran	2023	Effects of developmental exposures to Bisphenol-A and Bisphinol-S on hepatocellular function in male Long-Evans rats	Bisphenol S (BPS) is a current substitute for Bisphenol A (BPA) in various commercial products (paper, plastics, protective can coatings, etc.) used by all age groups globally. The current literature indicates that a drastic increase in the consumption of BPS has occurred in response to the restrictions placed on the use of BPA in consumer products. Although BPS is considered a safer alternative to BPA, there are increasingly public health concerns that substituted Bisphenol-mediated effects may impact hepatocellular function, particularly in sensitive exposures to BPA and BPS perinatally. However, the acute perinatal impact of BPS and BPA and the molecular mechanisms affecting hepatocellular functions are unknown. Therefore, the current study investigated the acute perinatal effect of BPA and BPS on the biomarkers of hepatocellular functions, including oxidative stress, inflammation, apoptosis, and mitochondrial activity in male Long-Evans rats. BPA and BPS (Low (0.4 mg/kg/day) and High (4 mg/kg/day)) were administered to SD dams by oral gavage from gestational day (GD) 6 to GD 20. Male offspring were euthanized on postnatal day (PND) 1. Liver tissues were collected for histological analysis. Results indicated that BPS is effectively absorbed in the gastrointestinal tract without crossing the blood-brain barrier. Likewise, BPA crosses the blood-brain barrier and is not a substrate of p-Glycoprotein and Cytochrome P450 enzymes. Thus, the current in vitro and in vivo findings revealed that acute perinatal exposure to BPS had no significant hepatotoxicity.	LiNe Sci Vol.326 Pages 122752	10.1016/j.lfs.2023.121752	37172818	動物	-	1	1	1	1	0	4、20 μg/L（胎仔中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1147	J. Liu, M. Liao, R. Huang, Y. You, X. Lin, H. Yang, L. Fan, Y. Zhong, X. Li, J. Li and X. Xiao	2022	Perinatal Combinational Exposure to Bisphenol A and a High-Fat Diet Contributes to Transgenerational Dysregulation of Cardiovascular and Metabolic Systems in Mice	Both bisphenol A (BPA) and high-fat diet (HFD) exert unfavorable effects on animals and humans; moreover, they could affect the health of their offspring. BPA and HFD often coexist in modern lifestyles; however, the long-term effects of simultaneous exposure of mothers to BPA and HFD during the perinatal period on the cardiovascular and metabolic systems of the offspring remain unclear. This study aimed to examine the effect of simultaneous exposure of mothers to BPA and HFD on the risk of metabolic and cardiovascular abnormalities in offspring. Institute of Cancer Research female mice (F0) were exposed to BPA and fed with HFD before and during pregnancy. Male offspring (F1) were fed a normal diet after weaning. Male offspring (F2) were obtained by mating F1 males with normal females. Male offspring (F3) were obtained by mating F2 males with normal females (F3). Combined maternal exposure to BPA and HFD caused myocardial hypertrophy and aortic extra-medial thickening as well as increased the cross-sectional area of cardiomyocytes and blood pressure in the male F1 and F2 generation. These cardiovascular changes might be associated with reduced endothelial nitric oxide synthase (eNOS) levels. The sacrificed female F2 was more likely to be obese than the sacrificed male F2. Re-feeding with a HFD induced a more significant weight gain and reduced energy expenditure. However, the aforementioned effects were not observed with exposure to BPA alone during the perinatal period. Our findings suggest that perinatal combinational exposure to BPA and HFD could cause metabolic and cardiovascular disorders in the offspring. Further, our findings demonstrate that the synergistic effects of BPA and HFD could be transmitted to future generations in a sex-dependent manner.	Front Cell Dev Biol Vol.10 Pages 834346	10.3389/fcell.2022.834346	35281091	動物	-	1	1	1	不明	0	500 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1148	H. Liu, F. Liu, G. Wang, Y. Ma and L. Wang	2021	[Effect of the reactive oxygen species-induced by bisphenol A on liver lipid metabolism disorder]	OBJECTIVE: To explore the toxic effect of bisphenol A on the liver, as well as the influence of the on lipid metabolism.METHODS: The toxic effects of bisphenols on human health were studied by using in vivo experiments of bisphenol A exposure in rats and in vitro experiments of human liver cell line HL-7702. Male SD rats were divided into the control group(Con), 1 mg/(kg·d) group(Low), 5 mg/(kg·d) group(Medium) and 25 mg/(kg·d) group(High) for 12 days subacute exposure of bisphenol A, to evaluate the toxic effect of bisphenol A on the liver in terms of body weight, liver organ index, liver pathological changes, serum biochemical indicators. Then HL-7702 was divided into liver groups: control group(Con), low concentration treatment group(L), 10 μ mol/L, medium concentration treatment group(M), μ mol/L and high concentration treatment group(H), 100 μ mol/L, to evaluate the toxic effects of bisphenol A on liver cells in terms of cell viability, reactive oxygen species (ROS) level, and mitochondrial membrane potential (MMP). The results showed that bisphenol A exposure can damage liver tissue structure. Serum biochemical indicators of total bile acid(TBA) were significantly reduced in the high dose group, which was(0.76 ± 0.35) μmol/L, creatinine(Cr) was significantly increased in the medium and high dose group, which was(8.38 ± 0.78) μmol/L and(8.83 ± 0.78) μmol/L, respectively. TC, high-density lipoprotein(HDL-C) and low-density lipoprotein(LDL-C) were significantly reduced in the middle and high dose groups(P<0.05), which were(1.24 ± 0.17), (0.14 ± 0.02)mmol/L, (0.40 ± 0.05), (0.43 ± 0.07)mmol/L, and(1.11 ± 0.30), (0.14 ± 0.02)mmol/L, (0.40 ± 0.05), (0.43 ± 0.07)mmol/L, respectively. The results of in vitro experiments showed that the ROS level of HL-7702 cells in the high concentration group of bisphenol A(H) was significantly increased, and the mitochondrial membrane potential(MMP) was significantly decreased in the high concentration group(P<0.05). DISCUSSION: Bisphenol A may cause oxidative stress by inducing excessive ROS production in liver cells, leading to liver damage and disorder of lipid metabolism in the body, thereby causing liver toxicity.	Wai Sheng Yan Jiu. 2021 Mar;50(2):289-300.	10.19813/j.cnki.weishengyanjiu.2021.02.021	33985639	動物、in vitro	肝	-	1	1	1	0	0.01、10 mg/kg体重/日	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1149	B. Lirdlio-Pradillo, L. Rancan, S. D. Paredes, M. Schrupf, M. Lichtenberger, E. Vara and F. Tresguerres JA	2023	Low Dose of BPA Induces Liver Injury through Oxidative Stress, Inflammation and Apoptosis in Long-Evans Lactating Rats and Its Perinatal Effect on Female PND6 Offspring	Bisphenol A (BPA) is a phenolic compound used in plastics elaboration for food protection or packaging. BPA monomers can be released into the food chain, resulting in continuous and ubiquitous low-dose human exposure. This exposure during prenatal development is especially critical and could lead to alterations in the programming of tissues increasing the risk of developing liver pathologies in adulthood. The aim was to evaluate whether BPA administration (0.038 mg/kg b.w./day and 3.42 mg/kg b.w./day) in pregnant rats could induce liver injury by generating oxidative stress, inflammation and apoptosis, and whether these effects may be observed in female pups exposed due to PVMA offspring. Antioxidant enzymes (CAT, SOD, GR, GPx and GST), glutathione system (GSH/GSSG) and lipid (TBA) damage markers (MDA, LPO, 4d, 8-HAE) were measured using colorimetric methods. Indexes of oxidative stress (ROS 16, ROS, eNOS), inflammation (IL-1,β) and apoptosis (AIF, BAX, Bcl-2 and BCL-XL) were measured by qRT-PCR and Western blotting in liver of lactating dams and offspring. Hepatic serum markers and histology were performed. Low dose of BPA caused liver injury in lactating dams and had a perinatal effect in female PND6 offspring by increasing oxidative stress levels, triggering an inflammatory response and apoptosis pathways, in the organ responsible for detoxification of the endocrine disruptor.	Int J Mol Sci Vol.24 Issue 5	10.3390/ijms24054585	36902016	動物	-	1	1	1	1	0	0.038、 90 mg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1150	Y. Ling, X. Huang, A. Li, J. Zhang, J. Chen, J. Ren, Y. Liu and M. Xie	2023	Bisphenol A exposure induces testicular oxidative damage via FTO/m6A/Nrf2 axis during postnatal development in mice	Bisphenol A (BPA), a commonly used plasticizer in the production of polycarbonate plastics and epoxy resins, has been shown to induce male reproductive toxicity. However, the effects of BPA exposure on early testicular development have not been thoroughly studied, and the underlying mechanism is yet to be elucidated. In the current study, neonatal male mice were exposed to BPA at 0, 0.1, and 5 mg/kg, respectively, by daily administration from postnatal day (PND) 1 to PND 21. Our results showed that BPA exposure at 5 mg/kg significantly reduced the testis weight and the number of spermatogonia. BPA exposure significantly reduced expression of testicular cells (c-kit and α-1-GSK) and α-1-GSK2 and reduced the thickness of seminiferous epithelium (p < 0.01). In addition, BPA exposure significantly increased testicular antioxidant capacity by tests, and levels of transcription factor Nrf2 as well as its downstream antioxidant molecules of NQO1 and GPx 1 (p < 0.05 and p < 0.01). Furthermore, global m6A modifications of mRNAs were upregulated accompanied by decreased m6A demethylase FTO in the testes of BPA groups (p < 0.05 and p < 0.01). MeRIP quantitative real-time polymerase chain reaction (qPCR) demonstrated that BPA exposure markedly increased the m6A modification of Nrf2 mRNA (p < 0.05 and p < 0.01). These findings suggest that upregulation of m6A induced by inhibited FTO may be involved in BPA-induced testicular oxidative stress and developmental injury during prenatal development, which provides a new idea to reveal the mechanisms underlying BPA-interfering with testicular development.	J Appl Toxicol Vol.43 Issue 5 Pages 694-705	10.1002/jat.4417	36451259	動物	-	1	0	1	不明	1	0、 0.1、 5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1151	T. Lind, M. H. Lejonklou, L. Dunder, M. M. Kushnir, C. Ohman-Mägi, S. Larsson, H. Malhaug and P. M. Lind	2019	Developmental low-dose exposure to bisphenol A induces chronic inflammation, bone marrow fibrosis and reduces bone stiffness in female rat offspring only	BACKGROUND: Developmental exposure to low doses of the endocrine disruptor bisphenol A (BPA) is known to alter bone tissue in young rodents, although here bone tissue is affected in aged animals is not well known. We have recently shown that low dose developmental exposure to BPA increases preadipogen type I/III terminal propeptide (PINP) levels, a peptide formed during type I collagen synthesis, in plasma at 12 weeks old female rat offspring while male offspring showed reduced bone size. OBJECTIVE: To analyze offspring bone phenotype at 52 weeks of age and clarify whether the BPA-induced increase in PINP levels at 3 weeks is an early sign of BPA-induced bone pathology. METHODS: Female Wistar Han rats were exposed to BPA (0.5 or 50 μg/kg bw/day) or vehicle (corn oil) via gavage from gestational day 9 until weaning. Offspring were euthanized at 52 weeks of age. Bone mineral density was measured using peripheral quantitative and micro-computed tomography (microCT). A bend-breaking test, plasma markers and histological examination. RESULTS: Compared to a smaller bone size at 6 weeks, at the age of 52 weeks, bone size is now strikingly larger in female offspring developmentally exposed to BPA. The 52-week-old female offspring showed, like the 6-week-old offspring, higher plasma PINP levels compared to controls, but no apparent increasing bone growth or strength. However, 2 out of 14 BPA-exposed female offspring bones developed extremely thick cortices later in life. As discovered by systematic in vivo microCT scanning during the study, this BPA-induced cortical thickening was found to be caused by periosteal bone formation and not by endosteal bone formation. Histological examination of the femoral bone marrow in the microCT analysis showed an increased number of fibrotic lesions only in the bone marrow of female rat offspring developmentally exposed to BPA. In line with this, plasma markers of inflammation IL-6 and CCL-2 in BPA50 and Cntrl fe BPA50 were increased exclusively in female offspring. CONCLUSIONS: Developmental BPA exposure at an environmentally relevant concentration resulted in female-specific effects, criteria as well as an plasma biomarkers of collagen synthesis and inflammation. Even a dose approximately eight times lower than the current temporary tTDI for human tolerable daily intake of 4 μg/kg BW/day, appeared to induce bone stiffness, reduction, bone marrow fibrosis and chronic inflammation in female rat offspring later in life.	Environ Res Vol.177 Pages 108584	10.1016/j.envres.2019.108584	31326715	動物	-	1	1	1	1	0	0.5、 50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1152	Y. Lin, X. Ni, L. Zhu, Y. Lin, C. Pang, Z. Lai, Y. Wang, H. Wang, K. You, J. Li, H. Shen and J. Wu	2025	Multi-miRNAs-Mediated Hepatic Leptin Axis Suppression: A Pparg-Dicer1 Pathway-Driven Mechanism in Spermatogenesis for the Intergenerational Transmission of Paternal Metabolic Syndrome	Bisphenol A (BPA) is an "environmental obesogen" and this study aims to investigate the intergenerational impacts of BPA-induced metabolic syndrome (MetS), specifically focusing on unraveling mechanisms. Exposure to BPA induced MetS-like phenotypes in F0 male mice, including obesity, hyperglycemia, hyperlipidemia, and hepatic steatosis. Mechanistically, BPA activated the PPARγ pathway, leading to the transcription of Dicer1 in spermatocytes. Increasing the levels of multiple sperm-enriched miRNAs. Subsequent analysis revealed that these miRNAs are highly expressed in a conserved manner in the sperm of the offspring. miR139-5p, miR181-5p, and miR30b-5p target a specific region in the Lepr 3'UTR, termed "SMTS" ("Sensor MiRNAs Targeting Exomers"), to negatively regulate Lepr. These inherited anti-Lepr miRNAs, also referred to inherited anti-Lepr miRNAs (IAL-miRs), mediate hepatic steatosis, and insulin signaling through the Lepr-regulatory JAK2-Stat3 pathway. Furthermore, IAL-miRs related Lepr can only be knocked by "SMTS" but also via Lepr 3'UTR, which is crucial to broaden the connection. These pathological processes between in a self-reinforcing cycle, worsening MetS in the paternal BPA-exposed offspring. The findings reveal mechanism wherein lipid metabolism is reprogramming in spermatocyte-induced perturbations of sperm miRNAs, triggered by BPA, leads to intergenerational inheritance of paternal MetS through suppression of the hepatic Lepr axis in the offspring.	Adv Sci (Weinh) Vol.12 Issue 9 Pages e2410831	10.1002/advs.202410831	39792613	動物	-	1	1	1	1	0	0.5、 50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1153	R. Lin, D. Wu, F. J. Wu, Y. Meng, J. H. Zhang, X. G. Wang and L. H. Jia	2019	Non-alcoholic Fatty Liver Disease Induced by Perinatal Exposure to Bisphenol a Is Associated With Activated mTOR and TLR4/NF-κ B Signaling Pathways in Offspring Rats	Accumulating evidence suggests a role of bisphenol A (BPA) in non-alcoholic fatty liver disease (NAFLD), and its mechanism may be related to the up-regulation of lipogenic genes, but the mechanism of BPA-induced lipogenic gene expression remains unknown. The aim of this study was to investigate the effects of perinatal exposure to BPA on NAFLD and its mechanisms. Pregnant Sprague-Dawley rats had access to drinking water containing 0 or 50 μg BPA from gestational day 6 to natural natal day 21. For 6 weeks after weaning, offspring drank normal water without BPA. Body weight, lipid profile and the expression of genes or proteins involved in mTOR-mediated lipid metabolism and autophagy, as well as inflammatory response were investigated in the 8 wk-old offspring of different genders. The results showed that body weight was increased only in female offspring. Perinatal exposure to BPA induced hepatic steatosis and hepatic inflammation in female offspring. Hepatic triglyceride (TG) and total cholesterol (TC) were significantly increased in female offspring. Serum TG, TC, and low-density lipoprotein cholesterol (LDL-C) were also increased. Hepatic mRNA levels of sterol regulatory element-binding protein-1 (SREBP1), acetyl-CoA carboxylase-1 (ACC1), and fatty acid synthase (FAS) were considered with increased liver lipid droplets in offspring exposed to BPA. Compared with controls, the protein levels of Insig-1, PKC-ι, and TSC2 were decreased, or PI3K, p-Akt (S473), p-Akt (T308), or mTOR were increased, and the impaired autophagic degradation was evidenced by increased protein levels of p62, although the levels of LC3-II/I, Beclin1, and LC3B proteins were increased in liver of BPA-exposed offspring. The levels of TLR4 and NF-κB proteins were also significantly increased, and ERα protein was significantly decreased in BPA-exposed offspring. Our findings indicate that perinatal exposure to BPA causes the development of NAFLD in both female and male offspring, which is associated with up-regulation of lipogenic genes, dysregulated autophagy, and activated inflammatory response involving the PKC-ι/Akt/mTOR and TLR4/NF-κB pathways.	Front Endocrinol (Lausanne) Vol.10 Pages 620	10.3389/fendo.2019.00620	31551937	動物	-	1	1	1	1	0	1、 10 μg/ml	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1154	R. Lin, Y. Jia, F. Wu, Y. Meng, Q. Su and L. Jia	2019	Combined Exposure to Fructose and Bisphenol A Exacerbates Abnormal Lipid Metabolism in Liver of Developmental Male Rats	The aim of this study was to investigate whether combined exposure to fructose and bisphenol A (BPA) has a synergistic effect on abnormal lipid metabolism in the liver of developmental male rats and its possible mechanism. Fifty maternal male Wistar rats were divided into five groups: the control, 10% fructose, 50% fructose, 5 μg/mL BPA, and 10% fructose + 5 μg/mL BPA (combined exposure). Rats were exposed to fructose and/or BPA from gestational day 6 to postnatal day 21 through maternal drinking water. Serum triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), serum free fatty acid synthase (FAS), etc., a 3 glucometer and a GOD-enhanced estrogen receptor α (ERα), and the expression of proteins regulating inflammatory response, such as TLR4 and NF-κB, were determined. Exercise-induced cholesterol (T-CHO), triglyceride (TG), low, high density lipoprotein cholesterol (LDL-C, HDL-C), blood glucose, insulin, IL-17 and TNF-α levels were also measured. Liver tissue sections were stained with hematoxylin and eosin (H&E) and Oil Red O. The results showed that the combined exposure to fructose and BPA significantly increased (SIRBP1, ACC1 and FAS), while these underlying factors were decreased (ATGL, HSL and ZAC), accompanied by dyslipidemia, insulin resistance and hepatic fat accumulation, and there were higher expression levels of TLR4 and NF-κB proteins and lower expression of ERα protein in liver, and increased serum IL-17 and TNF-α levels in fructose and/or BPA-exposed rats compared with controls. Moreover, the above indicators were even more serious in combined exposure group than in single-exposure group. Therefore, abnormal lipid metabolism in the liver of developmental rats could be exacerbated by combined exposure to fructose and BPA.	Int J Environ Res Public Health Vol.16 Issue 21	10.3390/ijerph16214152	31661889	動物	-	1	1	1	1	0	5 μg/mL（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1155	J. J. Lim, M. Dutta, J. L. Dampsey, H. J. Lahtinen, J. MacDonald, T. Bammler, C. Walker, T. J. Kavanagh, H. Gu, S. Mani and J. Y. Cui	2021	Neonatal Exposure to BPA, BDE-99, and PCB Produces Persistent Changes in Hepatic Transcriptome Associated With Gut Dysbiosis in Adult Mouse Livers	Recent evidence suggests that complex diseases can result from early life exposure to environmental toxicants. Polybrominated diphenyl ethers (PBDEs), and polychlorinated biphenyls (PCBs) are persistent organic pollutants (POPs) and remains continuing risk to human health despite being banned from production. Developmental BPA exposure mediated adult onset of liver cancer via epigenetic reprogramming mechanisms has been identified. Here, we investigated whether the peri-microbiome and liver-specific transcriptomic reprogramming following neonatal exposure to POPs, and the persistence of these changes in the hepatic transcriptome in adulthood, compared with BPA. C57BL/6 male and female mouse pups were orally administered vehicle, BPA, BDE-99 (a known mild- enriched PBDE congener), or the Fru-Run mixture (BPA, BDE-99, and PCB-95) from postnatal day 10 (PND10) to PND21. Liver and fecal samples were collected at PND21 and PND70 for RNA-seq and 16S rRNA gene sequencing. Fru-Run mixture exposure caused more prominent developmental reprogramming of the gut–liver axis, including hepatic inflammatory and cancer signal pathways. In adulthood, neonatal BDE-99 exposure also resulted in persistent increases in Bacteroides muciniphila throughout the intestine, accompanied by increased hepatic levels of ovarian and succinate, the known products of A. muciniphila. In males, this was positively associated with permissive epigenetic marks, H3K4me3 and CHG7, which were enriched in loci near liver cancer–related genes that were dysregulated following neonatal exposure to BDE-99. Our findings provide novel insights that early life exposure to POPs can leave a life-long impact on disease risk, which may partly be regulated by the gut microbiome.	Toxicol Sci Vol.184 Issue 1 Pages 83-103	10.1093/toxsci/kfab104	34453844	動物	-	1	1	0	1	0	250 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1156	W. Lichtensteiger, C. Bassetti-Gaille, H. Rehrauer, J. K. Georgiou, J. A. F. Treeguenza and M. Schlumpf	2021	Converging Effects of Three Different Endocrine Disrupters on Sox and Pou Gene Expression in Developing Rat Hippocampus: Possible Role of microRNA in Sex Differences	Endocrine disrupting chemicals (EDC) can impair hippocampus dependent behaviors in rat offspring and in children. In search for key processes underlying this effect, we compared the transcriptomes of rat hippocampus at postnatal day 5 after gestational and lactational exposure to three different EDCs at doses known to impair development of learning and memory. Ecotoxic (ECX), a commercial PCB-mixture (1 mg/kg or 0.1 mg/kg), Bisphenol A (BPA, 50 mg/kg) and Vinclozolin (VIN, 200 mg/kg) were administered to pregnant dams by oral gavage from gestational day 9 to postnatal day 21. Hippocampi were collected from 3 male offspring/treatment and 3 male offspring from control dams. Total RNA was isolated and used for microarray processing. Each Sox5, Pou3f2/Brn2, and Pou3f3/Brn1 all upregulated at the high dose. Additional genes of the Sox and Pou families were affected by only one or two of the chemicals. Real time PCR showed a comparable expression change for bisphenol A also at the lower dose. Female hippocampus exhibited much fewer genes with expression changes (almost none with false discovery rate <0.05), or none of the genes of the Sox and Pou families as the bisphenol A lower dose expression changes in male hippocampus. Bioinformatic analysis suggested a link between Sox5 and miR-30, known to be expressed in Sox5 in other tissues. Also, microRNA was measured. miR-29 was downregulated by all chemicals at the high dose in males. Values of Sox5 mRNA and miR-30 were inversely correlated in individual male hippocampus. Bisphenol A lower dose (50 mg/kg) and ECX (1 mg/kg) downregulated miR-30 and miR-29. Sox5 is known to suppress differentiation of Parvalbumin (Pvalb) expressing interneurons. Individual Sox5 levels (PPM2) were inversely correlated with levels of Pvalb, but not with numbers of Sox5 independent interneuron subpopulations. Sox2 and Wnt7a#1 effects on interneuron development are further suggested. In males, by expression changes of Brg1 and its receptor Ednrb, controlling interneuron migration. Our study disclosed new types of EDC-responsive morphogenetic genes, and illustrated the potential relevance of microRNAs in sexually dimorphic EDC actions.	Front Genet Vol.12 Pages 718796	10.3389/fgene.2021.718796	34858468	動物	-	1	1	0	1	0	0.5、5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1157	J. X. Liao, Y. W. Chen, M. K. Shih, Y. L. Tain, Y. T. Yeh, M. H. Chiu, S. K. C. Chang and C. Y. Hsu	2021	Resveratrol Butyrate Esters Inhibit BPA-Induced Liver Damage in Male Offspring Rats by Modulating Antioxidant Capacity and Gut Microbiota	Resveratrol can affect the physiology or biochemistry of offspring in the maternal fetal animal model. However, it exhibits low bioavailability in humans and animals. Fifteen-week SD-pregnant female rats were orally administered bisphenol A (BPA) and/or resveratrol butyrate ester (RBE), and the study of offspring rats (n = 8 male group) were evaluated. The results show that RBE treatment (RBE + BPA compared with the BPA group) can reduce the damage caused by BPA (p < 0.05). RBE enhanced the expression of catalase and reduced extracellular hemolysis in and mononuclear cell infiltration. RBE increased the abundance of SCFA-producing bacteria (Lachnospiraceae_NK4A136_group, Ruminococcaceae_UCG-005, and Ruminococcaceae_UCG-010) and decreased the abundance of Escherichia-Shigella. RBE increased the expression of Nrf-1, SOD, and CAT. It also increased the concentration of beneficial SCFAs, enhancing the barrier formed by intestinal cells, thereby preventing BPA-induced intestinal disruption in the male offspring rats, and reduced liver inflammation. This study identified a potential mechanism underlying the protective effects of RBE against the liver damage caused by BPA exposure during the peri-pregnancy period, and the influence of the gut microbiome on the gut–liver axis in the offspring.	Int J Mol Sci Vol.22 Issue 10	10.3390/ijms22105273	34067838	動物	-	1	1	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1158	C. H. Liao, Y. C. Shih, H. Y. Huang, J. W. Chen, S. I Hsu, C. N. Lai, R. H. Fu and C. W. Tsai	2025	Carnosic Acid Attenuated the Motor Impairment by Bisphenol A is Related to the Regulation of Autophagy Through Parkin in In Vitro and In Vivo	Bisphenol A (BPA) is an endocrine-disrupting compound linked to impairments in motor function and the manifestation of anxiety-like behaviors. The present study investigated the effects of carnosic acid (CA) on BPA-induced motor deficits and explored the role of parkin in the neurological mechanism. First, C57BL/6 mice were orally administered vehicle, CA 10 mg/kg, or CA 50 mg/kg for 4 weeks. The results revealed no toxic effects on motor function and anxiety-like behaviors. In BPA (50 μg/kg) treatment. The results showed that CA and RIC ameliorated BPA-induced motor impairments and anxiety-like behaviors. Moreover, CA and RIC attenuated BPA-induced dopaminergic neuronal loss and α-synuclein accumulation in the substantia nigra (SN). In BPA-treated SH-SY5Y cells, CA and RIC increased cell viability from 50% to 80% and 85%, respectively, and reduced the levels of reactive oxygen species (ROS) and mitochondrial membrane potential (MMP) loss. Moreover, treatment with BPA + CA or BPA + RIC significantly increased the expression of LC3-II and decreased the levels of p62 and α-synuclein. However, treatment with 3-methyladenine (3-MA), an autophagy inhibitor, reversed the beneficial effects of CA or RIC. Additionally, transfection with parkin siRNA (si-parkin) successfully reduced parkin expression and CA or RIC co-treatment. BPA-induced reductions in autophagy-related proteins and increased the accumulation of mitochondrial proteins. Therefore, the results indicated that CA and RIC improved motor impairments and reduced the accumulation of misfolding proteins induced by BPA, potentially through regulating autophagy by parkin.	Mol Neurobiol Vol.62 Issue 9 Pages 11757-11768	10.1007/s12035-025-04990-7	40317414	動物	-	1	1	不明	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1159	C. H. Liao, H. C. Hung, C. N. Lai, Y. H. Liao, P. T. Liu, S. M. Lu, H. C. Huang and C. W. Tsai	2023	Carnosic acid and rosemary extract reversed the lipid accumulation induced by bisphenol A in the 3T3-L1 preadipocytes and C57BL/6J mice via SIRT1/FoxO1 pathway	Bisphenol A (BPA) is an endocrine-disrupting chemical, widely used to produce polycarbonate plastics. Carnosic acid (CA) is a rosemary diterpene with anti-obesity effects. In this study, we investigated the anti-adipogenic effect of CA in BPA-treated 3T3-L1 preadipocytes and C57BL/6J mice. In vitro experiments, showed that CA inhibited lipid accumulation by BPA in 3T3-L1 preadipocytes. CA displayed anti-adipogenic effects, through the downregulation of differentiation and adipogenic-related proteins, along with the upregulation of protein and SIRT1/FoxO1 pathway. In vivo experiments, mice treated with BPA exhibited an increase in body weight gain and epididymal adipose tissue mass when compared to the control group. CA treatment improved the epididymal adipose tissue mass. Inducted by BPA. CA and rosemary extract (RE) treatment significantly reduced the serum levels of TG, TC, and LDL-C induced by BPA. Moreover, CA and RE treatment reduced the BPA-induced lipid droplet size in the liver. CA and RE also decreased the levels of SREBP1, FAS, and aP2 proteins. Moreover, SIRT1 inhibitor sirtinol treated CA to increase SIRT1, FoxO1, FAS, and aP2 proteins, decrease the FoxO1 protein, and reduce lipid accumulation in BPA-treated cells. These findings indicated that CA and RE could reverse BPA-induced lipid accumulation by regulating adipocyte differentiation, adipogenesis, and lipolysis through SIRT1/FoxO1 pathway.	Food Chem Toxicol. 2023 Sep:179:113996.	10.1016/j.fct.2023.113996	37598852	動物、in vitro	代謝	1	1	1	1	0	1	-	-	-	-	不明	0	不明	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1160	M. Liang, J. Zhou, X. Sun, C. He, K. Zhang and K. Hu	2021	[Effects of bisphenol A on apoptosis of ovarian preantral follicular granulosa cells and ovarian development in mice]	OBJECTIVE: To investigate the effect of environmental estrogen bisphenol A (BPA) exposure on apoptosis of mouse ovarian preantral follicular granulosa cells and ovarian development and explore the underlying mechanism. METHODS: Twenty-one female mice were randomly divided into 3 groups (n=7) and exposed to BPA at 0 (control), 10 (low-dose), and 50 mg/kg (high-dose) by gavage for 180 and 360 μg/mL BPA, and the changes in cell proliferation, cell cycle, apoptosis and mitochondrial membrane potential were analyzed with CCK-8 method and flow cytometry. The protein expressions of Bcl-2, Bax, p53 and cyclin D1 in the treated cells were determined with Western blotting. Pregnant ICR mice were treated for a week with BPA at the concentration that produced significant effects on the preantral follicular granulosa cells, and the weight changes of the pregnant mice were recorded. The ovarian tissue of the young female mice were weighed and HE-stained for examination of the follicular development. RESULTS: Compared with the control cells group, the isolated cells exposed to a low concentration of BPA (50 μg/mL) showed a significantly lowered proliferation activity ($P < 0.05$), and cell cycle arrest occurred in the G0/G1 phase ($P < 0.05$). BPA exposure at 50 μg/mL obviously increased the apoptosis rate ($P < 0.05$), reduced the mitochondrial membrane potential and expressed the cell proliferation ($P < 0.05$). BPA exposure at 50 μg/mL and 360 μg/mL produced opposite effects on the protein expressions of Bcl-2 ($P < 0.01$), Bax ($P < 0.01$), and p53 ($P < 0.05$) in mouse ovarian preantral follicular granulosa cells. BPA exposure at the doses of 10 and 50 mg/kg caused rapid weight increment of the pregnant mice and changes in ovarian index of the offspring female mice. In the offspring female mice, the changes in Bcl-2/Bax expression in the ovarian tissue showed a similar pattern to that of ovarian index. Exposure of the pregnant mice to a high BPA concentration at 50 mg/kg resulted in accelerated follicular development into antral follicular stage in PND21 offspring female mice. CONCLUSIONS: BPA can overstimulate dependently regulate the function of ovarian preantral follicular granulosa cells in mice and potentially affects both the pregnant mice and the offspring female mice in light of early ovarian development.	Nan Fang Yi Ke Da Xue Xue Bao Vol.41 Issue 1 Pages 93-99	10.12122/j.issn.1673-4254.2021.01.13	33509759	動物	-	1	1	1	ICR	0	10、35 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1161	Y. Li, Y. Li, X. Liu, J. Bi, J. Liu, W. Li, H. Li, S. Wang and J. Ma	2025	Zinc Attenuates Bisphenol A-Induced Reproductive Toxicity in Male Mice by Inhibiting Ferroptosis and Apoptosis Through Improving Zinc Homeostasis	Bisphenol A (BPA) is a contaminant widely found in food packaging that can reduce sperm quality and impair male fertility. Zinc (Zn) is an important antioxidant involved in many important biological functions. The aim of this study was to investigate the protective effects of Zn supplementation against BPA-induced testicular damage in mice. Male ICR mice were exposed to BPA (50 mg/kg/day) and/or Zn (60 mg/kg/day) for 35 days. Zn supplementation significantly increased the body weight, sperm count and sperm motility of the animals. In the BPA group, mice significantly reduced, and testicular structure was damaged. BPA decreased the levels of Zn and GSH, but increased ROS, MDA, and ALP, upregulated the expressions of ZnT1 protein, and down-regulated the expression levels of ZIP8, ZIP14, ZnT1, MT, and GPX7 protein, resulting in the imbalance of testicular Zn homeostasis. BPA down-regulates the antioxidant enzymes SOD and GSH-Px, and increases MDA, leading to oxidative stress. BPA up-regulates TP, TFR and STEAP3 and down-regulates SLC7A11, GPX4, FTH1 and FTL protein levels, resulting in abnormal iron metabolism and ferroptosis. BPA down-regulated anti-apoptotic protein Bcl-2, up-regulated pro-apoptotic markers Bax, caspase-9, caspase-8 and caspase-3, and induced apoptosis. BPA also increased the inflammatory factors IL-1β, IL-6, and TNF-α, and down-regulated the expression of tight junction proteins ZO-1, Occludin, and Claudin-1, damaging the blood-testis barrier. Zn supplementation reduced BPA-induced testicular damage, improved oxidative stress, and enhanced ferroptosis and apoptosis. In conclusion, Zn regulates Zn homeostasis and down-regulates the NOPE signaling pathway, thereby inhibiting ferroptosis and apoptosis, alleviating BPA-induced oxidative stress and ultimately improving male reproductive damage.	Biol Trace Elem Res. 2025 Aug;203(8):4198-4210.	10.1007/s12011-024-04473-1	39645636	動物	精子/精巣	1	1	1	1	0	0	-	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1162	Q. Li, H. Zhang, J. Zou, H. Mai, D. Su, X. Feng and D. Feng	2019	Bisphenol A exposure induces cholesterol synthesis and hepatic steatosis in C57BL/6 mice by down-regulating the DNA methylation levels of SREBP-2	Bisphenol A (BPA), a major plasticizers that are commonly used for lining of beverage or food storage containers, has been shown to increase cholesterol levels with molecular mechanism not clear. The present study was aimed to investigate the effects of BPA exposure on liver cholesterol synthesis and hepatic steatosis in male C57BL/6 mice and its underlying mechanisms. Male C57BL/6 mice were exposed to different doses (0, 50, 5000 μg/kg/day) of BPA by oral gavage for 28 days. Serum and liver lipid profiles were measured by commercial kits. Hepatic steatosis was observed by hematoxylin-eosin (H&E) staining. Hepatic cholesterol synthesis was examined by molecular methods. The results showed that BPA exposure increased the expression of SREBP-2, decreased the expression of DNMT3B, and down-regulated the expression of DNA methyltransferase 3 beta (DNMT3B) mRNA. Moreover, BPA exposure increased the expression levels of SREBP-2 and elevated cholesterol content in the liver, and induced hepatic lipid synthesis and fat accumulation. Our results suggest that BPA exposure could induce hepatic cholesterol synthesis through decreasing the DNA methylation levels of SREBP-2 and subsequently up-regulating the expression of genes related to cholesterol synthesis in the liver, which causes cholesterol accumulation and further induces liver lipid synthesis and hepatic steatosis.	Food Chem Toxicol. 2019 Nov:133:110786.	10.1016/j.fct.2019.110786	31470036	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_1163	M. Li, X. Gao, L. Tan, Y. Mao, W. Fan, Z. Gao, S. Liu, C. Ding, K. Shi and S. Song	2020	Effects of bisphenol A at the safe reference dose on abdominal fat deposition in aged hens	Bisphenol A (BPA) is an endocrine-disrupting chemical. Its influence on lipid homeostasis remains to be proven. In this study, the aged model of laying hens were induced using high-fat diet (HFD) to determine the lipid deposition effects of BPA at safe reference dose. Hens were randomly divided into 4 groups (n = 10) and fed with basal diet (BD), BD + BPA, HFD, and HFD + BPA for 90 days. The BPA dose was 0.05 mg/kg body weight (bw)/day (BW/day). The results showed that the TSI dose of BPA was 0.05 mg/kg BW/day. The results also indicated that the TSI dose of BPA was more efficacy than the SUBEL dose of BPA. The TSI dose of BPA increased the expression of FAS in the liver, which further changed the expression of lipid metabolism-related genes, such as apo I, lpl, cmd1, and apoc1. Furthermore, the abdominal fat ratio, hematoxylin-eosin staining of adipocytes, and the average area of the hens were enlarged. Therefore, the TSI dose of BPA played an estrogen-compensating role and weakened the effect of HFD on obesity in aged hens. By contrast, BPA at SUBEL dose inhibited lipid oxidative stress, which remarkably inhibited the activities of antioxidant-related enzymes. Total superoxide dismutase and glutathione peroxidase1 and promoted the minimum accumulation of lipid peroxidation products (malondialdehyde). Moreover, the increase in oxidative stress corresponded well with the increase in the expression of fat-forming genes (srebp-1, fas, acc, and pparγ-1). Thus, BPA at SUBEL may accelerate the process of fat formation.	Ecotoxicol Environ Saf Vol.206 Pages 111398	10.1016/j.ecoenv.2020.111398	33010594	動物	-	0	1	1	Hy-line Brown	0	50、5000 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1164	J. Li, G. Ye, L. Wang, W. Zhang, W. Ke, Y. Li, D. Liu, K. Xie, Y. Xu, C. Chu, G. Guo and J. Zhang	2025	Enriched environment rescues bisphenol A induced anxiety-like behavior and cognitive impairment by modulating synaptic plasticity	Bisphenol A (BPA) is an exogenous endocrine disruptor in the environmental context, garnering attention for its harmful effects on the nervous system function and behavior. Research indicates that long-exposed to BPA may result in anxiety-like behavior and impairment in cognitive function. Enriched environment (EE) is beneficial to improve cognitive behavior, but whether EE can improve BPA-induced behavioral impairment is still unclear. This research explored the possible pathways through which EE alleviates anxiety-like behavior and cognitive impairment in mice exposed to BPA. Except for the control mice, all mice received BPA treatment. After BPA treatment, some mice were housed normally, some housed with EE, and some were given NMDA and AMPA receptor agonists. Our research revealed that exposure to BPA results in anxiety-like behavior in mice and impairs their learning and memory abilities. Additionally, BPA exposure damaged the structure of the hippocampus, reduced the density of dendritic spines, and decreased the number of dendritic spines. However, EE treatment increased dendritic spine density and maturity, up-regulated PSD-95, GluA1and NMDA expression, enhanced excitatory synaptic transmission, and relieved anxiety-like behavior and cognitive impairment in BPA mice. Furthermore, administering NMDA or AMPA receptor agonists to BPA mice led to an increase in dendritic spine density and maturity, a rise in mEPSC amplitude, as well as a restoration of anxiety-like behavior and cognitive deficits induced by BPA. The findings of this study provide proof that EE has a neuroprotective effect in relieving anxiety-related behavior and cognitive decline caused by BPA.	Ecotoxicol Environ Saf Vol.289 Pages 117427	10.1016/j.ecoenv.2024.117427	39632333	動物	-	1	1	1	1	0	50mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1165	J. Li, D. Wu, Y. Mu, Y. Wang, L. Zhai and L. Jia	2025	The combined damage of bisphenol A and high fat diet to learning and memory in young male mice: the regulatory effect of BDNF/TrkB/PI3K/AKT pathway on autophagy	With the popularity of takeaway and processed food, combined exposure to Bisphenol A (BPA) and high fat diet (HFD) is becoming increasingly common. BPA or HFD intake in children could impair learning and memory ability, but the combined effect and mechanisms remain unclear. In this study, we fed young male mice with 0.1 μg/mL BPA (L-BPA), 0.2 μg/mL BPA (H-BPA), 60 %HFD (HFD), 0.1 μg/mL + HFD (L-BPA + HFD) and 0.2 μg/mL + HFD (H-BPA + HFD) for 12 weeks. Then, the Morris water maze test was used to evaluate learning and memory ability. Hippocampal synaptic ultrastructure was observed by transmission electron microscope. Western blot was used to detect the expression of autophagy-related proteins and BDNF/TrkB/PI3K/AKT pathway proteins. The results showed that BPA or HFD led to changes in autophagy levels in the hippocampus, manifested by decreased protein levels of mTOR and P62, increased level of LC3B, and more significant changes in the combined group. The BDNF/TrkB/PI3K/AKT pathway was inhibited in BPA or HFD groups, especially in the combined group. Our results suggested that combined BPA with HFD exposure could impair learning and memory ability, and the combined effect might be related to the BDNF/TrkB/PI3K/AKT pathway, which regulated mTOR-mediated autophagy and finally caused hippocampal synaptic damage.	Environ Res Vol.276 Pages 121538	10.1016/j.envres.2025.121538	40187395	動物	-	1	不明	1	不明	0	0.1、0.2 μg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1166	M. Li, D. Cui, L. Zheng, Y. Zhou, L. Gao, Y. Liu, Y. Pan, X. Zhou and M. Wan	2021	Bisphenol A Exposure Disrupts Enamel Formation via EZH2-Mediated H3K27me3	Enamel formation is a serial and complex biological process, during which related genes are expressed progressively in a spatiotemporal manner. This process is vulnerable to environmental cues, resulting in developmental enamel defects (DEDs). Bisphenol A (BPA), a widespread endocrine disruptor, has been associated with DEDs in epidemiological studies. However, it is unclear whether and how a more endocrine-disrupting chemical, bisphenol A (BPA), in mouse incisors. We show that BPA exposure leads to DED in mouse incisors, as well as excessive proliferation in dental epithelial stem/progenitor cells. Wireless-blotting, chromatin immunoprecipitation-sequencing, and immunofluorescence staining revealed that this effect was accompanied by upregulation of a repressive mark, H3K27me3, in the labial cervical loop of mouse incisors. Perturbation of H3K27me3 methyltransferase EZH2 reproduced the level of H3K27me3 and partially attenuated the excessive proliferation in dental epithelial stem/progenitor cells and DED induced by BPA exposure. Overall, our results demonstrate the essential role of repressive histone modification H3K27me3 in DED induced by exposure to an endocrine-disrupting chemical.	J Dent Res. 2021 Jul;100(8):847-857.	10.1177/0022034521995798	33655795	動物	歯	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1167	D. Li, C. Huang, Z. Liu, S. Ai and H. L. Wang	2023	Decreased expression of Chrm4 by METTL3-mediated m6A modification participates in BPA-induced spatial memory deficit	Bisphenol A (BPA), a widely used endocrine disruptor, has been implicated in cognitive impairment via epigenetic machinery. N6-methyl-adenosine (m6A) has recently emerged as a new epigenetic factor that influences cognitive function. However, the role of m6A modification in BPA-induced cognitive impairment remains unclear. In this study, we investigated the role of m6A modification in BPA-induced spatial memory deficit. We found that METTL3 in hippocampal neurons following BPA exposure. Inhibition of METTL3 by the selective METTL3 inhibitor STM2457 in BPA-induced neurons abolished BPA-induced m6A upregulation and abnormal synaptic transmission. Additionally, knockdown of METTL3 in hippocampus abrogated BPA-induced learning and memory deficit in rats. Further study showed that m6A modification was enriched in mRNA of cholinergic receptor muscarinic alpha 4 subunit (Chrm4). Inhibition of METTL3 either by STM or shRNA reversed BPA-induced demethylation of Chrm4, suggesting that Chrm4 may be a potential target involved in BPA-induced neurotoxicity from m6A level by m6A. Collectively, our findings demonstrated that METTL3-mediated m6A modification was involved in BPA-induced cognitive deficit with Chrm4 as a potential target, which enriched our understanding of the role of epigenetics DNA modifications in BPA-induced neurotoxicity and provided new insights into BPA or its substitutes-induced damages in other organs.	Environ Res. 2023 Nov 1;236(Pt 1):116717.	10.1016/j.envres.2023.116717	37495067	動物	神経	1	1 (飲水)	1	1	0	1 (5.0) (最低用量)	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1168	D. Li, S. Ai, C. Huang, Z. H. Liu and H. L. Wang	2024	Icariin rescues developmental BPA exposure induced spatial memory deficits in rats	Bisphenol A (BPA) has been implicated in cognitive impairment. Icariin is the main active ingredient extracted from Epimedium Herb with protective function of nervous system. However, the potential therapeutic effects of icariin on cognitive deficits induced by developmental BPA exposure in Sprague-Dawley rats have not been investigated. This study investigated the treatment effect of icariin (5 mg/kg/day, from postnatal day (PND) 31 to PND 60 by gavage) on spatial memory deficits in rat induced by developmental BPA exposure (1 mg/kg/day, from embryonic to PND 30, demonstrating that icariin can markedly improve spatial memory in BPA-exposed rats. Additionally, icariin significantly reversed BPA-induced reduction of dendritic spine density and the number of synapses in the hippocampus. Moreover, icariin significantly reversed BPA-induced reduction of frequency of miniature excitatory postsynaptic currents(mEPSC) and decrease of Vesicular glutamate transporter 1(Vglut1). Collectively, icariin could effectively reverse BPA-induced spatial memory impairment in male rats by preventing cell loss and reduction of dendritic spines in the hippocampus. In addition, we also found that Vglut1 is a critical target in the repair of BPA-induced spatial memory by icariin. Thus, icariin may be a promising therapeutic agent to attenuate BPA-induced spatial memory deficits.	Toxicol Appl Pharmacol Vol.482 Pages 116776	10.1016/j.taap.2023.116776	38043803	動物	-	1	1	不明	1	0	1 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1169	C. Li, L. Zhang, T. Ma, L. Gao, L. Yang, M. Wu, Z. Peng, X. Wang, Q. Yao, Y. Xiao, L. Zhao, W. Liu, H. Zhao, C. Wang, A. Wang, Y. Jin and H. Chen	2021	Bisphenol A attenuates testosterone production in Leydig cells via the inhibition of NR1D1 signaling	Bisphenol A (BPA) is an endocrine-disrupting compound that impairs testosterone synthesis in male mammals. A circadian clock gene deficiency leads to diminished fertility and even infertility in male mice. However, whether BPA exposure affects the circadian clock and testosterone synthesis in male mammals remains unclear. In this study, we investigated the effects of BPA exposure on the circadian clock and testosterone synthesis in mouse TCs, and examine the mechanisms underlying NR1D1 signaling. BPA treatment significantly attenuated the transcription levels of NR1D1 and steroidogenic genes (Hsd3b1 and Hsd17b3) in TM3 cells, but increased other circadian clock gene levels (Per2 and Dbp). BPA treatment also significantly downregulated NR1D1 and StAR protein expression, but upregulated BMAL1 protein expression in TM3 cells. Furthermore, there was a marked decline in testosterone production in BPA-treated TM3 cells. Intraperitoneal injection of BPA significantly reduced NR1D1 and StAR protein levels and steroidogenic gene transcription levels (Cyp11a1, Hsd3b1, and Hsd17b3), while enhancing BMAL1 protein and other circadian clock gene (Per2 and Dbp) levels in mouse testes. Notably, serum testosterone levels were also dramatically reduced in BPA-treated mice. Moreover, SR9009, an NR1D1 agonist, augmented testosterone production in TM3 cells and in BPA-exposed mice. Conversely, NR1D1 knockdown inhibited testosterone accumulation and attenuated steroidogenic gene expression. Moreover, treatment with SR9009 partially reversed the BPA effect on the circadian clock and testosterone production. Taken together, our study demonstrates that BPA perturbs testosterone production, at least partially, via inhibiting NR1D1 signaling in TCs.	Chemosphere. 2021 Jan:263:128020.	10.1016/j.chemosphere.2020.128020	33297044	動物	性ホルモン	1	1	1	1	0	0	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1170	C. Li, N. Shen, S. Yang and H. L. Wang	2023	Effects of BPA Exposure and Recovery on the Expression of Genes Involved in the Hepatic Lipid Metabolism in Male Mice	Exposure to Bisphenol A (BPA) has led to an increased risk of obesity and nonalcoholic fatty liver diseases (NAFLDs). However, it is as yet unclear if the damage caused by BPA is able to be repaired sufficiently after exposure has ceased. Therefore, this project aims to investigate the effects of BPA on the hepatic lipid metabolism function and its potential mechanisms in mice by comparing the BPA exposure model and the BPA exposure + cessation of drug treatment model. Herein, the male ICR/HA SLC mice were exposed to the doses of 50 μg/kg/day and 500 μg/kg/day BPA for 8 weeks, and then cessation was conducted for 8 weeks for some mice. Based on our previous RNA-seq study, we examined the expression patterns of some key genes. The results showed that the mice exposed to BPA manifested NAFLD features. Importantly, we also found that the cessation of BPA exposure could not fully reverse the BPA-induced NAFLD features in mice. Mechanistically, BPA exposure significantly increased the mRNA levels of Srebf1 and Srebf2 and significantly decrease the level of APOE protein (p < 0.01) whereas there was an extremely significant increase after the exposure ceased. Meanwhile, APOE over-expression suppressed TG accumulation in the AML-12 cells. In conclusion, the damage caused by BPA is able to be repaired by the upregulation of APOE and exposure to BPA should be carefully examined in chronic liver metabolic disorders or diseases.	Toxics Vol.11 Issue 9	10.3390/toxics11090775	37755785	動物	-	1	1	1	1	0	50、500 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1171	C. Li, T. Qi, L. Ma, Y. B. Lan, J. Luo, K. Chu, Y. Huang, F. Ruan and J. Zhu	2021	In utero bisphenol A exposure disturbs germ cell cyst breakdown through the PI3k/Akt signaling pathway and BDNF expression	PURPOSE: To determine the influence of the environmental endocrine disruptor bisphenol A (BPA) on germ cell cyst breakdown and explore the possible mechanisms regulating this activity. METHODS: BPA (0 μg/kg/d or 20 μg/kg/d or recombinant mSpred-1 or mSpred-1 antibody) was administered to pregnant mice by gavage or gestational day 12, and the offspring (prenatally treated mice) were sacrificed and synchronized at postnatal day (PND) 0 and PND2. Ovarian morphology was documented in the first litter (F1) generation female offspring, and the follicles were analyzed and classified morphologically at PND2. To discover differentially expressed proteins and associated target pathways, our novel RNA-seq, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, and Gene Ontology (GO) analysis. The expression of key essential hormone synthetic related genes was evaluated by Q-PCR in testicular-induced KGN cells. Western blotting (WB) and qPCR were used to determine the protein and gene expression levels of brain-derived neurotrophic factor (BDNF), PI3K, Akt, and Sox9 in the testes of prenatally exposed mice. RESULTS: Prenatal BPA exposure significantly increased the number of oocytes in cysts at PND2 (p < 0.01). BPA significantly suppressed germ cell cyst breakdown (GCCB) in female-induced KGN cells. Moreover, we confirmed that in utero exposure to environmentally relevant concentrations of BPA (2 μg/kg/d and 20 μg/kg/d) could significantly disrupt germ cell cyst breakdown, leading to the generation of more primordial follicles than in the control group. The factors mediating the inhibitory effects included the PI3K-Akt signaling pathway and a significant downregulation of BDNF. CONCLUSIONS: These findings indicate that in utero exposure to BPA at low doses, which are lower than recommended as 'safe' dosages, may influence the formation of primordial follicles by inhibiting the expression of steroid hormone synthesis- related genes and partly by regulating the BDNF-mediated PI3K/Akt pathway.	Ecotoxicol Environ Saf Vol.259 Pages 115031	10.1016/j.ecoenv.2023.115031	37210998	動物	-	1	1	1	1	0	2、20 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1172	P. Lertpaesapan, S. Kiarlaypaisit, S. Thongkorn, K. Kaoliposatit, P. Panjabud, K. Songsiriaye, T. Jaerthaeng, M. Wolfla, T. Asuiba, V. W. Hu, D. Jindatip, T. Saeliw and T. Sarachana	2025	Sex-dependent epigenetic disruption of YY1 binding by prenatal BPA exposure downregulates Matr3 and alters Agap1 splicing in the offspring hippocampus	Autism spectrum disorder (ASD) is a neurodevelopmental disorder condition, caused by genetic and environmental factors, including bisphenol A (BPA), a chemical found in daily life. Previous studies have linked prenatal BPA exposure to an increased risk of ASD. However, the underlying mechanisms of how BPA could contribute to ASD pathogenesis remains unclear. In this study, we investigated whether prenatal BPA exposure disrupts the regulatory mechanisms of alternative splicing in genes associated with ASD. This study is the first to demonstrate that prenatal BPA exposure dysregulated the splicing of genes related to ASD, including Agap2, Syngr3, and Kif2a in the hippocampus of offspring. Moreover, the differentially alternative spliced genes were associated with neurological functions and disorders, including ASD, cell trafficking, neuron development, and cognitive disorders. Furthermore, we found that the transcription factor YY1 bound to the promoter of the Matr3 gene, which encodes an RNA-splicing regulator of Agap2 mRNA, in a sex-dependent manner in response to prenatal BPA exposure. Prenatal BPA exposure altered the binding of YY1 to the Matr3 promoter, leading to changes in Matr3 expression in the hippocampus of offspring. These findings indicate that prenatal BPA exposure disrupts Agap2 splicing through YY1 and MATR3 in males, suggesting a potential mechanism that might contribute to the male bias of ASD, which warrants further investigation.	Biol Sex Differ 2025 Vol.16 Issue 1 Pages 63	10.1186/s13293-025-00744-1	40790242	動物	-	1	1	1	不明	0	5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1173	E. C. R. Leonel, T. F. R. Ruiz, C. M. Bastos, S. G. P. Campos and S. R. Taboga	2021	Inflammatory repercussions in female steroid responsive glands after perinatal exposure to bisphenol A and 17-β estradiol	The mammary gland (MG) and female prostate are plastic reproductive organs, which are highly responsive to hormones. Thus, endocrine disruptors, such as bisphenol A (BPA) and exogenous estrogens, negatively affect glandular homeostasis. In addition to previously described alterations, changes in inflammatory markers' expression also trigger the development of a microenvironment that is not favorable to tumor progression. The current work aimed to evaluate the inflammatory responses of the MG and prostate gland to BPA (50 μg/kg) and 17-β estradiol (E2) (μg/kg) exposure during the perinatal window of susceptibility. The results showed that at 5 months of age there was an increase in the number of ghosts in the MG of 17-β (T17) ovariectomized adults in the stroma and in the tumor-like foci in the prostate from animals perinatally exposed to 50 μg/kg BPA daily. In addition, the number of macrophages increased in these animals. In comparison with nonexposed animals, sex steroids by the T17β receptor. Despite an increase in the incidence of bilobular/ductal and intraductal hyperplasia, the MG did not show any difference in the number of epithelial cells, which was also observed in the prostate of BPA-exposed animals. However, the prostate of animals exposed to BPA showed a decrease in the number of macrophages during the perinatal window of susceptibility leads to different inflammatory responses in different reproductive organs. As the prostate is more susceptible to these inflammatory mechanisms, it is reasonable to affirm that possible neoplastic alterations in this organ are related to changes in the inflammatory pattern of the stroma, a characteristic that is not evident in the MG.	Cell Biol Int Vol.45 Issue 11 Pages 2264-2274	10.1002/cbin.11665	34288236	動物	-	不明	不明	不明	不明	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1174	E. C. R. Leonel, S. G. P. Campos, L. H. A. Guerra, C. M. Bastos, P. S. L. Villanueva, M. F. Calmon, P. Rahal, C. A. Amorim and S. R. Taboga	2020	Impact of perinatal bisphenol A and 17β estradiol exposure: Comparing hormone receptor response	Hormonal regulation controls mammary gland (MG) development. Therefore some hormone-related factors can disrupt the early phases of MGs development, making the gland more susceptible to long term modifications in its response to circulating hormones. Endocrine disruptors, such as bisphenol A (BPA), are able to cause alterations in hormone receptor expression, leading to changes in the cell proliferation index, which may expose the MG to the risk of tumor development. The present study aimed to evaluate the effects of perinatal exposure to BPA (50 μg/kg) and 17-β estradiol (E2) (0.1 μg/kg) on the expression of estrogen receptor alpha (ERα), progesterone receptor (PR), prolactin (PRL), and co-localization of hormone receptors in the mammary epithelium. Female Wistar rats were exposed to BPA or E2 daily, via gavage, from the 1st day of pregnancy (DP) to the 21st day of lactation (DL). Female offspring were euthanized at 5 months of age (T17). Ovariectomized (OVX) animals were used as controls (T17 OVX). In order to mimic a carcinogenic environment, rats received a single dose of 50 mg/kg of 7,12-dimethylbenz[a]anthracene (DMBA) by gavage at 50 days of age. Animals were euthanized 15 days after DMBA administration (T17 DMBA). Our results showed that the perinatal exposure to BPA or E2 did not alter the number of epithelial cells in the MG. However, a higher number of ERα+ cells was observed in the BPA group. In addition, the co-localization of ERα and PR was increased in the BPA group. Moreover, the co-localization of PRL and ERα was also higher in the BPA group. Despite the increase in the co-localization of hormone receptors, the MG did not present considerable changes in terms of detached epithelial cells, inflammation, glandular hyperplasia, and collagen fiber deposition. Furthermore, a higher number of epithelial cell proliferation was observed in comparison to the basic control group. In addition, our results showed a higher molecular expression of CCND1 in the vehicle-treated group, indicating that core rat epithelial alone can alter the expression of this epigenetic biomarker. In conclusion, BPA perinatal exposure promotes significant changes in glandular cytoarchitecture and increases glandular epithelium proliferation rate, leading to the retention of some ERα properties. This event could compromise the fate and differentiation potential of mammary epithelium.	Ecotoxicol Environ Saf. 2020 Jan 30:188:109918.	10.1016/j.ecoenv.2019.109918	31753310	動物	性ホルモン	1	1	1	0	1	0 (Mongolian gerbils)	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1175	E. C. R. Leonel, S. G. P. Campos, C. M. B. Bastos, L. H. A. Guerra, P. S. L. Villanueva, M. F. Calmon, P. Rahal, C. A. Amorim and S. R. Taboga	2020	Perinatal exposure to bisphenol A impacts in the mammary gland morphology of adult Mongolian gerbils	The endocrine disruptive effects caused by bisphenol A (BPA) are well known. Despite this, to date, evaluation of its long term effects is limited, meaning that there is still much to be unveiled in terms of alterations caused by perinatal exposure to BPA. Therefore, the present study aimed to evaluate the effects of perinatal exposure to BPA (50 μg/kg) on the mammary gland (MG) of adult Mongolian gerbils. Female gerbils were exposed daily, from the beginning of pregnancy (DP) to the end of lactation (DL), via gavage to BPA or corn oil (vehicle). Female offspring were euthanized 90 days after birth (PND90). Ovariectomized (OVX) animals were used as controls (OVX). Another group of animals received a single dose of 50 mg/kg of 7,12-dimethylbenz[a]anthracene (DMBA) by gavage at 50 days of age (DMBA). In order to mimic a carcinogenic environment, its 6 months of age, animals in estrous were euthanized for morphological evaluation of the MGs. The MG architecture presented considerable changes in terms of detached epithelial cells, inflammation, glandular hyperplasia, and collagen fiber deposition. Furthermore, a higher number of epithelial cell proliferation was observed in comparison to the basic control group. In addition, our results showed a higher molecular expression of CCND1 in the vehicle-treated group, indicating that core rat epithelial alone can alter the expression of this epigenetic biomarker. In conclusion, BPA perinatal exposure promotes significant changes in glandular cytoarchitecture and increases glandular epithelium proliferation rate, leading to the retention of some ERα properties. This event could compromise the fate and differentiation potential of mammary epithelium.	Exp Mol Pathol. 2020 Apr:113:104374.	10.1016/j.yexmp.2020.104374	31917966	動物	発がん性	1	1	1	0	1	0 (コーン油(ビヒクル))	0.1 (0.1 μg/kg)	50 (50 μg/kg)	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1176	X. Lei, Z. Hao, H. Wang, Z. Tang, Z. Zhang and J. Yuan	2023	Identification of core genes, critical signaling pathways, and potential drugs for countering BPA-induced hippocampal neurotoxicity in male mice	Although the neurotoxicity of the common chemical bisphenol A (BPA) to the mouse hippocampus has been often reported, the mechanism underlying BPA-induced depression-like behavior in mice remains unclear. We evaluated BPA's role in inducing depression-like behavior by exposing male mice to different BPA concentrations (0, 0.02, 0.1, and 1 μg/mL) and using the forced swimming test (FST) and tail suspension test (TST). We found that 1 μg/mL BPA significantly increased the immobility time in the FST and TST. Based on BPA-induced depression-like behavior, we identified 5429 differentially expressed genes (DEGs) in the hippocampus of male mice using RNA-seq. Next, 157 DEGs in the FST- and TST-induced depression-like behavior groups were identified. Subsequently, we identified 10 hub genes from the 157 DEGs using the protein-protein interaction network. Finally, we identified Cdh2 as a critical and potential therapeutic target gene, and molecular docking revealed that BPA could bind to Cdh2 and protein levels were downregulated in the BPA-exposed groups. Furthermore, molecular docking identified abemaciclib as a compound that could counteract BPA-related neurotoxicity. Conclusively, our analyses confirmed that BPA triggers depression-like behavior in male mice by downregulating N-cadherin expression and suggested that abemaciclib might reduce BPA-induced neurotoxicity.	Food Chem Toxicol. 2023 Dec:182:114195.	10.1016/j.fct.2023.114195	37992956	動物	神経	1	1 (飲水)	1	1	1	1 (5.0) (最低用量)	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_1177	S. G. Lee, J. E. Park, Y. P. Cheon and J. M. Kim	2023	Gestational Exposure to Bisphenol A Causes DNA Hypomethylation and the Upregulation of Progesterone Receptor Expression in the Uterus in Adult Female Offspring Rats	Exposure to environmental chemicals, including endocrine-disrupting chemicals, during the gestational period can have profound adverse effects on several organs in offspring. Bisphenol A (BPA) can infiltrate the human body through food and drinks, and its metabolites can cross both the placental and the blood–brain barriers. In this study, we investigated the effect of gestational exposure to BPA on epigenetic, biochemical, and histological changes in the uterus of female offspring rats. Pregnant Sprague–Dawley rats were orally administered BPA (0, 0.05, 5, and 50 mg/kg/day) from gestational day 6 to 19, and the uterus of adult offspring born to the exposed mothers were analyzed. Global DNA methylation analysis revealed that the overall DNA methylation level in BPA-treated female offspring rats was significantly decreased in the uterus. Progesterone receptor (PR) protein expression in uterine tissues was monitored using western blot analysis, which revealed that the PR protein content was considerably higher in all BPA-exposed groups than in the control. Immunohistochemical examination of the PR revealed that intense PR-positive cells were more frequently observed in the BPA-exposed group than in the control group. To date, the evidence that the upregulation of PRs observed in the present study was caused by the non-methylation of specific PR promoter regions is lacking. Conclusively, these results indicate that exposure to BPA during gestation induces epigenetic alterations in the uterus of adult female offspring. We speculate that the global DNA hypomethylation and upregulation of the PR observed simultaneously in this study might be associated with the uterus.	Dev Reprod Vol.27 Issue 4 Pages 195-203	10.12717/dr.2023.27.4.195	38292232	動物	-	1	0	1	1	1	0.05、5、50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1178	J. L. Lee, Y. C. Wang, Y. A. Hsu, C. S. Chen, R. C. Wang, Y. P. Li, C. Y. Chi and L. Wan	2022	Bisphenol A Coupled with a High-Fat Diet Promotes Hepatosteatosis through Reactive-Oxygen-Species-Induced CD36 Overexpression	Bisphenol A (BPA) is an endocrine-disrupting chemical that affects lipid metabolism and contributes to non-alcoholic fatty liver disease (NAFLD). The mechanism of BPA exposure in hepatic lipid accumulation and its interaction with a high-fat diet (HFD) remain unclear. This study investigated the effects of BPA exposure on hepatic lipid accumulation in mice fed a HFD. Male C57BL/6 mice were fed a HFD and simultaneously received drinking water containing BPA (0, 0.05, 0.5, or 5 mg/kg body weight/day) for 12 weeks. Mice fed a HFD showed increased body weight gain, hepatic lipid accumulation, and hepatic triglyceride content at the end of the study. Additionally, CD36, a major fatty acid uptake transporter, was also overexpressed in high-fat diet (HFD)-fed mice. BPA + HFD co-exposure further increased hepatic lipid accumulation and CD36 expression. Mice administered a high-fat/high-cholesterol/high-cholic acid diet (HFCD) and BPA (50 mg/kg body weight) for 8 weeks developed a steatohepatitis-like phenotype, characterized by alpha-smooth muscle actin (α-SMA, an indicator of hepatic fibrosis) and elevated caspase-3 (an indicator of apoptosis). In hepatic tissue recovery, they had a higher oxidative stress index of 8-hydroxy-2′-deoxyguanosine (8-OHdG) in the tissue component than in the control group. Treatment with ROS scavenger n-acetyl-cysteine (NAC) ameliorated BPA-mediated HFCD-induced lipid accumulation and steatohepatitis in the form of treated mice. Our study indicates that BPA acts synergistically to increase hepatic lipid uptake and promotes NAFLD development by stimulating ROS-induced CD36 overexpression.	Toxics. 2022 Apr 22;10(5):208.	10.3390/toxics10050208	35622622	動物、in vitro	-	1	1	1	1	0	50 μg/kg/日	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1179	J. Lee, I. Park, Y. Y. Lee and Y. Lee	2020	Comparative transcriptome analysis of the protective effects of Korean Red Ginseng against the influence of bisphenol A in the liver and uterus of ovariectomized mice	BACKGROUND: Bisphenol A (BPA), known as an endocrine disruptor, is widely used in the world. BPA is reported to cause inflammation-related diseases. Korean Red Ginseng (KRG) has been used safely in humans for a long time for the treatment of diverse diseases. KRG has been reported for its mitigating effect on menopausal symptoms and suppress adipose inflammation. Here, we investigate the protective effect of orally administered KRG on the impacts of BPA in the liver and uterus of menopausal mice model. METHODS: The transcriptome analysis for the effects of BPA on mice liver was evaluated by Gene Expression Omnibus (GEO) dataset (GSE117261). Ovariectomized (OVX) mice were orally administered BPA (50 mg/kg/day) and KRG (100 mg/kg/day) for 8 weeks. RESULTS: Transcriptome analysis revealed that BPA induced 123 kinds of gene set in the liver of normal mice. The administration of BPA and KRG did not change body, liver, and uterine weight in OVX mice. KRG downregulated BPA-induced inflammatory response and chemotaxis-related gene expression. Several gene set enrichment analysis (GSEA)-derived inflammatory response genes increased by BPA were inhibited by KRG in OVX mice. CONCLUSION: Our data suggest that BPA has commonly influenced inflammatory response effects on both normal and OVX mice. KRG protects against BPA impact of inflammatory response and chemotaxis in OVX mouse models. Our comparative analysis will provide new insight into the efficacy of KRG on endocrine disrupting chemicals and OVX mouse.	J Ginseng Res Vol.44 Issue 3 Pages 519-526	10.1016/j.jgr.2020.01.008	32372874	動物	-	1	1	1	1	0	200 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則として再検査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1180	C. Y. Lee, S. A. Hoan, M. Y. Ku, H. R. Kim, J. Rhu, K. K. Kim, W. Y. Kim and M. Ka	2021	Maternal Bisphenol A (BPA) Exposure Alters Cerebral Cortical Morphogenesis and Synaptic Function in Mice	Early life exposure to bisphenol A (BPA), synthetic compound used in polycarbonate plastics, is associated with altered cognitive and emotional behavior later in life. However, the brain mechanism underlying the behavioral deficits is unknown. Here, we show that maternal BPA exposure disrupted cell removal and cell differentiation of newborn neurons during cortical development. The BPA exposure reduced the neuron number, whereas it increased glial cells in the cerebral cortex. Also, synaptic formation and transmission in the cerebral cortex were suppressed after maternal BPA exposure. These changes appeared to be associated with aberrant gene ontology analysis of RNA-seq identified an autophagy decode in the BPA condition. Mouse behavioral tests revealed that maternal BPA caused hyperactivity and social deficits in adult offspring. Together, these results suggest that maternal BPA exposure leads to abnormal cortical architecture and function likely by activating autophagy.	Cereb Cortex Vol.31 Issue 12 Pages 5598-5612	10.1093/cercor/bhab183	34171088	動物	-	1	1	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1181	S. C. Lachy, H. E. Lapp, M. Salazar, S. Semyenko, D. Chauhan, A. E. Margolis and F. A. Champagne	2024	Postnatal maternal care moderates the effects of prenatal bisphenol exposure on offspring neurodevelopmental, behavioral, and transcriptomic outcomes	Bisphenols (BP), including BPA and "BPA-free" structural analogs, are commonly used plasticizers that are present in many plastics and are known endocrine disrupting chemicals. Prenatal exposure to BPA has been associated with negative neurodevelopmental and behavioral outcomes in children and in rodent models. Prenatal BPA exposure has also been shown to impact postnatal maternal care practices by which care also affects offspring neurodevelopment and behavior. However, it is unknown whether BPA exposure alters the quality of maternal care and whether variations in maternal care mediate or moderate associated maternal care or adult behavior. The purpose of the current study was to determine the impact of prenatal bisphenol exposure and postnatal maternal care on maternal behavior and behavior in rats. Our findings suggest that the effects of prenatal bisphenol exposure on pup-seeking, adult attentional set-shifting and anxiety-like behavior in the open field are dependent on maternal care in the first five days of life. Interestingly, maternal care might also attenuate the effects of prenatal bisphenol exposure on pup-seeking and adult attentional set-shifting. Finally, transcriptomic profiles, from adult female medial prefrontal cortex, also highlight a subset of genes that are impacted by the interactive effects of prenatal bisphenol exposure and postnatal maternal care converge on estrogen receptor signaling and are involved in biological processes related to gene expression and neuronal function. Together, these findings suggest that maternal care can moderate the effects of prenatal bisphenol exposure on offspring neurodevelopment, behavior, and transcriptomic outcomes. Understanding the underlying biological mechanisms involved might allow us to identify potential avenues to mitigate the adverse effects of prenatal bisphenol exposure and improve health and well-being in human populations.	PLoS One Vol.19 Issue 6 Pages e0305256	10.1371/journal.pone.0305256	38861567	動物	-	1	1	不明	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1182	S. C. Lachy, I. Agarwal, H. E. Lapp, M. Salazar, S. Semyenko, D. Chauhan, A. E. Margolis and F. A. Champagne	2025	Interplay between prenatal bisphenol exposure, postnatal maternal care, and offspring sex in predicting DNA methylation relevant to anxiety-like behavior in rats	Prenatal exposure to endocrine disrupting chemicals, such as bisphenols, can alter neurodevelopmental trajectories and have a lasting neurobehavioral impact through epigenetic pathways. However, outcomes associated with prenatal bisphenol exposure may also be shaped by the postnatal environment and collectively these environmental effects may be sex-specific. Thus, an integrative research design that includes multiple early life exposures and considers sex differences may be essential for predicting outcomes. In the current study, we use a multivariate approach to examine the contributions of prenatal bisphenol exposure, postnatal maternal care, and offspring sex to anxiety-like behavior and DNA methylation of a well-studied candidate gene, Oxtr[1]. BDNF. Oxtr[1] is a neural hypothesized, and amygdala of adult rat offspring and Exons 1 and 4 were chosen as they are differentially regulated by maternal care and interactions with prenatal bisphenol exposure were consistently found for DNA methylation within the NAC[1] gene (ventral hippocampus) and within the BDNF and Oxtr[1] genes (amygdala). Sex-specific effects were also found across all analyses. Overall, our findings suggest that both early life factors (prenatal and postnatal) and offspring sex contribute in variation in DNA methylation of genes and neurotypes relevant to the expression of anxiety-like behavior. These results highlight the need to consider the brain region-specific effects of multiple exposures in males and females to understand the lasting effects of early environments.	Horm Behav. 2025 Jun:172:105745.	10.1016/j.yhbeh.2025.105745	40273582	動物	免連神経	1	※神経（胎生6.5）	1	1	0	0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1183	H. E. Lapp, A. E. Margolis and F. A. Champagne	2022	Impact of a bisphenol A, F, and S mixture and maternal care on the brain transcriptome of rat dams and pups	Products containing BPA structural analog replacements have increased in response to growing public concern over adverse effects of BPA. Although humans are regularly exposed to a mixture of bisphenols, few studies have investigated the effects of bisphenol mixtures. Additionally, maternal care has been shown to moderate the effects of bisphenol exposure on offspring outcomes. Here, we exposed dams to a mixture of BPA, BPF, and BPS during gestation via the basic bisphosphonate in Long-Evans rats and dams using Tag-RNA-sequencing. We also examined the association between licking and grooming, which also has mediating effects on pup neural development, and the transcriptome. Associations between licking and grooming and the transcriptome were region-specific, with the hypothalamus having the greatest number of differentially expressed genes associated with licking and grooming and the hippocampus having the least. Prenatal bisphenol exposure altered the transcriptome of the medial preoptic area (MPOA) in offspring more robustly than later gene expression. In dams, the prefrontal cortex had the greatest number of differentially expressed genes associated with prenatal bisphenol exposure. Prenatal bisphenol exposure changed the relationship between the MPOA transcriptome and maternal behavior, suggesting that bisphenol exposure may alter the neural circuitry that underlies maternal behavior. Together, these results suggest that bisphenol exposure may have long-term consequences for the brain transcriptome and maternal behavior, and that the effects of bisphenol exposure may be dependent on the brain region examined. Finally, hypothesis-driven analysis of genes related to estrogen response, parental behavior, and epigenetic regulation of gene expression revealed region-specific expression associated with licking and grooming and bisphenol exposure that were distinct in dams and pups. These data highlight the effects of bisphenols on multiple physiological process that are highly dependent on timing of exposure (prenatal vs. adulthood) and brain region, and reiterate the contributions of multiple environmental and experiential factors in shaping the brain.	Neurotoxicology Vol.93 Pages 22-36	10.1016/j.neuro.2022.08.014	36041667	動物	-	1	1	0	1	0	150 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1184	A. Lama, F. Del Piano, C. Annunziata, F. Comella, N. Opallo, S. Melini, L. Grumetto, C. Pirozzi, G. Matteo Raso, R. Meli and M. C. Fenaroli	2023	Bisphenol A exacerbates anxiety-like behavior and neuroinflammation in prefrontal cortex of adult obese mice	ABBS Bisphenol A (BPA) is an endocrine-disrupting chemical inducing several damages, such as neurotoxicity, immunotoxicity, and metabolic disorders. Obesity is the main risk factor for the increased occurrence of metabolic alterations as well as mood disorders. Here, we investigated in obese mice the effects of BPA on anxiety-like behavior, associated with neuroinflammation and immune activation. MAIN METHODS Male C57BL/6J mice were fed a high-fat diet (HFD) for 12 weeks to induce obesity. Then, HFD mice were exposed to BPA (50 μg/kg/day) for 4 weeks. Control groups received vehicle (HFD) or BPA treatment and were fed a standard diet (Control). KEY FINDINGS Behavioral results showed that BPA treatment induced anxiety-like behavior in HFD + BPA group mice compared to HFD + BPA group mice and Control mice, which showed no obesity-like behavior. The analgesic effects of BPA also emerged from hyperactivation of the hypothalamus-pituitary-adrenal gland axis, demonstrated by the increased transcription of CRF and its receptor in the prefrontal cortex (PFC). Furthermore, BPA-treated HFD mice showed an increased number of microglia in the PFC, accompanied by a shift toward a pro-inflammatory phenotype (M1/M2 = 1.4 ± 0.1 in PFC. Furthermore, it induced inflammation and monocyte recruitment in hypothalamus and amygdala. Contextually, BPA significantly amplified the immune activation caused by lipid overload as evidenced by the increased expression of TLR-4 and MCP-1 in the PFC and triggered monocytosis in the hypothalamus under lean (FC) mice. SIGNIFICANCE Of these data show that sub-chronic BPA exposure represents an additional risk factor for mood disorders strictly related to obesity, enhancing neuroinflammation and immune activation triggered by HFD feeding.	Life Sci Vol.313 Pages 121301	10.1016/j.lfs.2022.121301	36535405	動物	-	1	不明	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1185	E. Krieger, F. Fischer, J. Hosaroğlu, M. Wagner, F. Romanelli, B. Fink, M. Bauer, A. Schumacher, T. Kretschmer and A. C. Zenclussen	2025	Implications of a combined perinatal exposure to BPA and BP-3 for offspring folliculogenesis and ovarian function in mice	Endocrine-disrupting chemicals (EDCs), like bisphenol A (BPA) and benzophenone-3 (BP-3), can interfere with hormone systems, posing risks to fertility and reproduction. Exposure to EDCs is unavoidable making it a relevant environmental health topic, however the impact of real-life EDC mixtures is largely unknown. This study explored the effects of a combined BPA and BP-3 exposure at realistic intake levels for humans during pregnancy and early life on ovarian development and function in an established mouse model. Mice were daily exposed to concentrations of 4 µg/kg BPA orally, 10 mg/kg BP-3 dermally, and the combination of BPA+BP-3 from gestational day 0.5 until weaning of the offspring. Ovaries were collected from female offspring at 3 weeks and 6 months of age. Ovarian RNA-sequencing revealed that BPA and BP-3 co-exposure led to stimulation in mitotic regulation and stimulation in mature ovulatory oocyte-specific pathways in 3-week-old offspring. Histological analysis revealed that co-exposure to BPA and BP-3 led to more atretic follicles and fewer corpora lutea, and genes linked to hormone signaling, hormone synthesis, and ovarian tissue remodeling were altered relative to unexposed controls. These findings suggest that early life exposure to BPA and BP-3 at environmentally relevant levels impairs ovarian development and function in mice indicating that known safe and hormonal signaling in the ovaries, even at single, of endocrine disruptors at relevant concentrations. Such findings may be compromising fertility and reproductive health in later life. Our research underscores the importance of investigating the impact of combined EDC exposure on the reproductive system.	Ecotoxicol Environ Saf Vol.302 Pages 118750	10.1016/j.ecoenv.2025.118750	40714391	動物	-	1	1	1	1	0	4 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1186	D. Kousar, D. E. H. Asfi, M. Brahmi, F. K. Akhtsifi, F. F. Bin Dayel, M. Asdiq, M. L. Fauconnier, B. Bouzouita, K. Kahlaoui, M. Slimani and S. H. Saviliam	2025	Role of Thymus ciliatus (Thyme) to Ameliorate the Acute Neurotoxicity Induced by Bisphenol A: In Vivo Supported with Virtual Study	Background/Objectives: The purpose of this research was to investigate the effects of bisphenol A (BPA) exposure on neurobehavioral testing in young Wistar rats and to evaluate the therapeutic potential of Thymus ciliatus (TCI) essential oil to attenuate the damage induced by this chemical toxin. Methods: The essential oil was extracted by hydro-distillation (yield of 2.26%), and the characterization by GC-MS indicates that the major compounds are thymol (40.2%), carvacrol (25.1%), and p-cymene (15.3%). Male Wistar rats were divided into five groups (n = 6/group): Control, BPA (50 mg/kg), and BPA + TCI (50, 100, and 200 mg/kg). Behavioral tests were performed using a comprehensive set of tests, including the hot-cold cube test, daily flight test, Morris water maze, open field test, and novel preference test, clearly demonstrated that bisphenol A (BPA) exposure induced significant neurobehavioral impairments. Results: These impairments included reduced exploratory behavior, indication of heightened stress, anxiety, and depressive-like states, as well as deficits in memory and learning. Furthermore, BPA intoxications are associated with metabolic disturbances such as hyperglycemia along with histopathological evidence of brain tissue damage. However, TCI treatments showed these adverse effects by reversing neurobehavioral function. Molecular docking analysis revealed an affinity between the major essential oils identified in T. ciliatus, BPA, and the 5HT2C receptor and the GSK3, ACHE, and BCHE enzymes, which may explain the observed neuroprotective effects. Conclusions: Overall, this study highlights the neurotoxic potential of BPA and the therapeutic benefits of TCI essential oil, which is rich in thymol, carvacrol, and p-cymene. These findings underscore the promising role of TCI in mitigating the cytotoxic effects of BPA and lay the way for additional research into the molecular mechanisms and therapeutic uses of natural compounds for the prevention and treatment of toxic diseases. Thymol, the major component in TCI, exhibited activity related to the dopamine and serotonin pathways, so it could have potential antidepressant properties. Conclusions: Thymol might be a promising candidate for the treatment of neurodegenerative and neurological disorders such as depression, Parkinson's disease, and Alzheimer's disease while also preventing histological damage in the brain.	Pharmaceuticals (Basel) Vol.18 Issue 4	10.3390/ph18040509	40283944	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1187	K. M. M. Karlem	2022	Fertaric acid amends bisphenol A-induced toxicity, DNA breakdown, and histopathological changes in the liver, kidney, and testis	BACKGROUND: Bisphenol A (BPA) is present in many plastic products and food packaging. On the other hand, fertaric acid (FA) is a hydroxycinnamic acid. AIM: To investigate the effect of FA on BPA-related liver, kidney, and testis toxicity, DNA breakdown, and histopathology in male rats. METHODS: Thirty male albino rats were divided into five equal groups (6 rats/group): Control, paraffin oil, FA - BPA - and FA + BPA treated groups. The control and paraffin oil groups were administered orally with 1 mL distilled water and 0.5 mL paraffin oil, and FA (50 mg/kg bw) followed by BPA (5 mg/kg, bw), respectively. All these treatments were given once orally for 4 weeks. RESULTS: BPA administration significantly (p < 0.05) increased the activities of serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, lactate dehydrogenase, lactate, urea, creatinine, uric acid, substituting hormone, follicle stimulating hormone, sex hormone binding globulin, blood urea nitrogen, and testis cholesterol levels. Also, FA inhibited the degradation of liver, kidney, and testis DNA content. Oral administration of FA to BPA-treated rats restored all the above parameters to normal levels. CONCLUSION: FA ameliorates BPA-induced liver, kidney, and testis toxicity, DNA breakdown, and histopathological changes in the brain.	World J Hepatol Vol.14 Issue 3 Pages 535-550	10.4254/wjh.v14.i3.535	35582291	動物	-	1	1	1	1	0	4 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1188	A. Kobroob, W. Peerapanyasut, S. Kumfu, N. Chattipakorn and O. Wongmekiat	2021	Effectiveness of N-Acetylcysteine in the Treatment of Renal Deterioration Caused by Long-Term Exposure to Bisphenol A	Human health hazards caused by bisphenol A (BPA), a precursor for epoxy resins and polycarbonate based plastics, are well documented and are closely associated with mitochondrial impairment and oxidative imbalance. This study aimed to assess the therapeutic efficacy of N-acetylcysteine (NAC) on renal dysfunction caused by long-term BPA exposure and examine the signaling molecules involved. Male Wistar rats were given vehicle or BPA orally for 12 weeks then the BPA-treated group was subdivided to receive vehicle or NAC concurrently with BPA for a further 5 weeks, while the vehicle-treated normal control group continued to receive vehicle. Long-term BPA exposure induced renal dysfunction, glomerular and tubular damage, and renal fibrosis. Mitochondrial dysfunction was also observed in the kidneys of BPA-exposed rats. Long-term BPA exposure also induced mitochondrial swelling, decreased mitochondrial membrane potential, increased mitochondrial reactive oxygen species production, and the loss of mitochondrial membrane potential. The benefit of NAC was related to the modulation of signaling proteins in the AMPK-SIRT3-SOD2 axis. The present study shows the potential of NAC to restore mitochondrial integrity and oxidative balance after long-term BPA exposure, and suggests that NAC therapy is an effective approach to tackle renal deterioration in this condition.	Biomolecules Vol.11 Issue 5	10.3390/biom11050655	33946939	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1189	A. Kobroob, S. Kumfu, N. Chattipakorn and O. Wongmekiat	2024	Modulation of Sirtuin 3 by N-Acetylcysteine Preserves Mitochondrial Oxidative Phosphorylation and Restores Bisphenol A-Induced Kidney Damage in High-Fat-Diet-Fed Rats	Bisphenol A (BPA) and high-fat diets (HFD) are known to adversely affect the kidneys. However, the combined effects of both cause, on kidney health and the potential benefits of N-acetylcysteine (NAC) in mitigating these effects have not been investigated. To explore these aspects, male Wistar rats were fed with HFD and allocated to receive a vehicle or BPA. At week twelve, the BPA-exposed rats were subdivided to receive a vehicle or NAC for a further 5 weeks, while the vehicle-treated normal control group continued to receive a vehicle. The results revealed that BPA exposure in HFD-fed rats induced renal dysfunction, glomerular and tubular damage, and renal fibrosis. Mitochondrial dysfunction was also observed in the kidneys. BPA exposure in HFD-fed rats also led to mitochondrial swelling, decreased mitochondrial membrane potential, increased mitochondrial reactive oxygen species production, and the loss of mitochondrial membrane potential. The benefit of NAC was related to the modulation of signaling proteins in the AMPK-SIRT3-SOD2 axis. The present study shows the potential of NAC to restore mitochondrial integrity and oxidative balance after long-term BPA exposure, and suggests that NAC therapy is an effective approach to tackle renal deterioration in this condition.	Curr Issues Mol Biol Vol.46 Issue 5 Pages 4935-4950	10.3390/cimb46050296	38785564	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1190	K. Kobayashi, Y. Liu, H. Ichikawa, S. Takemura and Y. Minamiyama	2020	Effects of Bisphenol A on Oxidative Stress in the Rat Brain	We investigated the effect of bisphenol A (BPA) on oxidative stress and key-related proteins in adult rat testis. BPA (10 mg/L) was administered to rats for eight weeks through their drinking water. The reactive oxygen species (ROS) scavenging capacity for hydroxyl radicals in the plasma was reduced after two weeks. In the hippocampus, four and eight weeks of BPA increased the ratio of oxidized (2) 1/2 (+) (PdHPC). The ratio of phosphorylated ERK1/2/ERK1/2 and phosphorylated JNK/JNK1 increased after one week of BPA treatment. The ratio of phosphorylated JNK/JNK and phosphorylated ERK/ERK increased after eight weeks of BPA. No alteration could be related to tau phosphorylation. Protein phosphatase 2A (PP2A) in the hippocampus decreased after eight weeks of BPA treatment. At that time, SOD1 was significantly reduced, but no changes in SOD2 and catalase were observed. Glutathione peroxidase (GPx) activity was also reduced after eight weeks of BPA. Nuclear factor erythroid 2-related factor 2 (Nrf2) in the hippocampus was not changed. However, Nrf2 in the nuclei tended to be increased after eight weeks. In the hippocampal of rats, BPA induced systemic oxidative stress and could change ROS-induced signaling pathways in the brain. These results suggest that mitochondrial dysfunction possibly is not responsible for oxidative stress and neurodegeneration due to low doses of BPA.	Antioxidants (Basel) Vol.9 Issue 3	10.3390/antiox9030240	32187996	動物	-	1	1	1	1	0	10 mg/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1191	R. D. Kini, S. Kumar, A. K. Nayarattara and G. Megha	2024	A study on bisphenol induce renal damage and role of vitamin c as an antioxidant on bisphenol induced renal damage in wistar rats. A case control study	INTRODUCTION: Bisphenol A (BPA) is considered one of the most common industrial manufactured chemicals and a pollutant. oxidative stress has been induced by bisphenol by dysregulate the cytokines. Oxidative stress is a condition in which the production of free radicals and the body's ability to neutralize them are out of balance. Vitamin C is a powerful antioxidant that can help protect cells from oxidative damage. This study was focused to evaluate the damaging effect on BPA on kidney and the role of vitamin c as anti-oxidant on BPA induced kidney toxicity. MATERIAL & METHODS: Three control two groups of rats(6 rats in each) Group 1: Control (Only Oral treated) Group 2:Vitamin C treated), Group 3: (Bisphenol treated), Group 4: (Vitamin C + Bisphenol treated). Oral kidney homogenized to measure Malondialdehyde level and glutathione and other kidney was used to measure histopathological changes. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by post hoc tests to determine significant differences between the groups. RESULTS: Results showed that Bisphenol A treatment significantly increased ROS and decreased GSH and increased in MDA level as well as SOD, catalase and potassium level. Biochemical results were supported by histo-pathological changes. The treatment with Vitamin C showed an how in the rats of GSH, catalase and potassium level and fall in MDA. Vitamin C per treatment also showed some beneficial changes in histology of kidney also. CONCLUSION Our result demonstrated that exposure to Bisphenol induced oxidative stress in rat kidney and vitamin C could act as an antioxidant protecting against BPA induced cellular stress.	Clin Ter. 2024 Nov-Dec;175(6):450-454.	10.7417/ct.2024.5153	39584766	動物	腎	1	1	単独あり	Wistar rat	0	25 mg/kg:0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1192	S. H. Kim, S. H. Shin, S. M. Kim, S. E. Jung, B. J. Shin, J. S. Ahn, K. T. Lim, D. H. Kim, K. Lee and B. Y. Ryu	2025	Bisphenol Analogs Downregulate the Self-Renewal Potential of Spermatogonial Stem Cells	PURPOSE: In this study, we investigated the effect of bisphenol A (BPA) and its major analogs, bisphenol F (BPF), and bisphenol S (BPS), on spermatogonial stem cells (SSCs) of populations using in vitro SSC culture and in vivo transplantation models. METHODS: SSCs were isolated from 6-day-old mice and cultured in the presence of BPA, BPF, or BPS at concentrations ranging from 0.1 to 10 μM. Cell proliferation, apoptosis, and bisphenol-induced cytotoxicity and changes in SSC characteristics. Mitochondrial Rex-proximity, immune polymerase chain reaction (PCR), and transcriptome analysis. The functional alteration of SSCs were further investigated by examining donor SSC-derived spermatogenesis restoration through in vivo transplantation and subsequent testis analysis. RESULTS: BPF exhibited a similar inhibitory effect on SSCs as BPA, demonstrating a significant decrease in SSC survival, inhibition of proliferation, and induction of apoptosis. On the other hand, while BPS was comparatively weaker than BPA and BPF, it still showed significant SSC cytotoxicity. Importantly, SSCs exposed to BPA, BPF, and BPS exhibited a significant reduction in donor SSC derivergerm cell colonies per total number of cultured cells, indicating that, like BPA, BPF, and BPS can also impair the self-renewal potential of SSCs. Transcriptome analysis revealed that BPA, BPF, and BPS commonly altered the expression of genes related to cell cycle regulation and apoptosis. CONCLUSION: Our findings indicate that the major BPA substitutes, BPF and BPS, have significant cytotoxic effects on SSCs, similar to BPA. These effects may lead to a reduction in the functional self-renewal stem cell population and potential impacts on male fertility.	World J Mens Health. 2025 Jan;43(1):154-165.	10.5534/wjmh.230166	38606862	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1193	J. K. Kim, A. Khan, S. Cho, J. Na, Y. Lee, G. Bang, W. J. Yu, J. S. Jeong, S. H. Jee and Y. H. Park	2019	Effect of developmental exposure to bisphenol A on steroid hormone and vitamin D3 metabolism	High exposure to bisphenol A (BPA) in children has been associated with the outcomes of several diseases, including those related to developmental problems. To elucidate the mechanism of BPA-mediated developmental toxicity, plasma and urine from rats exposed to BPA was analyzed with high-resolution metabolomics, beginning from post-natal day 0, for 10 days. Female and male rats were orally administered 5 different BPA doses (0, 0.02, 0.2, 2, and 20 mg/kg/day). Urine and plasma samples were collected at 3 weeks of age and analyzed using UPLC-QTOF/MS. Vitamin D3 was found to be a key metabolite in the rodent rats. It was increased by administration to female BPA dose and metabolic changes were more noticeable, showing overall metabolic changes in plasma and urine, respectively. Metabolic perturbation in the steroid hormone biosynthesis pathway was significantly associated with dose- and sex-specific BPA effects. Intermediate metabolites in the rate-limiting step of steroid hormone biosynthesis shown regulated steroid hormones in the 250 mg treatment. Further, our study identified that BPA increased urinary concentration of vitamin D3 and decreased its concentration in blood, suggesting that perturbation of vitamin D3 metabolism may be mechanistically associated with neurodevelopmental disorders caused by BPA. These metabolites showed a decrease in sex difference with high BPA dose because female rats were more affected than males, which can be related with early puberty onset in female. In brief, the results demonstrated that BPA induces dose- and sex-specific metabolic shifts and that perturbation of metabolism can explain developmental problems.	Chemosphere. 2019 Dec:237:124469.	10.1016/j.chemosphere.2019.124469	31549635	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1194	J. Kim, N. H. Kim, I. Your, E. K. Seo and C. Y. Kim	2023	Effects of Allium macrostemon Bunge Extract on Adipose Tissue Inflammation and Hepatic Endoplasmic Reticulum Stress in High-Fat Diet-Fed and Bisphenol A-Treated C57BL/6N Mice	The simultaneous exposure to a high-fat (HF) diet and to bisphenol A (BPA) from deformed foods and food delivery containers is on the rise in humans, according to the increased frequency of food delivery during the COVID-19 pandemic. This, co-exposure could cause harmful tissue toxicity in the human body. Here, the preventive effect of Allium macrostemon Bunge (AM) extract against dysfunction in adipose tissue and the liver was investigated in HF diet with or without BPA co-exposed C57BL/6N mice. Mice were divided into six groups: control (CON), HF diet (HF), HF diet with an oral injection of BPA (HF + BP), and HF diet with an oral injection of BPA and AM extract (HF + BP + AM). HF feeding increased body weight gain and fat mass (HF > BP > AM). HF feeding increased body weight gain and fat mass (HF > BP > AM). HF feeding increased body weight gain and fat mass (HF > BP >

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1206	S. Kaur, M. Sakaja, A. Aniqa and S. Sadwal	2021	Selenium attenuates bisphenol A incurred damage and apoptosis in mice testes by regulating mitogen-activated protein kinase signalling	Being a vital micronutrient, along with antioxidant, selenium (Se) protects the cells from oxidative stress (OS) in the form of selenoproteins. Bisphenol A (BPA) is a one toxicogenic compound that adversely affects the male reproductive system. The present study was aimed to elucidate the potentiative role of fenugreek seeds aqueous extract (FSE) and BPA-induced testicular damage in mice. Study included four different groups of male Balb/c mice: control (C), fenugreek (FSE), bisphenol A (BPA) and fenugreek + bisphenol A (FSE + BPA). After two months of treatment, assessment of sperm morphology, biochemical parameters, histological and immunohistochemical (IHC) analysis of testes was carried out. Results indicated that BPA treated animals demonstrated a marked decrease in antioxidant enzyme activities (superoxide dismutase, catalase, reduced glutathione and thiobarbituric acid reactive substances) in comparison to control group. Moreover, BPA induced significant (p < 0.05) decline in sperm count, viability and motility, while it increased the sperm abnormalities. Furthermore, BPA also induced histological changes in the testes of mice which was confirmed by IHC analysis. Nuclear factor erythroid 2-related factor 2 (Nrf2) signalling, Bax/Bcl-2 ratio and caspase-3 were studied to find out the apoptotic pathway. Results indicated that BPA treated animals demonstrated a marked increase in antioxidant enzyme activities (superoxide dismutase, catalase, reduced glutathione and thiobarbituric acid reactive substances) in comparison to control group. Moreover, BPA induced significant (p < 0.05) decline in sperm count, viability and motility, while it increased the sperm abnormalities. Furthermore, BPA also induced histological changes in the testes of mice which was confirmed by IHC analysis. Nuclear factor erythroid 2-related factor 2 (Nrf2) signalling, Bax/Bcl-2 ratio and caspase-3 were studied to find out the apoptotic pathway. Results indicated that BPA treated animals demonstrated a marked decrease

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統合_1219	A. Kaimal, J. M. Hoovenmitth, A. D. Cherry, J. T. Gaestly, M. H. Al Mansi, N. M. Martin, H. Buechner, P. V. Holmes, P. S. MohanKumar and S. M. J. MohanKumar	2023	Prenatal exposure to bisphenol A and/or diethylhexyl phthalate alters stress responses in rat offspring in a sex- and dose-dependent manner	Background: Prenatal exposure to endocrine-disrupting chemicals (EDCs) are correlated with adverse behavioral outcomes, but the effects of combinations of these chemicals are unclear. The aim of this study was to determine the dose-dependent effects of prenatal exposure to EDCs on male and female behavior, Methods: Pregnant Sprague-Dawley rats were orally dosed with vehicle, bisphenol A (BPA) (5 µg/kg body weight (BW)/day), diethylhexyl phthalate (DEHP) (5 µg/kg BW/day), or BPA + DEHP (5 µg/kg BW/day of each) from gestational day (GD) 6 to GD 19. Offspring were subjected to the Open Field Test (OFT), Elevated Plus Maze (EPM), and Novel Object Recognition (NOR) tests in adulthood. Body, adrenal gland, and pituitary gland weights were collected at sacrifice. Corticosterone (CORT) was measured in the serum. Results: Female EDC-exposed offspring showed anxiolytic effects in the OFT, while male offspring were unaffected. DEHP exposure increased the number of entries into the open arms in the EPM, while BPA exposure had no effect. Male offspring fostered less in the EPM, while their female counterparts showed reduced body reactivity, indicating sex-specific endocrine-driven behavioral alterations. Additionally, DEHP-F2 females had increased body weight, while BPA-F2 females had lighter adrenal glands. DEHP-F2 alone and in combination with BPA led to lower adrenal gland weights, but only in male offspring. Finally, females treated with a mixture of BPA + DEHP had elevated CORT levels. Conclusion: Prenatal exposure to BPA, DEHP, or a mixture at the two affects behavior, CORT levels, and adrenal gland weights in a sex- and dose-dependent manner.	Front Toxicol Vol.5 Pages 1264238	10.3389/ftox.2023.1264238	38152552	動物	-	1	1	1	1	0	5 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1220	A. Kaimal, J. M. Hoovenmitth, M. H. Al Mansi, A. D. Cherry, J. T. Gaestly, P. V. Holmes, P. S. MohanKumar and S. M. J. MohanKumar	2024	Prenatal bisphenol A and/or diethylhexyl phthalate exposure followed by adult estradiol treatment affects behavior and brain monoamines in female rat offspring	HIGHLIGHTS. Women are at increased risk for mood disorders, which may be partly attributed to exposure to endocrine-disrupting chemicals (EDCs) during sensitive periods such as pregnancy. Exposure during these times can impair brain development in the offspring, potentially leading to mood disorders in later life. Additionally, fluctuating levels of endogenous estrogens, as seen during pregnancy, or the use of oral contraceptives can further enhance this risk. This study examines the combinatorial effects of prenatal EDC exposure combined with chronic low-dose 17β-estradiol (E2) treatment in adulthood on behavioral outcomes. METHODS. Pregnant Sprague-Dawley rats were orally dosed with vehicle, bisphenol A (BPA) (5 µg/kg body weight (BW)/day), low-dose (LD) diethylhexyl phthalate (DEHP) (5 µg/kg BW/day), high-dose (HD) DEHP (15 mg/kg BW/day), or a mixture of BPA + DEHP (LD) from gestational day (GD) 6 to GD 19. Female offspring were ovariectomized at postnatal day (PND) 60 and treated with vehicle or E2 (0.2 µg/kg BW/day) for 21 days. Behavioral testing was conducted, and serum hormones and brain monoamine levels were analyzed. RESULTS. Chronic E2 treatment in controls increased anxiety and reduced active coping behaviors. In BPA- and BPA+DEHP-exposed offspring, E2 treatment reversed some of these effects. Dose-dependent alterations in circulating hormone levels and brain monoamines were observed. Dysregulation of the stress axis was particularly notable with the higher dose of BPA+DEHP (DEHP-HD). Overall, prenatal EDC exposure altered behavior, hormones, and brain monoamines, with adult E2 treatment further exacerbating some of these effects in female offspring.	Front Endocrinol (Lausanne) Vol.15 Pages 1479838	10.3389/fendo.2024.1479838	39839474	動物	-	1	1	1	1	0	5 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1221	A. Kaimal, M. H. Al Mansi, J. B. Daghir, C. Pope, M. G. Varghese, T. B. Bud, A. E. Almond, L. A. Cagle, H. K. Beyene, W. T. Bradford, B. B. Whitsett, B. D. K. Bougouma, K. J. Rita, Y. J. Chuang, E. J. Campbell, A. Marcal, P. S. MohanKumar and S. M. J. MohanKumar	2021	Prenatal exposure to bisphenols affects pregnancy outcomes and offspring development in rats	The objective of this study was to evaluate the effects of gestational exposure to low doses of bisphenol S (BPS), bisphenol G (BPG), and bisphenol F (BPF) on pregnancy outcomes and offspring development. Pregnant Sprague-Dawley rats were orally dosed with vehicle, 5 µg/kg body weight (BW)/day of BPS, BPF, or BPF, or 5 µg/kg BW/day of BPF or gestational days 6-21. Pregnancy and gestational outcomes, including number of abortions and stillbirths, were monitored. Male and female offspring were subjected to anxiety(open field test), followed by pre- and post-weaning body weights, post-weaning food and water intakes, and adult organ weights. Results: Exposure to BPS, BPF, or BPF+BPF did not affect pregnancy outcomes, but BPS and BPF+BPF increased the number of pregnant rats dosed with BPF+BPF. Exposure to BPS, BPF, or BPF+BPF during gestation affected offspring, while BPF

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性発現基準不適合と判断されるものは作成根拠評価への適用。当該物質評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1232	H. Jiao, Y. Chen, T. Han, Q. Pan, F. Gao and G. Li	2023	GGA1 participates in spermatogenesis in mice under stress	BACKGROUND: Infertility is recognized as a common and worrisome problem of human reproductive ecotoxicle. Based on previous studies, male factors account for about half of all infertility cases. Exposure to environmental isolants is an important contributor to male infertility. Bisphenol A (BPA) is the most prominent toxic environmental contaminant worldwide affecting the male reproductive system. BPA can impair the spermatogenic cells, leading to male infertility. Gallus gallinarum 1 (GGA1) is a member of the Gallus family and is highly conserved in vertebrates. GGA1 is a homolog of Drosophila melanogaster with spermatogenesis. In Drosophila, however, its function in mammalian spermatogenesis remains unclear. METHODS: Eight-week-old male mice were divided into the CONTROL and system. Eight (1 C) male mice and wild-type littermates received intraperitoneal (i.p.) injections of BPA (40 μg/kg) once daily for 3 weeks. Histological and immunofluorescence staining were performed to analyze the phenotypes of these mice. RESULTS: Male mice lacking Ggal had normal fertility without any obvious defects in spermatogenesis, sperm count and sperm morphology. Ggal ablation led to infertility in male mice exposed to BPA, along with a significant reduction in sperm count, sperm motility and the percentage of normal sperm. Histological analysis of the seminiferous epithelium showed that spermatogenesis was severely disorganized, while apoptotic germ cells were significantly increased in the Ggal-null mice exposed to BPA. Our findings suggest that Ggal protects spermatogenesis against damage induced by environmental pollutants.	Peerj Vol.11 Pages e15673	10.7717/peerj.15673	37551344	動物	-	1	1	1	0	0	40 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1233	W. Jiang, H. Zhao, L. Zhang, B. Wu and Z. Zha	2020	Maintenance of mitochondrial function by astaxanthin protects against bisphenol A-induced kidney toxicity in rats	Bisphenol A (BPA), a global environmental pollutant, has been reported to have the potential to induced organs toxicity. This study explored the potential benefits of astaxanthin (AST), a natural antioxidant, against BPA-toxicity in the kidney, and explored whether mitochondria are involved in this condition. Sixty Wistar rats were fed with a vehicle, BPA (BPA group), AST, and were evaluated after four weeks. AST treatment significantly reversed BPA-induced changes in body weight, kidney/body weight, and renal function-related markers. When treated simultaneously with AST, the imbalance of the oxidative-antioxidant status caused by BPA was also reversed. Moreover, AST treatment significantly reversed BPA-induced mitochondrial swelling, the collapse of the membrane potential, and the decrease in the mitochondrial respiratory chain complex enzyme activity. The beneficial of AST were associated with enhanced mitochondrial function, which led to increased mitochondrial-encoded gene expression, mitochondrial copy number, and increased mitochondrial morphology chain complex enzyme activity. Our results demonstrate the efficacy of AST in preventing BPA-induced kidney damage, in part by regulating oxidative imbalance and improving mitochondrial function. Collectively, these findings provide a new perspective for the rational use of ATX in the treatment of BPA-induced kidney disease.	Biomed Pharmacother Vol.121 Pages 109629	10.1016/j.biopha.2019.109629	31733573	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1234	C. Jiang, G. Gao, W. Sun, Y. Sun and J. Yu	2023	Molecular characterization of physis tissue and hormonal profiles of female rats neonatally exposed to low-dose bisphenol A	Physis is a complex cartilaginous structure that is critical for longitudinal bone growth. As one of the endocrine-disrupting chemicals, bisphenol A (BPA) can interfere with the physis by disrupting the complex networks of hormones. However, the molecular mechanisms underlying BPA-induced physis damage remain unclear. Kiss1 is a key regulator of the hypothalamic-pituitary-gonadal axis and is widely expressed in the physis. Therefore, understanding the molecular pathways involved in the physis after neonatal exposure to low-dose BPA may permit the identification of research targets for therapeutics, which may aid in modulating the process of growth plate closure. In the present study, female Sprague-Dawley rats were exposed to 0.05 mg kg(-1) day(-1) of BPA and corn oil (vehicle) from postnatal day 1 (PND1) to 15 via subcutaneous injection. Then gonadectomy (GDX) surgeries were performed for the rat(BPA) injected from the physis. The levels of sclerostin (SOST), growth hormone (GH), and insulin-like growth factor 1 (IGF-1) were measured in peripheral (BPA) groups (n = 10 for each group). We observed statistically significant enrichment of gene sets in the BPA(Bing)-tissues compared with the Vehicle tissues. Further analysis of the differentially expressed genes (DEGs) identified BPA(Bing)-specific networks of secreted proteins (LBP, SPP, SEC, ACE2, CAD, and CMPK) as well as those of heat-metronectin proteins (PSB2, LAMC2, ADAMTS18, and ADAMTS20). Furthermore, the levels of GC and ESI scores elicited by BPA exposure. Our results revealed the specific molecular characteristics of physis contaminated with BPA and may provide new clues for physis maturation and suspension of related processes and exceptional exposure.	Toxicol Ind Health Vol.39 Issue 3 Pages 146-157	10.1177/07482372231156666	36779543	動物	-	1	0	1	1	0	0.05 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1235	C. Jiang, W. Dang, G. Gao, W. Sun, Y. Wang, B. Zhan, Y. Sun and J. Yu	2024	Maternal oral exposure to low-dose BPA accelerates the onset of puberty by promoting prepubertal Kiss1 expression in the AVPV nucleus of female offspring	As the incidence of precocious puberty has risen in recent years and the age at puberty onset is younger, children may be at increased risk for health consequences associated with the early onset of puberty. Bisphenol A (BPA) is recognized as an endocrine disruptor chemical that is reported to induce precocious puberty. The effect of BPA exposure modes, times, and doses (especially low dose) were controversial. In the present study, female Sprague-Dawley rats were exposed to corn oil (vehicle) or BPA (0.05 mg kg(-1) day(-1)) via subcutaneous injection from postnatal day 1 (PND1) to 15 (PND1-15) or 21 (PND1-21). Then, BPA-treated rats were gonadectomized (BPA-GDX). Pregnant rats were exposed to corn oil vehicle, 0.05 mg kg(-1) day(-1) BPA, or 5 mg kg(-1) day(-1) 17α-propionate (PRO) (n = 10 per group). The vaginal opening (VO), ovarian follicular luteinization, and relevant hormone concentrations were measured. Hypothalamic Kiss1 and ERα/ERβ levels by western immunoblot analysis were also examined as indices of puberty onset. During in vitro exposure, low-dose BPA reactivated ERα-dependent Kiss1 and PRDM1, and subsequently accelerated puberty onset by promoting the expression of prepubertal Kiss1 and ERβ/ERα in the AVPV nucleus. In PND30, leading to advanced VO, an elevation in LH and FSH concentrations (on PND30). We also noted increased ERα mRNA on PND30 and PND35. Maternal oral exposure to low-dose BPA altered the ERα curve during the neonatal and prepubertal periods, and subsequently accelerated puberty onset by promoting prepubertal Kiss1 expression in the AVPV nucleus.	Reprod Toxicol Vol.124 Pages 108543	10.1016/j.reprotox.2024.108543	38232916	動物	-	1	1	1	不明	0	0.05, 5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1236	J. Jia, H. Xu, C. Chen, X. Zhang, X. Zhang, W. Li and J. Ma	2020	Quantitative proteomic analysis of mouse testis uncovers cellular pathways associated with bisphenol A (BPA)-induced male infertility	Quantitative proteomic analysis was performed using iTRAQ to explore the potential regulation of differentially expressed proteins (DEPs) by bisphenol A (BPA) in murine testis. BPA was intraperitoneally injected into male mice at 0, 50, 100, and 200 mg/kg/day for 5 consecutive days. Histological examination revealed that BPA exposure induced testicular damage in a dose-dependent manner. Tandem mass tag (TMT) labeling and nanoscale liquid chromatography-tandem mass spectrometry (nanoLC-MS/MS) identified 5,947 proteins in the mouse testis. The levels of 7 and 51 were affected by BPA exposure. The abundances of enzymes(cat-1 (Cbs1), haptoglobin (Hp), and insulin-like 3 (Insl3) were significantly lower in BPA-treated mice than those in control mice. The expression changes in the above-mentioned proteins were further validated at the protein level using Western blot analysis. We concluded that BPA affects testicular histological morphology of testis and sex hormone production. The regulation of the proteins, such as Cbs1, Hp and Insl3, may reflect that these proteins may serve as important factors in male reproductive disorders caused by BPA, and these proteins are probably biomarkers for infertility caused by endocrine-disrupting chemicals.	Gen Physiol Biophys Vol.39 Issue 4 Pages 331-341	10.4149/gpb_2020013	32902403	動物	-	1	0	1	不明	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1237	R. Ji, M. Cui, D. Zhou, X. Pan, Y. Xie, X. Wu, X. Liang, H. Zhang and W. Song	2023	Adulthood bisphenol A exposure induces anxiety in male mice via downregulation of alpha-1D adrenergic receptor in paraventricular thalamus	Bisphenol A (BPA), a ubiquitous endocrine disrupting chemical, is widely used in household plastic products. Large amounts of evidence indicate prenatal and postnatal BPA exposure causes neurodevelopmental disorders, such as anxiety and autism. However, the neuronal mechanisms underlying the neurotoxic effects of adulthood BPA exposure remain poorly understood. Here, we provided evidences that adult mice treated with BPA (0.5 mg/kg/d, 0.05 mg/kg/d) for 4 weeks displayed anxiety-like behaviors. Moreover, BPA exposure significantly decreased the excitability of glutamatergic neurons in the paraventricular thalamus (PVT). Acute chemogenetic activation of PVT glutamatergic neurons caused similar effects on anxiety as observed in male mice exposed to BPA. In contrast, acute chemogenetic inhibition of PVT glutamatergic neurons reduced BPA-induced anxiety in male mice. Concomitantly, the BPA-induced anxiety was related to a down-regulation of alpha-1D adrenergic receptor in the PVT. Taken together, the present study indicated a previously unknown target region in the brain for neurotoxic effects of BPA on anxiety and implicated a possible molecular mechanism of action.	Ecotoxicol Environ Saf Vol.262 Pages 115205	10.1016/j.ecoenv.2023.115205	37392660	動物	-	1	不明	1	1	0	0.45 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1238	H. Ji, N. Song, J. Rier, W. Li, B. Xu, H. Li and G. Shen	2020	Metabonomics reveals bisphenol A affects fatty acid and glucose metabolism through activation of LXR in the liver of male mice	Bisphenol A (BPA) is a representative environmental endocrine disrupting chemical that is widely used in the production of polycarbonate plastics and epoxy resins. Many studies have confirmed BPA is be closely associated with metabolic diseases, reproductive system diseases, and sex-hormone dependent cancers. In this study, we aimed to systematically elucidate the molecular action of BPA on liver fatty acid and glucose metabolism and the reasons for BPA-induced hepatic steatosis through a metabonomics approach. C57BL/6 mice were orally treated with BPA (1, 10, 50, 250 μg/kg/d) for 35 days. Histological examination and Histopathology, molecular docking, mRNA expression levels and activities of enzymes were analyzed. Based on the high-resolution mass spectrometry (MS) for metabonomics and on various software and bioinformatic analysis methods, we found that BPA could affect fatty acid and glucose metabolism. Both the TCA cycle and BPA also regulated the nuclear receptor in LXR-caused lipogenesis, thereby affecting the normal metabolic functions of the liver.	Sci Total Environ. 2020 Feb 10:703:134881.	10.1016/j.scitotenv.2019.134681	31715463	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-
統合_1239	B. O. Jamiloux, R. C. Knight, K. L. Abbott, S. R. Pondugula and B. T. Akingbemi	2021	Gonadal sex steroid hormone secretion after exposure of male rats to estrogenic chemicals and their combinations	Environmental chemicals can interfere with the endocrine axis; hence they are classified as endocrine-disrupting chemicals (EDCs). Bisphenol S (BPS) is used in the manufacture of consumer products because of its superior thermal stability and is thought to be a safer replacement chemical for its analog bisphenol A (BPA). However, the safety profile of these compounds alone or in the presence of other EDCs is yet to be fully characterized. In this study, we tested the hypothesis that BPS, alone or in combination with other estrogenic chemicals, would alter the secretion of gonadal sex steroid hormones. Using a rat model and chemical mixtures, we investigated the effects of BPS, BPA, EE2, and their combinations on steroid concentration in the growing male rat gonad. Prepubertal castrated male rats at 21 and 35 days of age were provided with test chemicals in drinking water (parts per billion) for 10 days. At termination of exposure, some individual chemical effects were modified by exposure to chemical combinations. Single chemical exposures markedly increased testosterone concentration, but when combinations (e.g., BPA + BPS + EE2) caused the opposite effect, i.e., increased Leydig cell T secretion. Also, the test chemicals varied in their combination-increased testosterone and Leydig cell 17,20 lyase/cytochrome P450 17A1 (CYP17A1) expression. Chemical-induced changes in T and E2 secretion were associated with altered testicular expression of the cholesterol side-chain cleavage (CyclaCleav) and 17,20 lyase/steroid dehydrogenase (Hsd17) enzyme protein. Additional studies are warranted to understand the mechanisms by which single and chemical combinations impact function of testicular cells and disrupt their paracrine regulation.	Mol Cell Endocrinol. 2021 Aug 1:533:111332.	10.1016/j.mce.2021.111332	34038751	動物	内分泌/精巣	1	1	1	1	0	低ホルモン(PND3～5)μg/L	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-
統合_1240	M. Javed, Sulaimya, A. Mangla, G. Jindal, H. N. Bhutto, S. Shahid, S. Kumar and S. Rekvadin	2025	Bisphenol A-induced polycystic ovary syndrome (PCOS) with hormonal and metabolic implications in rats	There is a rising incidence of polycystic ovary syndrome (PCOS) cases worldwide in women of reproductive age due to environmental factors. We evaluated the effects of an environmental estrogen, bisphenol A (BPA) for inducing PCOS in female Wistar albino rats and the therapeutic potential of Metformin (MET) and Pioglitazone (PIO). Thirty rats were divided into 5 groups (n = 6) and treated for 21 days. Group I received 1 mL/kg BPA, respectively. While normals treated with the positive control (dehydroepiandrosterone, DHEA) at 6 mg/100g caused 100% disorder. Cystic and atretic follicles along with less corpora lutea were found in the low dose group. However, no corpus luteum was found in the high dose group. Furthermore, hyperplasia and hypertrophy were found in the myometrium, endometrium, and luminal epithelium of the uterus of the last dose and DHEA groups. Additionally, 17,21 metabolic progesterone, DHEA, androstenedione, testosterone, dihydrotestosterone (DHT), dehydroepiandrosterone sulphate (DHEAS), estradiol/estrone hormone, LABH3, rats of 11ß-17ß and testosterone/DHT were increased significantly (P < 0.01) in BPA groups. A significantly higher TSH (P < 0.01) indicates hypothyroidism. Furthermore, hyperglycemia, hypercholesterolemia, HOMA-IR, and HOMA-ß indicate insulin resistance in the low-dose group. Thus, the low dose of BPA was found to be non-anemic as compared to the higher dose in defining the hyperandrogenic state. Our study revealed that BPA may not only be a causative factor in the induction of PCOS but also has metabolic implications bearing on its mutagenic nature.	Reprod Toxicol Vol.131 Pages 108750	10.1016/j.reprotox.2024.108750	39549768	動物	-	1	不明	1	不明	0	50, 500 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1241	N. S. Jardim, S. G. Müller, M. H. M. Sari and C. W. Nogueira	2020	Females are more susceptible than male mice to thermal hyperanalgesia behavior induced by early-life bisphenol-A exposure: Effectiveness of diphenyl diselenide	Humans are ubiquitously exposed to bisphenol A (BPA), one of the most used synthetic monomers for manufacturing polycarbonate plastics. BPA exposure leads to abnormal nociceptive perception and neuroinflammation in rodents. This study investigated whether diphenyl diselenide (PhSe)2), a diselenium substance containing redox molecule, would be effective against the hyperanalgesia behavior induced by the early-life BPA exposure to mice. Three-week-old male and female Swiss mice received intragastrically BPA (5 mg/kg) from 21st to 60th postnatal day. After, the mice received by the intragastric route (PhSe)2 (1.1 mg/kg) once a day for seven days. The BPA exposure induced thermal hyperanalgesia behavior in female mice, but not in male mice, in the hot plate test. Moreover, the BPA exposure increased the IL-1β levels in female mice. The results demonstrated that females were more susceptible than male mice to thermal hyperanalgesia behavior early BPA exposure in BPA. (PhSe)2 (but effective against the redox molecule) in female mice. Furthermore, (PhSe)2 restored the impairment in the levels of inflammatory proteins (COX-2, IL-1β, and p-JNK/JNK) but not those of apoptosis in the cerebral cortex of female mice exposed to BPA. Collectively, these data showed that females were more susceptible to thermal hyperanalgesia behavior induced by early-life exposure to BPA than male mice. The administration of (PhSe)2 reduced thermal hyperanalgesia behavior, a sex-independent effect, in BPA-exposed mice. (PhSe)2) modulated inflammatory protein levels in the cerebral cortex of female mice exposed to BPA.	Eur J Pharmacol Vol.879 Pages 173156	10.1016/j.ejphar.2020.173156	32360838	動物	-	1	1	1	1	0	5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1242	I. A. Jama, I. M. Usman, A. Oviosun, E. D. Eze, I. A. Adeniji, E. M. Ekukalo, E. Kwizera, E. Owembabazi and E. Anyanwu	2025	Assessment of the Impact of Bidens pilosa on Behavioral, Oxidative Stress and Cerebellar Cortical Histoarchitectural Alterations During Bisphenol A Exposure in Mice	PURPOSE: The use of medicine plants in the management of various human ailments have gained lots of attention in recent time; hence, the present study aimed to investigate the impact of Bidens pilosa on the behavioral, oxidative stress and cerebellar cortical histoarchitectural alterations during Bisphenol A exposure in mice. METHODS: Thirty (30) adult male mice were divided into six groups. Group 1 received distilled water only, group 2 received 50 mg/kg b.w. of BPA, group 3 received 100 mg/kg b.w. of BPA, group 4 received 50 mg/kg b.w. of BPA + 100 mg/kg b.w. of Bidens pilosa, group 5 received 100 mg/kg b.w. of BPA + 100 mg/kg b.w. of Bidens pilosa, while group 6 received vitamin C (50 mg/kg b.w.) along with BPA. The animals' anthropometrical traits were measured weekly, while behavioral tests (open field, hole board, and Y-maze) were evaluated following the last dosing. After sacrificing, oxidative stress biomarkers, and cerebellar histology. RESULTS: Animals treated with high doses of Bidens pilosa spent less time crossing the beam during the beam walking test and more time in the arms/long time than those treated with BPA alone. Elevated malondialdehyde level and higher catalase and superoxide dismutase activity was observed in Bidens pilosa treated groups than in the BPA only group. Histological examination revealed a significant improvement in the cerebellar tissue structure in Bidens pilosa treated groups, particularly at higher doses. CONCLUSION: Bidens pilosa demonstrated potential protective effects against BPA-induced oxidative stress and negative histological changes in the cerebellar cortex, suggesting its therapeutic potential for mitigating BPA neurotoxicity. Further research is needed to explore the therapeutic applicability.	J Exp Pharmacol Vol.17 Pages 403-416	10.2147/jep.S522973	40606320	動物	-	1	不明	1	不明	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1243	R. Iwell, A. M. Vinggaard, H. Soyama and R. Anand-Ivell	2022	Influence on the adult male Leydig cell biomarker insulin-like peptide 3 of maternal exposure to estrogenic and anti-androgenic endocrine disrupting compound mixtures: A retrospective study	Insulin like peptide 3 (INSL3) is a peptide biomarker secreted specifically by the mature Leydig cells of the testes. It is constitutive, has low within individual variance, and effectively measures the functional capacity of the adult testicular Leydig cell population. Here, we re-analyzed INSL3 data from a previous study in which pregnant rats were exposed to mixtures of anti-androgens and estrogens. The study aimed to determine maternal exposure to environmentally relevant mixtures of endocrine disrupting chemicals (EDC) at low-dose levels (known as no-observed-adverse-effect-level, NOAEL) and to identify the most sensitive endpoint. EDC mixtures were administered to pregnant Wistar rats from embryonic day (ED) 7 to postnatal day (PND) 18. Male offspring were euthanized at PND 90 (adult) from the F1 generation of females maternally exposed to varied doses of bisphenol A (BPA), butylparaben, vinclozolin, and flutamide as single compounds, as well as estrogenic and anti-androgenic mixtures of BPA and butylparaben and dE2 ethinylestradiol and vinclozolin and procymidone respectively. A mixture of BPA and butylparaben significantly reduced circulating INSL3 concentrations in adult male progeny. The remaining compounds or mixtures tested, though sufficient to induce other effects in the F1 generation were without significant effect. Maternal exposure to low concentrations of some EDCs may be a contributing factor to the variation in the Leydig cell biomarker INSL3 in young adulthood, though caution is warranted translating results from rats to humans.	Andrologia. 2022 Dec;54(11):e14566.	10.1111/and.14566	36054713	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-
統合_1244	J. I. Itodo, P. I. Rekwot, T. Akuwog, L. Allam, K. Olutimilehin Jolayemi, S. Kyari, K. O. Abah, S. Ibrahim, M. U. Dogara, A. T. Yunusa, M. M. Musa, H. L. Mundi and H. R. Abdullahi	2022	Azanza garckeana ameliorates Bisphenol A-induced reproductive toxicities in rabbit bucks	This study evaluated the ameliorative properties of Azanza garckeana in Bisphenol A-induced reproductive toxicities on weight, spermiogram, serum hormonal profile, sperm DNA integrity, histopathology of testes and testes tissues of rabbit bucks. Twenty-eight rabbit bucks, with live weight of 1.50-2.00 kg and aged 10-18 months. They were randomly divided into four groups of seven bucks each, group A was administered distilled water (1.5 ml/) daily for 12 weeks, group B was administered Bisphenol A (100 mg/kg) for 5 consecutive days in a week for a period of 12 weeks, group C was administered Azanza garckeana (500 mg/kg) daily for 12 weeks, group D was administered Bisphenol A (100 mg/kg) for 5 consecutive days in a week and Azanza garckeana (500 mg/kg) daily for 12 weeks. The results showed that Bisphenol A significantly ($p < 0.05$) affected significantly ($p < 0.05$) between group B (1.4 ± 0.23) when compared with groups A (0.3 ± 0.06), C (0.7 ± 0.19) and D (1.1 ± 0.18). There were significant differences ($p < 0.05$) in the mean testicular size, spermiogram, testosterone, follicle stimulating hormone, luteinizing hormone and sperm DNA fragmentation index between Bisphenol A-exposed groups and treatment groups. On histopathology, there was testicular vacuolization, interstitial hemorrhage, reduction in spermatogenic cells following Bisphenol A exposure. There were layers of dense basophilic cells in the pineal and pituitary parenchyma. In conclusion Bisphenol A has negative effects on reproduction but administration of Azanza garckeana may possess some therapeutic properties that can ameliorate such adverse effects.	Theriogenology Vol.192 Pages 150-165	10.1016/j.theriogenology.2022.08.023	36099805	動物	-	1	不明	1	不明	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1245	O. I. Ismail and M. M. S. El-Meligy	2022	Curcumin ameliorated low dose-Bisphenol A induced gastric toxicity in adult albino rats	Bisphenol A (BPA) is one of the most common endocrine chemicals involved in the industry of polycarbonate plastics, medical devices, and pharmaceuticals. Forty three-month-old albino rats were randomly classified into five groups (eight rats/group). Group I received a daily dose of 1% CMC-Na (carboxymethyl cellulose sodium) as a vehicle. Group II received a daily dose of BPA (0.5 µg/kg B.W) through a gastric tube for one month. Group III received a daily dose of BPA (0.5 µg/kg B.W) through a gastric tube for one month and then Curcumin (100 mg/kg B.W) for one month. Group IV received a daily dose of BPA (0.5 µg/kg B.W) through a gastric tube for one month and then Curcumin (200 mg/kg B.W) for one month. Group V received a daily dose of Curcumin as the regimen described in groups III and IV. The rats were sacrificed, and glandular portion of stomach was dissected and processed for light, immunohistochemical and ultrastructural study. BPA induced deteriorated gastric glands, dilated congested blood vessels, submucosal oedema, decreased PAS positive reactivity, increased collagen fibres deposition, decrease in the positive BCL2 immunoreaction, increased and the PCNA immunoreaction, reduction in the gastric mucosal height and destructive changes in the enterocytes like; chief and parietal cells. Curcumin coadministration provided an obvious improvement in the gastric structure. BPA exposure has toxic effects on the glandular portion of the stomach in rats. Otherwise, Curcumin coadministration has exhibited protective impact on the architecture of the stomach.	Sci Rep Vol.12 Issue 1 Pages 10201	10.1038/s41598-022-14158-1	35715475	動物	-	1	1	1	1	0	0.5 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1246	A. Ishtiaq, I. Mushtaq, H. Rehman, I. Mushtaq, I. Mushtaq, S. W. Abbasi, F. Liaqat, A. Rasheed, S. Ali mad, Z. Akhtar and I. Murtaza	2024	Tetra aniline-based polymers ameliorate BPA-induced cardiotoxicity in Sprague Dawley rats, in silico and in vivo analysis	ABBS Bisphenol A (BPA), xenoestrogen, is a environmental toxicant, that generates oxidative stress leading to cardiotoxicity. The oxidative stress can be neutralized by natural and synthetic antioxidants. The present study elucidates the highly selective antioxidative potential of synthetic tetra aniline polymers (tc-37 and tc-57 against Bisphenol A induced cardiac impairments and the role of miRNA-15a-5p in the regulation of different associated proteins. MATERIALS AND METHODS: The molecular docking was carried out by PyRx, Discovery Studio (DS) and Autodock tools. The polymers (tc-37 and tc-57 and 50 mg/kg BW/3x week) via oral gavage (OG) were administered to Sprague Dawley rats. The miRNA and target gene expression were confirmed by qRt-PCR and immunoblotting. KEY FINDINGS: In our results, the tc-37 and tc-57 showed significant binding affinity with the target proteins compared to SC-212 and the highest binding affinity was recorded for tc-57 polymer. Additionally, molecular docking of synthetic polymers validated that L-57 has a greater binding affinity with the target proteins compared to SC-212 and the highest binding affinity was recorded for the enzymatic protein cytochrome c. SIGNIFICANCE: These results suggest that both synthetic polymers (tc-37 and tc-57 have the potential to scavenge free radicals, boost up antioxidant enzyme activities, and avert BPA-induced toxicity, thus, may serve as cardioprotective agents. Moreover, this study first time proposes that miRNA-15a-5p overexpression is associated with oxidative stress and anomalies with BPA-induced cardiotoxicity, thus may serve as potential therapeutic target in future.	Life Sci Vol.358 Pages 123104	10.1016/j.lfs.2024.123104	39366552	動物	-	1	不明	1	1	0	1 mg/kg/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1247	A. Ishtiaq, A. Bakhtiar, E. Sitar, J. Saeed, S. Ajmal, I. Mushtaq, T. Ali, H. M. Wahid, W. Khan, U. Khan, M. Arsee, A. Sultan and I. Murtaza	2020	Pistacia integerrima alleviated Bisphenol A induced toxicity through Ubc13/p53 signalling	Exposure to environmental toxicants such as Bisphenol A (BPA) has raised serious health issues globally particularly in developing countries. It is ubiquitously used in the manufacturing of canned food and feeding bottles. BPA generated reactive oxygen species can lead to several diseases including cardiotoxicity. However, the endocrine stimulated in BPA is ubiquitously yet need to be investigated. The current study was aimed to investigate the underlying molecular pathways which may contribute in reversing the protective effects of Pistacia integerrima against BPA induced oxidative stress. The dose of 100 µg BPA of BPA, 100 mg/kg BW P. integerrima and 100 mg/kg BW P. integerrima + 100 µg BPA were administered to Sprague Dawley rats. The miRNA and target gene expression were confirmed by qRt-PCR and immunoblotting. KEY FINDINGS: In our results, Ubc13 a chain linked to BPA treated up-regulates p53, the tumor suppressor gene was found upon treatment with P. integerrima. Then the role of BPA in heart tissue apoptosis was further confirmed by the measurement of P-p53, cytochrome C and elucidated cellular architecture whereas the P. integerrima has shown its amelioration potential by mitigating the adverse effects of BPA. Moreover, the oxidant, antioxidant, lipid, and liver markers profile has also revealed the therapeutic potential of P. integerrima by maintaining the levels in the normal range. However, melatonin has also manifested the normalized expression of apoptotic markers, biochemical markers, and tissue architecture. Conclusively, the data suggest that P. integerrima may be a potential candidate for the treatment of BPA induced toxicity by neutralizing the oxidative stress through Ubc13/p53 pathway.	Mol Biol Rep Vol.47 Issue 9 Pages 6545-6559	10.1007/s11033-020-05706-x	32770526	動物	-	1	不明	1	1	0	100 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1248	A. Ishtiaq, T. Ali, A. Bakhtiar, R. Bibi, K. Bibi, I. Mushtaq, S. Li, W. Khan, U. Khan, R. A. Arsi, M. Arsee, A. Sultan and I. Murtaza	2021	Melatonin abated Bisphenol A-induced neurotoxicity via p53/PUMA/Drp-1 signaling	Bisphenol A (BPA), an endocrine disruptor, is widely used in the manufacture of different daily life products. Accumulating evidence supports the association between the increasing incidence of neurodegenerative diseases and the BPA load in the environment. In the present study, we aimed to evaluate the neuroprotective role of melatonin against BPA induced mitochondrial dysfunction-mediated apoptosis in the brain. Herein, BPA was administered to Sprague Dawley rats at a dose of 100 µg/kg BW, 100 mg/kg BW melatonin, and 100 mg/kg BW melatonin + 100 µg/kg BW BPA for 30 consecutive days. BPA increased the oxidative stress as demonstrated by increased lipid peroxidation, nitric oxide, and decreased antioxidant enzymes including SOD, CAT, GPX, HSA, and GSH levels. Additionally, BPA treatment increased the expression of PUMA, p53, and Drp-1 resulting in apoptosis in the brain tissues of rats. However, melatonin treatment significantly attenuated BPA-induced toxic effects by scavenging ROS, boosting antioxidant activities, and chromatin/cell remodeling-mediated brain apoptosis by normalizing p53, PUMA, and Drp-1 expressions at both trans-cytosol and mitochondrial level. Moreover, the histo-tissue histology also revealed the therapeutic potential of melatonin by normalizing the cellular architecture. Conclusively, our finding suggests that melatonin could alleviate oxidative stress and mitochondrial dysfunction-linked apoptosis, rendering its neuroprotective potential against BPA-induced toxicity.	Environ Sci Pollut Res Int Vol.28 Issue 14 Pages 17789-17801	10.1007/s11356-020-12129-5	33398767	動物	-	1	不明	0	1	1	100 µg/kg, 1 mg/kg, 10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1249	K. Ishida, M. Furukawa, M. Kurihari, R. Yamagiwa, Y. Hiromori, D. Matsumaru, J. Hu, H. Nagase and T. Nakanishi	2023	Novel, highly sensitive, in vivo screening method detects estrogenic activity at low doses of bisphenol A	Low doses of bisphenol A (BPA), a typical endocrine-disrupting chemical (EDC), have been reported to exhibit estrogenic action in animals; however, the effects have not been fully clarified because of their non-monotonicity. Here, we developed a novel, short-term screening tool for estrogen like chemicals, using a bioluminescence imaging system. Ovariectomized female rats received a single intramuscular injection of 17β-estradiol (positive control), BPA (20 mg/kg), BPA + TDG (20 mg/kg + 10 mg/kg) and TDG (10 mg/kg). BPA exposure significantly decreased the activities of catalase (CAT), superoxidase dismutase (SOD), peroxidase (POD), glutathione reductase (GSR), glutathione S-transferase (GST), and glutathione (GSH) contents in the cytosolic fraction, increased the malondialdehyde and reactive substances (TBARS) and hydrogen peroxide (H2O2) levels. Cytochrome c increase in the levels of plasma antioxidant levels (AL-T, alkaline phosphatase (ALP), aspartate aminotransferase (AST) was also observed in BPA treated rats. Moreover, BPA significantly increased the inflammatory markers, including tumor necrosis factor - α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), interleukin-8 (IL-8), interleukin-12 (IL-12) and Thromboxane-A2 (TXA2). Histopathological observation of the liver, kidney, and testis of BPA-treated rats revealed significant biochemical, inflammatory, and histopathological impairments in all of them. The present study shows that TDG has significant potential to exert BPA-induced liver damage to its antioxidant and anti-inflammatory properties.	J Hazard Mater. 2023 Mar 5:445:130461.	10.1016/j.jhazmat.2022.130461	36436451	動物	性ホルモン	1	1	1	0 (E-Rep)	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1250	J. H. Im, J. S. Lim, X. Han, X. Mao, G. Oh, X. Fu, G. H. Cho, W. S. Hwang, S. I. Choi and O. H. Lee	2025	Anti-obesogenic effect of standardised Brassica juncea extract on bisphenol A-induced 3T3-L1 preadipocytes and C57BL/6J obese mice	Bisphenol A (BPA) is a representative obesogen that induces adipocyte differentiation and lipid accumulation by mimicking the action of hormones. Brassica juncea is a plant belonging to the mustard family, and has antioxidant, anti-inflammatory, and anti-obesity effects. However, its efficacy against obesogen-induced obesity requires further investigation. In this study, we investigated the anti-obesogenic effects of Brassica juncea extract (BJE) on BPA-induced 3T3-L1 preadipocytes and C57BL/6J obese mice. BJE significantly inhibited the accumulation of lipid droplets and triglycerides in 3T3-L1 preadipocytes induced by BPA-induced obesogen. Investigation of differentiation, adipogenesis, and lipolysis protein expression in 3T3-L1 cells. Oral administration of BJE reduced body weight, adipose tissue mass, and adipocyte size in BPA-induced obese C57BL/6 mice. BJE also regulated the expression of proteins involved in adipocyte differentiation, adipogenesis, and lipolysis. These data demonstrate that BJE is a natural functional substance with anti-obesogenic effects.	Food Sci Biotechnol. 2024 Aug 17;34(3):781-791.	10.1007/s10068-024-01688-9	39958180	動物	代謝	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1251	M. U. Ijaz, M. S. Shahab, A. Samad, A. Ashraf, K. Al-Ghanim, S. S. Mvchtnl and S. Mahboob	2022	Tangeretin ameliorates bisphenol induced hepatocyte injury by inhibiting inflammation and oxidative stress	Bisphenol A (BPA) is an industrial toxicant that can potentially damage the liver. Tangeretin (TAN) is a natural flavonoid that displays various pharmacological activities. This experiment was carried out to evaluate the protective effects of TAN against BPA-induced hepatic impairment in the male albino rat. Twenty-four male albino rats were equally divided into four different groups (control, BPA (50 mg/kg), BPA + TAN (50 mg/kg + 10 mg/kg) and TAN (10 mg/kg). BPA exposure significantly decreased the activities of catalase (CAT), superoxidase dismutase (SOD), peroxidase (POD), glutathione reductase (GSR), glutathione S-transferase (GST), and glutathione (GSH) contents in the cytosolic fraction, increased the malondialdehyde and reactive substances (TBARS) and hydrogen peroxide (H2O2) levels. Cytochrome c increase in the levels of plasma antioxidant levels (AL-T, alkaline phosphatase (ALP), aspartate aminotransferase (AST) was also observed in BPA treated rats. Moreover, BPA significantly increased the inflammatory markers, including tumor necrosis factor - α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), interleukin-8 (IL-8), interleukin-12 (IL-12) and Thromboxane-A2 (TXA2). Histopathological observation of the liver, kidney, and testis of BPA-treated rats revealed significant biochemical, inflammatory, and histopathological impairments in all of them. The present study shows that TAN has significant potential to exert BPA-induced liver damage to its antioxidant and anti-inflammatory properties.	Saudi J Biol Sci Vol.29 Issue 3 Pages 1375-1379	10.1016/j.sjbs.2021.11.007	35280594	動物	-	1	不明	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1252	A. O. Ige	2025	Gastroprotective biochemicals in Wistar rats orally exposed to Bisphenol A and co-treated with either Garcinia kola (Heckel) seeds or its biflavonoid, Kolaviron	This study evaluated gastroprotective biochemicals in Wistar rats exposed to both Bisphenol A and either Garcinia kola or its biflavonoid, kolaviron. Fifty-six rats (140-160g) shaded into 7 groups (n=8), and treated orally for 28 days, as follows; Group I was the control (distilled water, 1.5mL/kg) while group II (vehicle control) received corn oil (1.5mL/kg), group III were exposed to BPA (50mg/kg/kg) only and treated with distilled water (1.5mL/kg), Garcinia kola extract (200mg/kg/kg) and kolaviron (100mg/kg), respectively. Animals in groups IV and VII received Garcinia kola (200mg/kg) and kolaviron (100mg/kg) orally, respectively. Thereafter and under anaesthesia, the stomach was dissected out, reckoned for mucin (n=3), homogenized (n=5), centrifuged, and the clear supernatant obtained was analyzed for malondialdehyde, superoxide dismutase, catalase, reduced glutathione, glutathione peroxidase, glutathione-S-transferase, and myeloperoxidase activities. Histopathological examination was also carried out on the stomach of the rats. Bisphenol A (BPA) induced gastric glands dilation, congestion, and oedema of the mucosa and submucosa layers of the stomach, while values in animals exposed both BPA and either Garcinia kola or kolaviron were elevated. Exposure to Garcinia kola and kolaviron alone also showed a potentiation of gastric antioxidant and anti-inflammatory activities. This study shows that Garcinia kola and especially its biflavonoid, kolaviron, protects the gastric mucosa against Bisphenol A induced impairment by potentiating gastroprotective biochemicals in male Wistar rats.	Niger J Physiol Sci Vol.39 Issue 1 Pages 57-63	10.54548/njps.v39i1.8	40156803	動物	-	1	1	1	不明	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1253	A. Ibrahim Salih, H. Mohammad Saleh, A. Sulaiman Wahdi and H. Sabbar Ayed	2022	Effect of Moringa oleifera Leaves against Hepatotoxicity Induced by Bisphenol A	Bisphenol A (BPA) is a synthetic compound with alterations in the liver, antioxidant enzymes, and reproductive hormones. The therapeutic potential of Moringa oleifera extract has recently been considered. The present study aimed to increase the leaf extract of M. oleifera against hepatotoxicity induced by BPA. In total, 42 adult male rats were used in this study, and the experiment was conducted on 7 groups (6 animals per group). The rats were administered (orally) with 5 and 10 mg/kg BPA and treated (orally) with 100, 200, 300, and 400 mg/kg of the aqueous extract of M. oleifera. After 28 days of challenge, liver enzymes, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin, were measured. The histopathological changes in the liver were also examined. The results showed that in the AST, ALT, and ALP in the BPA groups with different histological changes that included the necrosis of the bile duct surrounded by fibrocytes and lymphocytes infiltration. After treatment with M. oleifera, the liver enzymes and tissue returned to a normal state and showed non-significant (P>0.05) differences, compared to the control group. According to the results, it can be concluded that the aqueous extract of M. oleifera has a good potential to prevent and improve liver damage of BPA.	Arch Razi Inst Vol.77 Issue 3 Pages 1083-1089	10.22092/ari.2022.357266.2005	36618322	動物	-	1	1	1	不明	0	5, 10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1254	S. A. Hyun, M. Y. Ko, S. Jang, B. S. Lee, J. Rho, K. K. Kim, W. Y. Kim and M. Ka	2023	Bisphenol-A impairs synaptic formation and function by RGS4-mediated regulation of BDNF signaling in the cerebral cortex	Bisphenol A (BPA) is a representative endocrine disruptor, widely used in a variety of products including plastics, medical equipment and receipts. Hence, most people are exposed to BPA via the skin, digestive system or inhalation in everyday life. Furthermore, BPA crosses the blood brain barrier and is linked to multiple neurological dysfunctions found in neurodegenerative and neuropsychological disorders. However, the mechanisms underlying BPA-induced neurological dysfunctions remain unclear. Using primary cortical neurons and mice, we report that BPA exposure impairs excitatory synaptic morphology and function in the cerebral cortex. Cortical pyramidal neurons treated with BPA showed reduced size and number of dendritic spine puncta. The density of the excitatory synapses was also decreased by BPA treatment. More importantly, we found that BPA disrupted normal synaptic transmission and physiological neuronal consequences related to a potent endocrine modifier.	Dis Model Mech Vol.15 Issue 7	10.1242/dmm.049177	35781563	動物	-	1	不明	1	0	50 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1255	Z. Huang, R. Niu, Q. Xu, R. Zhang, W. Hu, Y. Qin, X. Wang, Q. Xu, Y. Xia, Y. Fan and C. Lu	2025	Impact of Maternal BPA Exposure during Pregnancy on Obesity in Male Offspring: A Mechanistic Mouse Study of Adipose-Derived Exosomal miRNA	BACKGROUND: The widespread use of bisphenol A (BPA) has led to universal exposure among the population, raising concerns about its health effects. Epidemiological studies have linked environmentally relevant levels of BPA exposure to obesity. OBJECTIVES: We aimed to uncover the complex mechanisms by which oral exposure during pregnancy with BPA affects the offspring. METHODS: We conducted a two-stage mouse study. In stage 1, we gavaged mice with BPA at 0.05, 0.5, and 5 mg/kg/day during pregnancy, and we tracked the offspring's weight and diet to 12 wk of age. In stage 2, exosomes from BPA-exposed dams and offspring were injected into pregnant mice and 3-wk-old males, respectively, and the mice were observed up to 12 wk. We then sequenced exosomal microRNAs (miRNAs) in male offspring whose dams had been exposed to BPA during pregnancy. RESULTS: Gavage of 0.05 mg/kg/day of BPA during pregnancy in dams led to obesity in male offspring mice, and injection of exosomes from male offspring with BPA exposure during pregnancy also induced similar outcomes in the next generation of male mice. Exosomal miRNA sequencing identified differentially expressed miRNAs associated with BPA-induced obesity in male offspring, revealing sustained high expression of miR30a-3 radiated tissue and a gradual increase in the liver and serum over time. Further mechanistic studies showed that exosomes derived from BPA-treated adipose-derived stems cells reduced the browning of white adipose tissue and increased lipid accumulation in the liver. DISCUSSION: Our findings suggest that BPA may be a potential therapeutic compound against metabolic diseases, including maternal exposure-induced metabolic abnormalities. In conclusion, low-dose of miR-30 3p or inhibition of exosome secretion rescued these effects. https://doi.org/10.1289/EHP14888.	Environ Health Perspect. 2025 Jan;133(1):17011.	10.1289/ehp14888	39886984	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-
統合_1256	W. C. Huang, K. Y. Liao, S. K. Hsieh, P. H. Pan, Y. H. Kuan, S. L. Liao, C. J. Chen and W. Y. Chen	2021	Magnesium lithospermate B supplementation improved prenatal Bisphenol A exposure-induced metabolic abnormalities in male offspring	Obesity is closely linked with metabolic diseases, while the and prenatal exposure to endocrine-disrupting chemicals has been implicated in the development of obesity. Magnesium lithospermate B (MLB), an active compound of Salvia miltiorrhiza (Danshen), has beneficial effects on insulin resistance and metabolic abnormalities in diet-induced obese rodents. These exposure to endocrine-disrupting Bisphenol A (BPA) during pregnancy mimics the effects of high fat diet-induced alterations of glucose and lipid metabolism in adult male offspring. the effects of daily MLB supplementation for 3 weeks on metabolic abnormalities in male offspring exposed to BPA during pregnancy. Pregnant Sprague-Dawley rats were orally administered BPA (50 mg/kg/day) during gestation days 9 to 18. Male offspring were randomly divided into 4 groups (n=8/group) and received oral gavage with distilled water, the maternal BPA-exposed offspring, and the maternal BPA-exposed offspring with MLB (10 mg/kg/day) supplementation for 3 weeks. Increased body weight, adiposity, and dyslipidemia, activation of adipocyte differentiation, adipogenesis, maturation, and gluconeogenesis, and reduction of thermogenesis in the adipose tissues were demonstrated in BPA-exposed rats. The aforementioned alterations were improved by MLB supplementation. Additionally, MLB displayed negative effects on glucocorticoid receptor action and inflammation, and promoted lipolysis and thermogenesis in the adipose tissues. In conclusion, our findings suggest that MLB may be a potential therapeutic compound against metabolic diseases, including maternal exposure-induced metabolic abnormalities.	Environ Toxicol. 2021 Sep;36(9):1932-1943.	10.1002/tox.23313	34165232	動物	代謝	1	0 (ip)	1	1	0	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1257	R. Huang, J. Li, M. Liao, L. Ma, I. Laurent, X. Lin, Y. Zhang, R. Gao, Y. Ding and X. Xiao	2022	Combinational exposure to Bisphenol A and a high-fat diet causes trans-generational Malfunction of the female reproductive system in mice	Bisphenol A (BPA) is a common endocrine disruptor and a high-fat diet (HFD) also affects fertility. However, little is known about the long-term consequences of simultaneous exposure to BPA and a HFD on reproductive health. Herein, we assessed the effects of maternal exposure to BPA in combination with a HFD on reproductive function in subsequent generations of female mice and evaluated its effects on the hypothalamic–pituitary–gonadal axis. We found that the combination of maternal exposure to BPA and a HFD led to increased serum BPA levels, anovulatory patterns, abnormal estrous cyclicity, decreased follicle numbers, and altered hypothalamic Kiss1 methylation status in F1 and F2 mice. Therefore, we demonstrated that maternal exposure to BPA in combination with a HFD exerts a trans-generational effect on female reproduction.	Mol Cell Endocrinol. 2022 Feb 5:541:111507.	10.1016/j.mce.2021.111507	34785282	動物	生殖能への影響	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

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別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1271	A. Horánszky, B. Shashikadze, R. Ekhteraei, S. D. Lombardo, F. Lamberto, M. Zana, J. Mercha, T. Fröhlich and A. Dönyes	2023	Proteomics and disease network associations evaluation of environmentally relevant Bisphenol A concentrations in a human 3D neural stem cell model	Bisphenol A (BPA) exposure is associated with a plethora of neurodevelopmental abnormalities and brain disorders. Previous studies have demonstrated BPA-induced perturbations in critical neural stem cell (NSC) characteristics, such as proliferation and differentiation, although the underlying molecular mechanisms remain underdefined. The present study evaluated the effects of a repeated dose exposure of environmentally relevant BPA concentrations during the in vitro 3D neural induction of human induced pluripotent stem cells (hiPSCs), modelling a chronic exposure scenario. Firstly, we demonstrated that our model is suitable for NSC, neuron, and glial cell differentiation, and the applied concentrations of BPA (0.01 nM, 0.1 nM, 1 µM) were not cytotoxic to the cells. Secondly, we revealed that BPA induced a dose-dependent reduction in cell viability (one-way ANOVA, Dunnett's post hoc test, p < 0.05), while the lowest concentration (0.01 nM) caused a significant increase in cell viability (one-way ANOVA, Dunnett's post hoc test, p < 0.05). Thirdly, we identified 1 µM BPA-induced changes in the proteomic profile of 3D neural cultures, which could be associated with the reduction in cell viability (one-way ANOVA, Benjamini–Hochberg post hoc test, FDR < 0.05). Fourthly, we revealed that BPA exposure altered the expression of key neural lineage and neurodevelopmental markers. Quantification of proteomics at 2D revealed several differentially abundant proteins across all BPA-treated groups with important functions in NSC proliferation and maintenance (e.g., FABP7, GSPT2, RAN, Rac-GBP, TPPP3). Additionally, a network analysis demonstrated alterations to the glycolysis pathway, potentially implicating BPA-induced changes to glycolytic signalling in NSC proliferation impairments, as well as the pathophysiology of brain disorders including intellectual disability, autism spectrum disorders, and amyotrophic lateral sclerosis. (ALS). This study enhances the current understanding of BPA-related NSC alterations, based mostly on acute, still high dose exposures of rodent in vivo and in vitro models and human C2BB1 data in a novel human 3D cell-based model with real life scenario relevant prolonged and low-level exposures, offering further mechanistic insights into the ramifications of BPA exposure on the developing human brain and consequently, later life neurological disorders.	Front Cell Dev Biol. 2023 Aug 16:11:1236243.	10.3389/fcell.2023.1236243	37664457	in vitro	-	-	-	-	-	-	-	-	-	1	0	0.01、0.1、1µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1272	T. Hong, J. Zou, J. Yang, H. Liu, Z. Cao, Y. He and D. Feng	2023	Curcumin protects against bisphenol A-induced hepatic steatosis by inhibiting cholesterol absorption and synthesis in CD-1 mice	Curcumin is a polyphenol extracted from the rhizome of turmeric, and our previous research showed that curcumin inhibited cholesterol absorption and had cholesterol-lowering effect. Bisphenol A (BPA), a common plasticizer, is widely used in the manufacture of food packaging and is associated with non-alcoholic fatty liver disease (NAFLD). We hypothesized that curcumin could protect against BPA-induced hepatic steatosis by inhibiting intestinal absorption and synthesis. Male CD-1 mice fed BPA-contaminated diet were supplemented with or without curcumin for 12 weeks. Curcumin supplementation in the BPA-exposed mice significantly increased the levels of serum triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol and the contents of liver TC and TG, resulting in liver fat accumulation and hepatic steatosis. Curcumin significantly reduced the expression of intestinal cholesterol absorption-related genes and proteins, including Niemann-Pick C1-like 1 (NPC1L1) and ATP-binding cassette transporter G5 (ABCG5). Curcumin also reduced the expression of intestinal cholesterol esterification-related genes and proteins, which was mediated by suppressing the expression of sterol regulatory element-binding protein 2 (SREBP-2), Sterenon Plus 2.1 (Ste1), hydroxymethylglutaryl-coenzyme A reductase (HMGCR) in the small intestine and liver. In addition, the expression levels of liver lipogenic genes such as liver X receptor alpha (LXRα), SREBP-1c, acetyl-CoA carboxylase 1 (ACC1), and ACC2 were also markedly down-regulated by curcumin. Overall, our findings indicated that curcumin inhibited BPA-induced intestinal cholesterol absorption and liver cholesterol synthesis by suppressing SREBP-2, NPC1L1, and HMGCR expression, subsequently reducing liver cholesterol accumulation and fat synthesis, thereby preventing hepatic steatosis and NAFLD.	Food Sci Nutr Vol.11 Issue 9 Pages 5091-5101	10.1002/fsn3.3468	37701206	動物	-	1	1	1	1	0	0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1273	T. Hong, J. Zou, Y. He, H. Zhang, H. Liu, H. Mai, J. Yang, Z. Cao, X. Chen, J. Yan and D. Feng	2023	Bisphenol A induced hepatic steatosis by disturbing bile acid metabolism and FXR/TGR5 signaling pathways via remodeling the gut microbiota in CD-1 mice	Dysregulation of gut microbiota-mediated bile acid (BA) metabolism plays an important role in the pathogenesis of hepatic steatosis and nonalcoholic fatty liver disease (NAFLD). Our previous studies found that bisphenol A (BPA) exposure induced hepatic steatosis and gut microbiota dysbiosis. However, whether the gut microbiota-dependent BA metabolism alterations were involved in BPA-induced hepatic steatosis remains unclear. Therefore, male CD-1 mice were exposed to BPA-contaminated diet (0.5 mg/kg) for 12 weeks. Fecal microbiota transplantation (FMT) and broad-spectrum antibiotic cocktail (ABX) treatment were further adopted to clear the role of gut microbiota in the adverse effects of BPA. We found that BPA induced hepatic steatosis in mice. Additionally, 16S rRNA gene sequencing showed that BPA reduced the relative abundance of Ruminiclibs, Ruminococcaceae_UCG-014, Romboutsia, and Lachnoclostridium, which are associated with BA metabolism. Metabolomic analyses demonstrated that BPA significantly altered the ratio of conjugated to unconjugated BAs and increased the total level of tauro-β- or γ-muricholic acid while decreasing the total bile acid. Also, inhibiting the activation of special receptors, including farnesoid X receptor (FXR) and Takeda G protein-coupled receptor 5 (TGR5), in the ileum and liver. The inhibition of FXR reduced short heterodimer partner and subsequently increased cholesterol 7α-hydroxylase (CYP7A1) and sterol 12α-hydroxylase (CYP8B1) expression to maintain BA homeostasis, which is related to hepatic BA and lipid levels. Furthermore, we found that mice that received FMT from BPA-exposed mice mimicked hepatic steatosis, and the influences of BPA on hepatic steatosis and FXR/TGR5 signaling pathways could be eliminated by ABX treatment, confirming the role of gut microbiota in BPA effects. Collectively, our new study illustrates that suppressed microbiota-BA-FXR/TGR5 signaling pathways may be a potential mechanism for hepatic steatosis induced by BPA, providing a new target for the prevention of BPA-induced NAFLD.	Sci Total Environ Vol.889 Pages 164307	10.1016/j.scitotenv.2023.164307	37211107	動物	-	1	不明	1	1	0	50 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1274	T. Hong, X. Jiang, J. Zou, J. Yang, H. Zhang, H. Mai, W. Ling and D. Feng	2022	Hepatoprotective effect of curcumin against bisphenol A-induced hepatic steatosis via modulating gut microbiota dysbiosis and related gut-liver axis activation in CD-1 mice	Chronic exposure to low-dose bisphenol A (BPA) has become a global problem of public health. Our previous work showed that low-dose BPA exposure caused gut microbial dysbiosis and hepatic steatosis. Curcumin, a polyphenol extracted from turmeric, has an inhibitory effect on liver lipid accumulation, whether curcumin can alleviate BPA-induced hepatic steatosis through improving intestinal flora and modulating gut-liver axis remains to be elucidated. Male CD-1 mice were fed with BPA-contaminated diet supplemented with or not with curcumin for 24 weeks. Curcumin supplementation markedly ameliorated liver fat accumulation and hepatic steatosis induced by BPA. Gut microbiota analysis (i.e. 16S rRNA sequencing revealed that the relative abundances of Proteobacteria and Escherichia-Shigella were increased in BPA-fed mice, and curcumin administration reversed by curcumin treatment. Bifidobacteria, which was recognized as a potential probiotic, was significantly reduced after BPA exposure and was restored to the control level with curcumin addition. Furthermore, curcumin administration significantly reduced the intestinal permeability and decreased the serum lipopolysaccharide (LPS) level by enhancing the intestinal barrier function in BPA-exposed mice. Curcumin also inhibited the activation of hepatic toll-like receptor 4 / nuclear factor -κB (TLR4/NF-κB) pathway induced by BPA. These results indicated that the protective effect of curcumin against hepatic steatosis induced by BPA and further revealed that its mechanism might be its prebiotic effect on maintaining intestinal flora homeostasis and improving intestinal barrier function, consequently reducing serum lipopolysaccharide-triggered inflammatory response in the liver. Our work provides evidence for curcumin as a potential nutritional therapy for BPA-mediated hepatic steatosis.	J Nutr Biochem. 2022 Nov:109:109103.	10.1016/j.jnutbio.2022.109103	35780999	動物	肝毒性	1	1	1	CD-1mice:1	0	50 µg/kg/日当:1	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1275	L. Hong, Y. Xu, D. Wang, Q. Zhang, X. Li, C. Xia, J. Wu, C. Zhong, L. Fu and S. Geng	2023	Sulforaphane ameliorates bisphenol A-induced hepatic lipid accumulation by inhibiting endoplasmic reticulum stress	The aim of the present study was to investigate the role of endoplasmic reticulum (ER) stress in bisphenol A (BPA) - induced hepatic lipid accumulation as well as the protective effects of Sulforaphane (SFN) in this process. Human hepatocyte cell line (L-02) and ICR/ddd mice were used to examine BPA-triggered hepatic lipid accumulation and the underlying mechanisms. Hyperlipidemia (HLP) mice, by the injection of tail vein of hyperlipidemia emulsion, were used to further confirm the role of ER stress in BPA-induced hepatic lipid accumulation. Results showed that BPA treatment increased the number of lipid droplets, the levels of TG and mRNAs expression of lipogenesis related genes, and proteins in the ER stress pathway were measured. It was revealed that BPA treatment increased the number of lipid droplets, the levels of TG and mRNAs expression of lipogenesis related genes, and proteins in the ER stress pathway were measured. It was revealed that BPA treatment activated ER stress, as indicated by increased expression of GRP78, p-PERK/PERK, p-IRE1α/IRE1α, and downstream CHOP, XBP1s, and ATF6 proteins. Moreover, BPA treatment also increased the expression of ER stress-associated apoptosis proteins. Meanwhile, BPA-induced ER stress-related markers. Together, these findings suggested that BPA activated ER stress to promote hepatic lipid accumulation, and that SFN exerted beneficial BPA effects by alleviating ER stress.	Sci Rep. 2023 Jan 20;13(1):1147.	10.1038/s41598-023-28395-5	36670177	動物、in vitro	-	1	0	1	1	0	100 µg/kg/day	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1276	S. M. Ho, R. Rao, B. Ouyang, N. N. C. Tam, E. Schurch, D. Sung, J. Ying, Y. K. Leung, V. Govindarajah and P. Tarapore	2021	Three-Generation Study of Male Rats Gestationally Exposed to High Butterfat and Bisphenol A: Impaired Spermatogenesis, Penetrance with Reduced Severity	Gestational high butterfat (HFB) and/or endocrine disruptor exposure was previously found to disrupt spermatogenesis in adulthood. This study addresses the data gap in our knowledge regarding transgenerational transmission of the disruptive interaction between a high fat diet and endocrine disruptor bisphenol A (BPA). F0 generation Sprague-Dawley rats were fed diets containing butterfat (21 kcal%) and/or bisphenol A (50 mg/kg HFB) with or without BPA (25 µg/kg body weight/day) during mating and pregnancy. Established exposed F1 generation offspring from different litters were mated to produce F2 offspring, and similarly, F2 offspring were mated to produce F3 offspring. Adult F1 males exposed to HFB + BPA had significantly reduced sperm counts, motility, and viability. Testicular histopathology revealed a mixed phenotype of impaired spermatogenesis, including germ cell depletion, tubule vacuolization, and sloughing of immature germ cells into the lumen. Sperm counts were significantly reduced in F2 males derived from HFB + BPA F1 dams, but not single exposure to either, disrupted spermatogenesis in F2 generation adult males. Interbreed F1 × F2 mated pairs and the naturally aged group. CYP19A1 localization to the acrosome and estrogen receptor beta (ERbeta) localization to the nucleus were associated with impaired spermatogenesis. Finally, exposure of methyl-CpG-binding domain 1 (MBD1) was consistently decreased in the HFB and HFB + BPA exposed F1 and F2 males, suggesting an epigenetic component to this inheritance. However, the severe atrophy within testes present in F1 males was absent in F2 males. In conclusion, the HFB + BPA group demonstrated transgenerational inheritance of the impaired spermatogenesis phenotype, but severity was reduced in the F2 generation.	Nutrients Vol.13 Issue 10	10.3390/nu13103636	34684636	動物	-	1	1	1	1	0	25 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1277	J. K. Hinchcliffe, M. Mendl and E. S. J. Robinson	2020	Investigating hormone-induced changes in affective state using the affective bias test in male and female rats	Recent clinical and pre-clinical research suggests that affective biases may play an important role in the development and perpetuation of mood disorders. Studies in animals have also revealed that similar neuropsychological processes can be measured in non-human species using behavioural assays designed to measure biases in learning and memory or decision making. Given the proposed links between hormones and mood, we used the affective bias test to investigate the effects of different hormone treatments in both male and female rats. Animals were pre-trained to lift ovarian doses of hormone or vehicle control prior to learning tasks designed to measure cognitive bias. Specifically, we investigated the effects of testosterone propionate (TP) in male rats and 17β-oestradiol (OE) in ovariectomised female rats. Hormone treatments were administered chronically, in both cases, and tested over the subsequent three consecutive days. Treatment with TP, but not OE, induced a negative bias in both cases, at the highest dose (25 mg/kg). The non-aromatisable androgen, dihydrotestosterone (DHT), also induced a negative bias in males. Blocking testosterone with flutamide induced a positive bias in both cases, at the highest dose (25 mg/kg). The non-steroidal oestrogen, diarylpropionitrile (DPN), also induced a positive bias in female rats only. These results provide evidence that modulating levels of hormones using exogenous treatments can induce affective biases in rats. They also suggest that hormone-induced affective biases influence cognitive and emotional behaviour and could have longer-term effects in some mood disorders.	Psychoneuroendocrinology Vol.115 Pages 104647	10.1016/j.psyneuen.2020.104647	32179367	動物	-	1	0	1	1	0	0.05、0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1278	A. D. Henriksen, A. Andrade, E. P. Harris, E. F. Rissman and J. T. Wolstenholme	2020	Bisphenol a Exposure in Utero Disrupts Hypothalamic Gene Expression Particularly Genes Suspected in Autism Spectrum Disorders and Neuron and Hormone Signaling	Bisphenol A (BPA) is an endocrine-disrupting compound detected in the urine of more than 93% of humans, easily crosses the placental barrier, and has been shown to influence gene expression during fetal brain development. The purpose of this study was to investigate the effect of in utero BPA exposure on gene expression in the anterior hypothalamus, the basal nucleus of the stria terminalis (BNST), and hippocampus in CD1® (Crl:CD1(ICR)) mice exposed in utero to human-relevant doses of BPA, and the BNST was dissected and analyzed via RNA-Sequencing (n = 4/group) that included the medial preoptic area (mPOA) and BNST to determine whether any genes were differentially expressed between BPA-exposed and control mice. A subset of genes was selected for further study using RT-qPCR on adult tissue from the same animals. Pathway analysis indicated that these DEGs were overrepresented in categories relating to neuronal development, cell-cell signaling, behavior, and nervous system development in BPA-exposed and control mice. Gene ontology analysis indicated that these DEGs were overrepresented in categories relating to neuronal development, cell-cell signaling, behavior, neurodevelopment, neurons, synapse formation, cognition, learning behaviors, hormone activity, and signaling receptor activity, among others. Ingenuity Pathway Analysis was used to interrogate novel gene networks and upstream regulators, indicating the top five common regulators as huntingtin, beta-estradiol, alpha-synuclein, Cre(e), and estrogen receptor (ER) alpha. In addition, 13 DE genes were identified that are suspected in autism spectrum disorders.	Int J Mol Sci Vol.21 Issue 9	10.3390/ijms21093129	32365465	動物	-	1	1	1	1	0	5 mg BPA/kg 体外曝露	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1279	B. Hadi, S. P. Nowski, S. A. Hosseini, A. Sabahi, L. Ahmandi, N. Aminejad, M. Mahdawisa, S. Rahmati and M. A. Dehghani	2024	The Protective Effects of Syringic Acid on Bisphenol A-Induced Neurotoxicity Possibly Through AMPK/PGC-1 α /Fndc5 and CREB/BDNF Signaling Pathways	Bisphenol A (BPA), an endocrine disruptor, is commonly used to produce epoxy resins and polycarbonate plastics. Continuous exposure to BPA may contribute to the development of diseases in humans and seriously affect their health. Previous research suggests a significant relationship between the increased incidence of neurological diseases and the level of BPA in the living environment. Syringic acid (SA), a natural derivative of benzoic acid, has various pharmacological properties, including antioxidant, anti-inflammatory, and neuroprotective effects. This study aimed to investigate the protective effects of SA on BPA-induced oxidative stress, apoptosis, memory and locomotor disorders, and mitochondrial function in the hippocampus of rats. Male Wistar rats received BPA (50, 100, and 200 mg/kg) and SA (50 mg/kg) for 21 days. The results showed that BPA exposure significantly altered the rats' neurobehavioral responses. Additionally, BPA, by increasing the level of ROS, and MDA level, increased the level of oxidative stress while reducing the level of antioxidant enzymes, such as SOD, CAT, GPx, and mitochondrial ETC4. The administration of BPA at 200 mg/kg significantly decreased the expression of PPAR-γ, TFAM, Irisin, PGC -1α, Bcl-2, and FNDC5, while it increased the expression of TNB, cytochrome C, caspase 3, and Bax. Moreover, the Western blotting results showed that BPA exposure at 200 mg/kg significantly reduced the expression of AMPK, PGC -1α, FNDC5, and CREB/BDNF, while it increased the expression of NF-κB. Interestingly, SA administration significantly reversed the molecular changes induced by high doses of BPA. Overall, BPA could lead to the development of AD by affecting the mitochondrial dysfunction-apoptosis pathway as well as AMPK/PGC -1α /FNDC5 and CREB/BDNF/TrkB signaling pathways, and finally, by increasing the expression of tau and Aβ proteins. In conclusion, SA, as an antioxidant, significantly reduced the toxicity of BPA.	Mol Neurobiol Vol.61 Issue 10 Pages 7767-7784	10.1007/s12035-024-04048-0	38430353	動物	-	1	不明	1	1	1	50、100、200 mg/kg	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1280	J. J. Heindel, S. Belcher, J. A. Flaws, G. S. Prins, S. M. Ho, J. Mao, H. B. Patisaul, W. Ricke, C. S. Rosenfeld, A. M. Soto, F. S. Vom Saal and R. T. Zoeller	2020	Data integration, analysis, and interpretation of eight academic CLARITY-BPA studies	Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA) was a comprehensive "industry standard" Good Laboratory Practice (GLP)-compliant 2-year chronic exposure study of bisphenol A (BPA) toxicity that was supplemented by hypothesis-driven independent investigator-initiated studies. The investigator-initiated studies were focused on integrating disease-associated, molecular, and pathological endpoints previously found by academic scientists into an industry-standard guideline-compliant toxicity study. Thus, the goal of this collaboration was to provide a more comprehensive dataset upon which to base safety decisions and to enable a thorough examination of the impact of research practices on study outcomes and interpretation. Here, we provide a brief overview of the eight investigator-initiated studies, into a comprehensive overview of the observed impacts of BPA across the multiple organs and systems analyzed. For each organ system, we provide the rationale for the study, an overview of methodology, and summarize major findings. We then compare the results of the CLARITY-BPA studies across organ systems with the results of previous peer-reviewed studies from independent labs. Finally, we discuss potential influences that contributed to differences between studies. Developmental exposure to BPA can lead to adverse effects in multiple organ systems, including the brain, prostate gland, urinary tract, mammary gland, and heart. As published previously, many effects were at the lowest dose tested, 2.5 µg/kg/day, and many of the responses were non-monotonic. Because the low dose of BPA affected endpoints in the same animals across organs evaluated in different labs, we conclude that these are biologically - and toxicologically - relevant.	Reprod Toxicol. 2020 Dec:98:29-60.	10.1016/j.reprotox.2020.05.014	32682780	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1281	Q. He, C. Xu, J. Guo, Y. Chen, N. Hu and J. Chen	2024	Bisphenol A exposure stimulates prostatic fibrosis via exosome-triggered epithelium changes	Fibrosis is the pathological basis for the clinical progression of benign prostatic hyperplasia (BPH). Prostatic fibrosis is an important risk factor in patients with BPH who experience lower urinary tract symptoms. Bisphenol A (BPA) is a widely used endocrine disruptor that has been associated with BPH. However, the role of BPA in prostatic fibrosis remains unclear. In this study, we found that BPA induced mouse prostatic fibrosis. It is characterized by collagen deposition and an increase in hydroxyproline content in prostatic tissue. Furthermore, BPA-exposed prostatic exosomes promote the epithelial-mesenchymal transition of epithelial cells. High-throughput RNA sequencing and functional enrichment analyses show that substantially altered miRNAs, lncRNAs, and circRNAs play roles in cellular interactions and the hypoxia-inducible factor-1 signaling pathway. The results showed that exosomes participated in the pro-fibrogenic effects of BPA on the prostate by mediating communication between stromal and epithelial cells and triggering epithelial changes.	Food Chem Toxicol. 2024 Mar:185:114450.	10.1016/j.fct.2024.114450	38215961	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1282	J. He, L. Zhang, H. Jin, D. Yang, L. Jia, B. Han, H. Sui and L. Sun	2025	Prediction of the exposure profile of bisphenol A in Chinese population by physiologically-based pharmacokinetics modeling	Bisphenol A (BPA) has emerged as a typical contaminant which can induce various adverse effects on human health and environment. BPA exposure and the corresponding human responses can vary across different regions. Therefore, it is necessary to investigate the exposure profile of BPA in Chinese population. Physiologically-based pharmacokinetic (PBPK) model is a powerful tool for chemical risk assessment. In this study, an emerging in vivo useful tool to predict the internal exposure profiles of chemicals. Herein, the present study was aimed to predict the exposure profile of BPA in Chinese population by PBPK modeling using external BPA exposure data. A PBPK model specific for oral BPA exposure in Chinese population was established using chimpanzee and rodent to make extrapolations using pharmacokinetic data from intravenous BPA exposure experiments. The model was then validated by comparing the predicted BPA concentrations in blood, urine, and tissues with the corresponding observed data from the published literatures. Afterward, this model was applied to simulate the internal exposure level of BPA in Chinese population by integrating external exposure data from the China Total Diet Study (CTDS) and physiological parameters specific to Chinese population. Parameter sensitivity and modelling uncertainty were analyzed. Based on the simulated BPA internal profile, human equivalent dose factors (HEDF) were calculated. Our results provide an important basis for assessment of the potential risk of BPA exposure in Chinese population and an essential reference for determination of the safe margin limits for BPA in China.	Environ Pollut Vol.373 Pages 126075	10.1016/j.envpol.2025.126075	40122328	ヒト	-	-	-	-	-	-	PBPKモデル	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1283	H. He, X. Li, J. Shen, S. Bai, C. Li and H. Shi	2022	Bisphenol A exposure causes testicular toxicity by targeting DPY30-mediated post-translational modification of PI3K/AKT signaling in mice	Bisphenol A (BPA), one of the chemicals with the highest volume of production worldwide, has been demonstrated to cause testicular toxicity via different pathways. However, there is little evidence concerning the mechanism of BPA exposure-induced histone modification alterations, especially regarding the effects on the histone H3 lysine 4 (H3K4) trimethyl modification. Our results demonstrated a new epigenetic regulation of BPA exposure on testicular damage using both cell culture and mouse models. With BPA treatment, disordered and circadian-unmatched rates, adults and sperm quality were observed in mice, and mouse spermatogonial GC-1 cells exhibited a decrease in cell viability, an increase in apoptosis, and a disruption of the cell cycle. Mechanistically, BPA exposure induced the overexpression of DPY30 in mouse testes and GC-1 cells, which contributed to reducing H3K4me3 recruitment at the PIK3CA transcriptional start site (TSS) in BPA-treated cells. The toxicity caused by BPA exposure was reflected in the reconstruction of atherosclerosis-expressing DPY30 transgenes, which resulted in the stimulation of PI3K/AKT with H3K4me3 enriched at the PIK3CA TSS. DPY30 promoted cell glycolysis via AMPK and proliferation through AKT/PCI. DPY30 was mainly located in the round and elongated spermatids. Its energy accumulation in mature sperm in GC-DPY30 -treated mice which showed higher sperm quality. Overall, our results indicated that BPA exposure causes testicular toxicity through a DPY30-mediated H3K4me3 epigenetic modification, which serves to regulate the PI3K/AKT/PCI pathway.	Ecotoxicol Environ Saf. 2022 Sep 15:243:113996.	10.1016/j.ecoenv.2022.113996	36030680	動物、in vitro	-	1	0	1	BALB/c	1	-	-	-	-	1	0	10% BSA	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

利用評価機関
●：該当

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価へ進め、当該時点情報取得で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	保険性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1284	H. He, X. Chen, X. Li, K. Yang, J. Li and H. Shi	2022	Lactoferrin alleviates spermatogenesis dysfunction caused by bisphenol A and cadmium via ameliorating disordered autophagy, apoptosis and oxidative stress	Contaminants in food have severely threatened human health, and appropriate antioxidants derived from food could reduce impairment risk. Lactoferrin from milk could control iron concentration in the blood to ameliorate oxidative stress, which is also inspired for sperm maturation, but the underlying mechanisms remain unclear. The present study used mice with spermatogenetic dysfunction caused by bisphenol A (BPA) and cadmium (Cd) co-exposure to explore the effects of lactoferrin on testicular damage. The results showed that lactoferrin could improve the reproductive parameters, including sperm quality, disordered apoptosis, oxidative stress, and autophagy; however these functions were impaired by co-exposure. A comprehensive and mechanistic spermatogenetic dysfunction model was established by the increased levels of BAX/BCL-2, CYP11A1, PS2, AMPK was involved in autophagic regulation, while ERK1/2 inhibition attenuated the protective effects of lactoferrin, including ameliorating apoptosis, oxidative stress, and arrested autophagic flux. Notably, PS2 was consistently stimulated with different ERK1/2 inhibitors, which was ubiquitin-dependent. The study provides evidence for the ameliorative effects of lactoferrin and milk in mice with spermatogenetic dysfunction through ERK1/2 mediated the ubiquitin-dependent degradation of PS2. The involved signals and molecules could be identified as novel therapeutic targets for male infertility, which contributes to expanding LF's interest in research and application.	Int J Biol Macromol Vol.222 Issue Pt A Pages 1048-1062	10.1016/j.ijbiomac.2022.09.260	36183753	動物	-	1	不明	不明	不明	不明	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1285	D. Herbagalu, M. Burak Ates, G. Sentürk, O. Kuca, A. Buha Iarović, N. Dzemidzic	2025	Neuroprotective role of Nigella Sativa seed oil in mitigating bisphenol a-induced neurodegeneration	The primary objective of this study was to investigate the adverse effects of Bisphenol A (BPA) on the central and peripheral nervous systems at molecular, histopathological, and immunohistochemical levels, as well as to evaluate the potential neuroprotective effects of Nigella Sativa seed oil (NSO). Rats were administered BPA at a dosage of 100 mg/kg body weight per day via gavage for 30 days, alongside NSO at a dosage of 5 ml/kg body weight per day via gavage. Our findings indicate that BPA exposure induces significant oxidative stress, as evidenced by increased malondialdehyde (MDA) levels and decreased glutathione (GSH) levels in brain tissues. BPA exposure resulted in neurotoxic effects in both the central nervous system (brain) and peripheral nervous system (sciatic nerve), leading to oxidative stress, apoptosis, and neurodegeneration. Specifically, glutathione (GSH) levels decreased, while malondialdehyde (MDA) levels increased in both tissues due to BPA administration. Additionally, BPA elevated the gene expression levels of nuclear factor erythroid 2-related factor 2 (Nrf2), Caspase-3, and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) mRNA transcripts, while decreasing the expression of nuclear receptor subfamily 1 group A member 2 (NR4A2). In contrast, NSO administration alongside BPA increased GSH content in both tissues and significantly reduced MDA levels. Moreover, NSO decreased the gene expression levels of Nrf2, NF-κB, and Caspase-3 mRNA transcripts, while increasing NR4A2 expression. Immunohistochemical analysis revealed that BPA exposure led to a significant increase in the number of glial fibrillary acidic protein (GFAP)-positive cells in the brain, a change mitigated by the concurrent administration of NSO, indicating its neuroprotective efficacy. In conclusion, this study provides promising evidence that NSO may therapeutically alleviate BPA-induced neurodegeneration.	Sci Rep Vol.15 Issue 1 Pages 22477	10.1038/s41598-024-80654-1	40595699	動物	-	1	1	不明	不明	不明	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1286	A. A. Hassan, S. S. Abdelgayed and S. Z. Mansour	2024	Liver and ovarian toxicities boosted by bisphenol and gamma radiation in female albino rats	Bisphenol A (BPA), a carbon-based synthetic polymer compound, was newly classified as an environmental toxicant and an endocrine-disrupting chemical leading to abnormalities in cell proliferation, apoptosis, or signaling that contribute to tumor development and progression. This study aims to evaluate the effects of the interaction of γ - radiation dose and BPA on the liver and ovaries of female rats. In this study, eighty female albino rats (150-180 g) were used in this work. Rats in this experiment received BPA in ethanol (50 mg/kg b.w.) at 1st 30 days, day after day, and in the irradiated groups, animals were administered BPA and then exposed to γ - radiation doses (1, 2, and 3 Gy) on alternate days. Several members of the cytochrome family are known to be induced by BPA and γ - radiation and BPA showed an increase in oxidative DNA damage. Moreover, BPA exposure and γ - radiation activate α and β estrogen receptors and also downregulate aromatase (CYP19) field change. The current results also revealed that BPA and/or γ - radiation regulate the protein expression of the PI3K/Akt signaling pathway. The immunohistochemistry assay positive (PCNA) appeared to be negative by BPA and γ - radiation and its relative expression was elevated significantly by raising the γ - radiation dose. In conclusion, exposure to BPA, an endocrine-disrupting chemical, leads to marked toxicity. Additionally, toxicity is heightened by increasing the γ - radiation dose, either alone or in combination with BPA.	Hum Exp Toxicol Vol.43 Pages 9603271231219264	10.1177/09603271231219264	38263794	動物	-	1	0	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1287	M. E. U. Haq, M. S. H. Akash, K. Rehman and M. H. Mahmood	2020	Chronic exposure of bisphenol A impairs carbohydrate and lipid metabolism by altering corresponding enzymatic and metabolic pathways	Bisphenol A (BPA), a widespread endocrine disrupting chemical, has been recognized as a risk factor for metabolic disorders. BPA is considered to be involved in the impairment of carbohydrate and lipid metabolism but the underlying mechanisms still need to be elucidated. Present study was aimed to investigate the impact of BPA exposure on enzymatic and metabolic pathways that are responsible for the carbohydrate and lipid metabolism. Experimental rats were exposed to different doses of BPA (50, 500, 2500 and 5000 µg/kg bw) orally dissolved in 1.5% dimethyl sulfoxide for a period of 3 months. Serum level of key metabolic enzymes i.e. amylase, α-glucosidase, hexokinase, glucose-6-phosphatase and HMG-CoA reductase were measured by ELISA method. BPA exposure significantly suppressed the mRNA expression of pancreatic and salivary

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統合_1297	D. Guignard, C. Cariel, M. Tremblay-Franco, E. Chalbos, B. Gaudin, V. Gayrard, N. Picard-Hagen, H. Schroeder, F. Jourdin, D. Zalko, C. Viguié and N. J. Cabaton	2022	Gestational exposure to bisphenol A induces region-specific changes in brain metabolomic fingerprints in sheep	Fetal brain development depends on maternofetal thyroid function. In rodents and sheep, perinatal BPA exposure is associated with maternal and/or fetal thyroid disruption and alterations in central nervous system development as demonstrated by metabolic modulations. In the xenoplata of mice, We hypothesized that a gestational exposure to a low dose of BPA affects maternofetal thyroid function and fetal brain development in a region-specific manner. Pregnant ewes, a relevant model for human thyroid and brain development, were exposed to BPA (5 µg/kg bw/d, n=7, the thyroid status of ewes during gestation and term fetuses at delivery was characterized by measurements of circulating thyroid hormones (TH) and TH-related genes expression in the liver and placenta. Fetal brain metabolomic fingerprints were established by 1H-nuclear magnetic resonance (1H-NMR) spectroscopy. In maternal TTH serum concentrations. For fetal brain regions, statistical models allowed discrimination of BPA-exposed fetuses from control lambs. Metabolic network computational analysis revealed that prenatal exposure to BPA modulated several metabolic pathways, in particular oxidative and inhibitory amino acid, cholinergic, energy and lipid homeostasis pathways. These pathways might contribute to BPA-related neurobehavioral and neurodevelopmental disorders. Overall, our results highlight the sensitivity of the sheep model to study the impact of BPA on fetal brain development. Moreover, as in rodents, the use of a large animal model allowed to examine specific brain areas, and pave the way to a more in-depth characterization of the distinct region-specific effects of fetal BPA exposure on the brain metabolome. These modifications occur concomitantly to subtle maternal thyroid function alteration. The functional link between such moderate thyroid changes and fetal brain metabolomic fingerprints remains to be determined as well as the potential implication of other modes of action triggered by BPA such as oestrogenic ones. Our results pave the ways for new scientific strategies aiming at linking environmental endocrine disruption and altered neurodevelopment.	Environ Int Vol.165 Pages 107336	10.1016/j.envint.2022.107336	35700571	動物	-	1	0	1	不明	0	5 µg/kg bw/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1298	L. H. A. Guerra, S. I. Collete, V. Grégo, S. A. de Oliveira, S. G. P. Campos, E. Sasso-Cerri, P. S. L. Villamair and S. R. Taboga	2025	Lifelong impact of BPA: Steroidogenic reprogramming in aged gerbil adrenal glands following developmental exposure	Endocrine-disrupting chemicals, particularly bisphenol A (BPA), are ubiquitous environmental contaminants that can profoundly affect hormonal systems and human health. The effects are variable and are contingent upon the developmental stage at which exposure occurs. This study aimed to investigate the effects of intrauterine and lactational BPA exposure on the adrenal glands of aged Mongolian gerbils (Meriones unguiculatus). In a controlled experimental set-up, pregnant gerbils were exposed to control or BPA-treated drinking water, with the BPA group receiving a high dose during critical periods of development to assess the subsequent effects on adrenal gland function in their offspring at senile age. Biometric and hormonal assessments (estradiol, cortisol and testosterone) were conducted. Immunohistochemical and immunofluorescence analysis assessed steroidogenic enzymes (CYP11A1, CYP17A1, and HSD3B1), estrogen receptors (ESR1 and ESR2), and androgen receptors (AR). Gene expression of Esr1, Esr2, and Ar was quantified via real-time PCR (RT-qPCR). Adrenal vascularization was evaluated using Doppler ultrasonography and histological analysis of vascular endothelial growth factor (VEGF). The results revealed that gerbils exposed to BPA exhibited increased body weight, alongside significant alterations in circulating hormone profiles, including decreased cortisol and elevated estradiol levels. Furthermore, there was an upregulation of steroidogenic enzymes, indicating BPA's disruptive effects on adrenal hormone production and regulation. Notably, intracellular testosterone levels were elevated despite the typical age-related declines observed in control groups. Additionally, increased expression of androgen receptors and CYP19A1 was noted, underscoring BPA's complex impact on steroidogenic pathways. These findings emphasize the potential for intrauterine BPA exposure to induce enduring endocrine disturbances.	Life Sci Vol.378 Pages 123825	10.1016/j.lfs.2025.123825	40623519	動物	-	1	1	1	不明	0	5000 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1299	J. Gu, N. Zhang, X. Jiang, L. Zhu, Y. Lou, S. Sun, L. Yin and J. Liu	2024	The Olfactory Receptor Olfr25 Mediates Sperm Dysfunction Induced by Low-Dose Bisphenol A through the CatSper-Ca(2+) Signaling Pathway	Bisphenol A (BPA), a typical endocrine disruptor, is known to have various adverse effects on the male reproductive system. However, the toxic effects and mechanisms of low-dose BPA have not yet been fully explored. In this study, male Kunming mice were orally administered low-dose BPA (0.02, 0.2 and 2 mg/kg/d) for ten consecutive weeks. Pathological sections of testicular tissue showed no significant morphological differences after BPA exposure. An analysis of the functional parameters of sperm revealed that exposure to low-dose BPA significantly decreased sperm motility, chemotaxis, and the acrosome reaction. An in vitro BPA exposure model was established to explore the mechanism underlying the effects of low-dose BPA on sperm function. Olfactory receptor 25 (Olfr25) was identified as a potential target of BPA. Knockdown of the Olfr25 olfactory receptor gene (Or25) in vivo and in vitro exposure models. Meanwhile, exposure to low-dose BPA reduced the intracellular calcium ion concentration and the mRNA levels of the CatSper subunit and its auxiliary subunits of the CatSper channel in sperm. Importantly, the knockdown of Or25 inhibited calcium ion levels and CatSper subunit expression in GC-2 cells. Olfr25 overexpression attenuated the BPA-induced downregulation of CatSper subunit expression in GC-2 cells. These findings indicate that Olfr25 might participate in low-dose BPA-induced sperm dysfunction by affecting the CatSper-Ca(2+) signaling pathway. This study reveals a new mechanism underlying the effects of low-dose BPA on sperm function and provides a reference for assessing the safety of low-dose BPA exposure.	Toxics. 2024 Jun 20;12(6):442.	10.3390/toxics12060442	38922122	動物	精巣	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1300	H. J. Gu, D. Y. Kim, S. H. Shin, M. S. Rahman, H. S. Lee, M. G. Pang, J. M. Kim and B. Y. Ryu	2024	Genome-wide transcriptome analysis reveals that Bisphenol A activates immune responses in skeletal muscle	Comelian human exposure to the environmental toxin, bisphenol A (BPA), has raised important health concerns in recent decades. However, the direct genomic regulation of BPA in skeletal muscle and its clinical significance are poorly understood. Therefore, we conducted a genome-wide transcriptome analysis after daily oral administration of BPA at the lowest observed adverse level (LOAEL, 50 mg/kg) to male mice for six weeks to explore the gene expression regulations in skeletal muscle induced by BPA. The primary Gene Ontology terms linked to BPA-dependent, differentially expressed genes at 1 (DEG, comprised oxidative immune response, positive regulation of T cell activation, and immune system process. The gene set enrichment analysis also disclosed increased complement associated genes (complement components C1S and C8B) and cytokines (tumor necrosis factor-β, complement receptor 2, and immunoglobulin lambda constant 2) in the group administered with BPA, with a false discovery rate of <0.05. Subsequent validation analysis conducted in BPA-fed animal skeletal muscle tissues revealed significantly increased mRNA expression of complement component 3 (C3) and tumor necrosis factor-α (TNF-α) in the BPA-administered group. Furthermore, the administration of BPA markedly upregulated the transcription of tumor necrosis factor-α (TNF-α) in C2C12 myoblasts and mouse skeletal muscle cells, which was substantially inhibited by the T-cosmetic and perfumable, providing further evidence of BPA-induced inflammation in muscle cells. Our bioinformatics and subsequent animal and in vitro validations demonstrate that BPA can activate inflammation in skeletal muscle, which could be a risk factor underlying chronic muscle weakness and wastage.	Environ Res Vol.252 Issue Pt 3 Pages 119034	10.1016/j.envres.2024.119034	38701888	動物	-	1	1	1	不明	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1301	D. Grami, K. Rtibi, I. Hammami, S. Selmi, L. De Tori, C. Foresta, L. Marzouki and H. Sebai	2020	Protective Action of Eruca sativa Leaves Aqueous Extracts Against Bisphenol A-Caused In Vivo Testicular Damages	Eruca sativa acts on the male reproductive system and fertility has not been precisely defined. In this study, the aim was to investigate the ameliorative activity of E. sativa aqueous extracts (ESAE) on reproductive toxicity associated with oxidative stress induced by bisphenol A (BPA). Wistar rats were used and divided into six groups of animals each: control (0.3 mL of corn oil/rat), ESAE at the higher dose (250 mg/kg), BPA (100 mg/kg body weight (b.w.)), amino[5-(p-fluorophenyl)-2-furoyl]guanidine sulfonate (EIPA) (1 mg/kg b.w.), BPA + ESAE, and BPA + EIPA. The BPA pathway plays an essential role in complex IV (CIV) formation, a rate-limiting oxygen-dependent CIV assembly factor. The results showed that BPA treatment produced a diminution of density, motility, and viability of sperm with disruption of spermatozoa morphology and fertilizing potential as well as testosterone, luteinizing hormone, and follicle-stimulating hormone levels. Moreover, BPA administration induced a significant increase in testicular lipid peroxidation (LPO) and nitric oxide (NO) levels and a decrease in the activities of superoxide dismutase (SOD), catalase, and glutathione peroxidase in spermatozoa as well as in reproductive tissue, which was marked. The oxidative stress was measured by malondialdehyde production. Vital group I BPA decline and established improved fertility disturbance, in particular superoxide dismutase, catalase, and glutathione peroxidase in reproductive tissues. ESAE coadministration at the two lower doses improved all histological and biochemical parameter injuries. These finding suggested the ESAE ability to prevent the testicular damages in rats, which might be linked to functional bioactive substances, such as phenolic compounds with higher antioxidant capacity.	J Med Food Vol.23 Issue 6 Pages 600-610	10.1089/jmf.2019.0170	31859581	動物	-	1	1	1	1	1	50、100、200 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1302	S. Goyal, S. Tiwari, B. Seth, A. Tandon, J. Shankar, M. Sinha, S. J. Singh, S. Priya and R. K. Chaturvedi	2021	Bisphenol-A inhibits mitochondrial biogenesis via impairment of GFER mediated mitochondrial protein import in the rat brain hippocampus	Mitochondrial biogenesis relies on different protein import machinery, as mitochondrial proteins are imported from the cytosol. The mitochondrial intermembrane space assembly (MIA) pathway consists of CFTR/OSU5 and CHCHD4/Mia40, responsible for importing proteins and their oxidative folding inside the mitochondria. The MIA pathway plays an essential role in complex IV (CIV) formation, a rate-limiting oxygen-dependent CIV assembly factor. The results showed that BPA treatment produced a diminution of density, motility, and viability of sperm with disruption of spermatozoa morphology and fertilizing potential as well as testosterone, luteinizing hormone, and follicle-stimulating hormone levels. Moreover, BPA administration induced a significant increase in testicular lipid peroxidation (LPO) and nitric oxide (NO) levels and a decrease in the activities of superoxide dismutase (SOD), catalase, and glutathione peroxidase in spermatozoa as well as in reproductive tissue, which was marked. The oxidative stress was measured by malondialdehyde production. Vital group I BPA decline and established improved fertility disturbance, in particular superoxide dismutase, catalase, and glutathione peroxidase in reproductive tissues. ESAE coadministration at the two lower doses improved all histological and biochemical parameter injuries. These finding suggested the ESAE ability to prevent the testicular damages in rats, which might be linked to functional bioactive substances, such as phenolic compounds with higher antioxidant capacity.	Neurotoxicology. 2021 Jul;85:18-32.	10.1016/j.neuro.2021.04.001	33878312	動物	神経	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1303	S. Goyal, S. Tiwari, B. Seth, Phoolmala, A. Tandon and R. Kumar Chaturvedi	2022	Bisphenol-A Mediated Impaired DRP1-GFER Axis and Cognition Restored by PGC-1α Upregulation Through Nicotinamide in the Rat Brain Hippocampus	The regulatory network of mitochondrial biogenesis and dynamics is vital for mitochondrial functions and cellular homeostasis. Any impairment in the mitochondrial network leads to neurodegenerative disorders. Our previous study has established that bisphenol-A (BPA) exposure impairs mitochondrial biogenesis in the rat brain hippocampus. The present study was focused on the mechanism of BPA-induced impairment of mitochondrial biogenesis. Mitochondrial protein import machinery is crucial for mitochondrial biogenesis. Glutaredoxin 2 (GRX2) and mitochondrial import protein (MTP18), which leads to demyelination, neurodegeneration, and cognitive deficits in the rats. In the present study, we found that chronic BPA exposure reduces PGC-1α levels, broader regulator of mitochondrial biogenesis, alters mitochondrial localization of DRP1 and GFER, and reduces the number of PGC-1α (Nuclear)+/and PGC-1α (β -tubulin)+/ neurons in the rat hippocampus, suggesting reduced PGC-1α -mediated neurogenesis. Nicotinamide significantly increased nuclear PGC-1α protein levels, PGC-1α (Nuclear) -co-labeled cells in BPA-treated rat hippocampus and PGC-1α (β -tubulin)+ co-labeled cells in neuron culture derived from hippocampal neural stem cells. Interestingly, PGC-1α upregulation by nicotinamide also resulted in increased GFER levels and restored mitochondrial localization of DRP1 in the hippocampus of BPA-exposed rats. Nicotinamide also restored BPA-induced reduction in mitochondrial membrane potential, ATP production, and mitochondrial number in the cortex and hippocampus, suggesting restored mitochondrial function. This resulted in reduced cytochrome c levels in improved cytosol and reduced hippocampal neurodegeneration-induced caspase-3/cleaved-caspase-3 (Cleaved-C-3+) (Active-caspase) following nicotinamide treatment in BPA-treated group. Consequently, activation of PGC-1α by nicotinamide restored BPA-mediated cognitive deficits in rats. Results suggest that the treatment of nicotinamide has therapeutic potential and rescues BPA-mediated neuronal death and cognitive deficits by upregulating the PGC-1α and GFER-DRP1 link, thus balancing mitochondrial homeostasis.	Mol Neurobiol. 2022 Aug;59(8):4761-4775.	10.1007/s12035-022-02862-y	35612786	動物	神経	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1304	Z. Gorowska-Wojtowicz, M. Dutkiban, M. Kuckyska, P. Durka, P. Pawlicki, A. Milon, M. Zarzycka, W. Plucha, M. Kotula-Balak, A. Ptak, J. K. Wolski and B. Bilinska	2019	Leydig cell tumorigenesis - implication of G-protein coupled membrane estrogen receptor, peroxisome proliferator-activated receptor and xenoestrogen exposure. In vivo and in vitro appraisal	The etiology and molecular characteristics of Leydig cell tumor (LCT) are scarcely known. From the research data stems that estrogen can be implicated in LCT induction and development, however it is not investigated in detail. Considering the above, herein we analyzed the relation between G protein-coupled membrane estrogen receptor, peroxisome proliferator-activated receptor and Insulin like family peptides Insulin like 3 peptide (INSL3) expression in LCT induced by xenoestrogen exposure. Female Wistar rats were treated with BPA, DES, and G1 (G protein-coupled membrane estrogen receptor agonist) for 2 years. Ovariectomized rats were used as a control group. Immunohistochemistry (IHC) and Western blot (WB) were used to assess GPER1 (G protein-coupled membrane estrogen receptor), PPARγ (peroxisome proliferator-activated receptor γ), and INSL3 expression in normal LCT being a possible source and in additionally affecting LCT. Moreover, in vitro experiments, two cell lines were used: MA-10 Leydig cell (MA-10) treated with BPA chemicals were examined. We revealed either diverse changes in expression or co-expression of GPER1 and PPARγ in normal LCT as well as in MA-10 cells after BPA analogues when compared to human LCT. Moreover, we found that BPA, DES, and G1 affected INSL3 expression in LCT. Our results indicate that BPA, DES, and G1 cells xenoestrogen-treated some basic differences, involvement of GPER, PPARγ, and INSL3 pathways not only in LCT development but also in hormonal receptors and hormones axes altered. Taken together, species, cell origin, experimental system used and type of used chemical differentiate may result in diverse molecular characteristics of LCT. Estrogen/xenoestrogen may play a role in tumor Leydig cell proliferation and biochemical potential of tumor but this issue requires further studies. Experimentally induced LCT in mouse, rats and MA-10 cells after BPA exposure seem to be additional models for understanding some aspects of human LCT biology.	Tissue Cell. 2019 Dec;61:51-60.	10.1016/j.tice.2019.08.001	31759407	動物、in vitro	精巣	1	0	1	0	不明	1	0	不明	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1305	A. C. Gore, T. Moore, M. J. Groom and L. M. Thompson	2022	Prenatal Exposure to an EDC Mixture, NeuroMix: Effects on Brain, Behavior, and Stress Responsiveness in Rats	Humans and wildlife are exposed to endocrine-disrupting chemicals (EDCs) throughout their lives. Environmental EDCs are implicated in a range of diseases/disorders with developmental origins, including neurodevelopmental disorders. Most studies have focused on single chemicals, but humans are exposed to complex mixtures of EDCs with unknown consequences for health and development. The choice of EDCs, which we refer to as "NeuroMix," was informed by evidence for neurobiological effects in single-compound studies and included bisphenols, phthalates, insecticides, and perfluorinated, polybrominated, and polychlorinated compounds. Pregnant Sprague Dawley rats were fed the NeuroMix or vehicle, and then offspring of both sexes were assessed for effects on postnatal development and behavior, and gene expression in the brain in adulthood. In order to determine whether early life EDC1 predisposed to subsequent vulnerability to postnatal life challenges, a subset of rats were also given a stress challenge in adolescence. Prenatal NeuroMix exposure decreased body weight and delayed puberty in males, but not females. In adulthood, NeuroMix caused changes in anxiety-like, social, and mate preference behaviors, only in females. Effects of stress were predominantly observed in males. Some interactions of NeuroMix and stress were found, especially for the male preference behavior and gene expression in the brain. These findings provide novel insights into how toxic metabolic environmental challenges lead to developmental and neurobehavioral deficits, both alone and in combination, in a sex-specific manner.	Toxics Vol.10 Issue 3	10.3390/toxics10030122	35324748	動物	-	1	1	0	1	不明	不明	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1306	M. González-Gómez, R. Reyes, M. D. C. Damas-Hernández, R. Plasencia-Cruz, I. González-Mariscal, R. Alonso and A. R. Bello	2023	NTS, NTSR1 and ERs in the Pituitary-Gonadal Axis of Cycling and Postnatal Female Rats after BPA Treatment	The neuropeptide neurotensin (NTS) is involved in regulating the reproductive axis and is expressed at each level of this axis. Bisphenolamic pituitary gonadal. This dependence on estrogen levels has been widely demonstrated in the hypothalamus and pituitary. We focused on confirming the relationship of NTS with estrogens and the gonadal axis, using a particularly important environmental estrogenic molecule, bisphenol A (BPA). We studied the expression of NTS, NTSR1, ERα, and ERβ in the pituitary gland of female rats at different stages of the estrous cycle and after BPA treatment. We found that the expression of NTS and estrogen receptors in the pituitary gland was dynamic during the estrous cycle and BPA treatment. The exposure to BPA (0.5 and 2 mg/kg body weight per day during gestation and lactation) also increased the number of neuronal cells in the porcine small intestine and containing serotonin (5-hydroxytryptamine, 5-HT). During this experiment, it was demonstrated that both applied BPA doses caused an increase in the number of 5-HT positive cells located in the mucosal layer of the intestinal epithelium and lamina. These changes may be connected with the direct impact of BPA on the intestinal mucosa, the pro-inflammatory and immunomodulatory properties of this substance, and/or the influence of BPA on the neurochemical characterization of nervous structures supplying the intestine.	Int J Mol Sci Vol.24 Issue 8	10.3390/ijms24087418	37108581	動物	-	1	0	1	1	0	0.5、2 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1307	S. Gorkowski	2020	Bisphenol A (BPA)-Induced Changes in the Number of Serotonin-Positive Cells in the Mucosal Layer of Porcine Small Intestine-the Preliminary Studies	Bisphenol A (BPA) is a substance used in the production of plastics which has a negative impact on many internal organs. Because BPA is normally toxic for the gastrointestinal (GI) tract, the intestine is especially vulnerable to the adverse effects of this substance. The aim of this investigation was to study the influence of two doses of BPA (0.05 mg and 0.5 mg/kg body weight/day) on the number of mucosal cells in the porcine small intestine and containing serotonin (5-hydroxytryptamine, 5-HT). During the experiment, it was demonstrated that both applied BPA doses caused an increase in the number of 5-HT positive cells located in the mucosal layer of the intestinal epithelium and lamina. These changes may be connected with the direct impact of BPA on the intestinal mucosa, the pro-inflammatory and immunomodulatory properties of this substance, and/or the influence of BPA on the neurochemical characterization of nervous structures supplying the intestine.	Int J Mol Sci Vol.21 Issue 3	10.3390/ijms21031079	32041147	動物	-	1	1	1	不明	0	0.05、0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1308	J. Gorkowski, S. Gorkowski, E. Dzika and J. Wojtkiewicz	2020	Changes in the Population Size of Calbindin D-28k-Immunoreactive Enteric Neurons in the Porcine Caecum under the Influence of Bisphenol A: A Preliminary Study	Calbindin D-28k (CB) is a calcium-binding protein widely distributed in living organisms that may act as a calcium buffer and sensory protein. CB is present in the enteric nervous system (ENS) situated in the gastrointestinal tract, which controls the majority of activities of the second-most extensive system of the human body. The influence of various doses of bisphenol A (BPA) on chemical composition and neurochemical plasticity production on the number and distribution of CB-positive enteric neuronal cells in the porcine caecum was investigated with an immunofluorescence technique. The obtained results showed that low dosages of BPA resulted in an increase in the number of CB-positive neuronal cells in the myenteric (MP) and inner submucous (SIP) plexuses, whereas it did not alter the number of neuronal cells in the outer submucous plexus (OSP). High dosages of BPA caused the increase in the amount of CB-positive perikarya in all the above-mentioned kinds of the caecal neuronal plexuses. These observations strongly suggest that CB's role in the ENS participates in the processes connected with the toxic activity of BPA. Most likely, the changes noted in the experiment result from the adaptive and protective properties of CB.	Toxics Vol.9 Issue 1	10.3390/toxics9010001	33379192	動物	-	1	1	1	Pitrain × Duroc	0	0.05、0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1309	A. Ghanbarzehi, S. Mokhtari, A. Piryaei, F. Asadi, A. Mohammadi and A. Shahbazi	2025	Prenatal exposure to Bisphenol A sex-specifically disrupts prepulse inhibition and decreases parvalbumin-positive neurons in the prefrontal cortex of adult rats	Early life exposure to bisphenol A (BPA) has adverse effects on neuronal development and behavioral performance; however, many aspects of its effects, remain unknown. Here, we aimed to investigate whether prenatal exposure to BPA can induce psychosis-like behaviors and impair certain schizophrenia-related GABAergic markers, including GAD67, NR2C, NR4B, and parvalbumin (PV), in the prefrontal cortex (PFC) of adult offspring rats. Pregnant Sprague Dawley rats were orally administered BPA (0.25 and 2.5 mg/kg/day) and/or haloperidol as a reference antagon, or a vehicle during the pregnancy period. On postnatal days (PNDs) 52–60, male and female offspring were subjected to behavioral tests, including the open field test (OFT), novel object recognition test (NORT), and prepulse inhibition (PPI). Prenatal BPA exposure within or significant changes were observed in male offspring. Moreover, in female offspring, a marked reduction in the density of PV-positive neurons in the PFC was observed in both BPA groups compared to the control group. In the locomotor activity test, neither sex showed significant changes. Meanwhile, the PPC expression of GAD67, NR2C, and PNR4 genes did not show significant alterations in either male or female rats. Overall, this study demonstrates that prenatal BPA exposure disrupts PPI and decreases PV-positive neurons in the PFC of adult female rats. In other words, early neurodevelopment can be sex-specifically impaired by BPA, which may consequently increase susceptibility to schizophrenia in adulthood. Therefore, the detrimental effects of BPA on embryonic and fetal brain development should be considered in health policies related to pregnancy.	Physiol Behav Vol.297 Pages 114933	10.1016/j.physbeh.2025.114933	40311724	動物	-	1	1	1	1	0	0.25、2.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1310	A. Gezer, H. Gürüldağ, N. Kılıç Başpınarlı, E. Erkaş and M. Özkanca	2024	The Protective Effect of Gallic Acid Against Bisphenol A-Induced Ovarian Toxicity and Endocrine Disruption in Female Rats	Purpose: This study aimed to investigate the protective effects of gallic acid (GA) against ovarian damage induced by bisphenol A (BPA) exposure in female rats. We evaluated whether GA can mitigate the adverse effects of BPA on ovarian structure, inflammatory markers, oxidative stress, apoptosis, and reproductive hormone levels. Methods: Thirty-two female rats were categorized into four groups: control, GA, BPA, and GA+BPA. Histopathological evaluations of ovarian tissue were performed using hematoxylin-eosin staining. The immunohistochemical analysis was conducted for inflammatory, oxidative DNA damage, and apoptotic markers. Biochemical parameters, including TAS, TOS, PON1, and MPO activities, were measured in serum samples. Results: Histopathological examinations revealed that BPA exposure caused significant damage to ovarian tissues. Furthermore, follicular stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and progesterone levels were quantified using enzyme-linked immunosorbent assay. Results: Histopathological outcomes revealed that BPA significantly induced follicular degeneration, which was effectively mitigated by GA treatment (P < 0.05). Immunohistochemical analysis highlighted the exacerbation of inflammatory and oxidative stress markers in BPA-exposed rats, which GA co-administration substantially reduced (P < 0.05). Biochemical assays revealed that BPA exposure induced significant oxidative stress, demonstrated by elevated TOS and decreased TAS and PON1 activity (P < 0.05). Hormonal profiling indicated that BPA treatment altered the levels of FSH, LH, estrogen, and progesterone, with GA treatment showing a capacity to modulate these changes, especially in progesterone levels (P < 0.05). Conclusions: The findings suggest that GA exhibits protective properties against BPA-induced ovarian damage through its antioxidative and anti-inflammatory activities, alongside its ability to modulate hormonal imbalances. This research underscores the therapeutic potential of GA in safeguarding reproductive health against environmental toxicants.	J Med Food Vol.27 Issue 7 Pages 651-660	10.1089/jmf.2024.0088	38975681	動物	-	1	不明	1	不明	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1311	C. A. Gilly, M. Z. Lacroix, B. B. Roques, P. L. Toutain, V. Gayrard and N. Picard-Hagen	2023	Comparison of toxicokinetic properties of eleven analogues of Bisphenol A in pig after intravenous and oral administrations	Due to the restrictions of its use, Bisphenol A (BPA) has been replaced by many structurally related bisphenols (BPs) in consumer products. The endocrine disrupting potential similar to that of BPA has been described for several bisphenols, there is therefore an urgent need of toxicokinetic (TK) data for these emerging BPs in order to evaluate if their internal exposure could increase the risk of endocrine disruption. We investigated TK behaviour of eleven BPs (abbreviations: BPE, BPG, BPAF, BPB, BPF, BPAP, BPZ, 12-BPA, BPS-2, BPAF-MP and BPF-MP) by intravenous and oral administrations of mixtures of three BPs in pigs and serial collection of blood over 72 h and urine over 24 h, to evaluate their disposition. Data were analysed using nonlinear mixed effects modelling and a comparison was made with TK predicted by the generic model PITH package. The low urinary excretion of BPE, BPG, BPAF, BPB, BPF, BPAP, BPZ, 12-BPA, BPS-2, BPAF-MP and BPF-MP (<1% dose) and the high oral bioavailability (>70%) of BPE, BPG, BPB, BPF, BPAP, BPZ, 12-BPA, BPS-2, BPAF-MP and BPF-MP analogues have been demonstrated. Bisphenols with higher systemic exposure (area under the plasma concentration-time curve (AUC) of the unconjugated Bisphenol than BPA (i.e. 1.6 to 3.1 fold for 12-BPA, BPAF, BPB and BPZ, 7–10 fold for BPE, 12-BPA, BPAF-MP and BPF-MP and 230 fold for BPG) due mainly to a considerable variation of oral bioavailability (proportion of BP administered by oral route that attains the systemic circulation unchanged). Given similarities in the digestive tract between pigs and humans, our TK data suggest that replacing BPA with some of its alternatives, particularly BPE, will likely lead to higher internal exposure to potential endocrine disruptive compounds. These findings are crucial for evaluating the risk of human exposure to these emerging BPs.	Environ Int Vol.171 Pages 107722	10.1016/j.envint.2022.107722	36584424	動物	-	1	1	0	不明	0	6 μmol/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1312	L. García-Motil, A. Fuster-Aparisi, M. D. M. Ribao-Taberner, J. Trujillo-Vives, G. Escamez-Garcia, M. Jiménez, F. A. Casado-Carmona, S. Tejada, M. D. Ferrer, J. Mercader-Barceló, A. Sureda and M. Miró	2025	Is bisphenol A sorbed onto microplastics less bioavailable than freely dissolved bisphenol A? Implications for the gut health in a murine model	There is scarcity of in vivo assays to investigate the potential deleterious effects of plastic-laden compounds in the gastrointestinal tract of mammals, compared to in vitro testing and notoriously assays to ascribe toxicity to MPs per se. Thus, the present study investigated the potential adverse effects of polystyrene microplastics (PS-MPs) sorbed with bisphenol A (BPA) in the gut health of mice. Male C57BL/6J mice (n = 30) received a gavage dose of 2000 μg BPA/kg bw/day (BPA) with a mean particle size of 236 μm, which were administered via oral gavage at a mere 0.67 mg BPA/kg body weight for 21 days using an elution method. The determination of plasma BPA (plasma-free) revealed that BPA accumulated in rich BPA is bioavailable, to a similar extent to that of freely dissolved BPA, with a free index (the Cmax (ng/L) values of 1249.3 ± 182 and 928.1 ± 270 μg/mL) for the 0–6 h interval (AUC(0–6h)), respectively. Besides, the AUC(0–24h) of free BPA was 1.5-fold higher than that of BPA sorbed onto MPs. Exposure to BPA sorbed onto MPs did not induce significant changes in the gut barrier function or in the ability to elucidate the potential deleterious effects of BPA. Instead, PS-MPs by themselves or sorbed with BPA were found to induce alterations in the abundance of the Akkermansia, multidrug resistance protein 1 (MDR1) and GSH-glucuronyltransferase (B1-GGT2B1) in the jejunum, particularly when PS and BPA co-exist together, likely due to the extended intestinal residence time of BPA when MPs. Endobiotic stress markers, such as superoxide dismutase activity, and inflammatory responses, evaluated by myeloperoxidase activity, were also elevated with PS-BPA, suggesting a reference response but without evidence of oxidative damage, as demonstrated by the malondialdehyde levels. In conclusion, the findings suggest that BPA associated with MPs exhibits similar bioavailability than that of freely dissolved BPA, with the subsequent activation of detoxification pathways and inflammatory responses.	Environ Pollut Pages 127019	10.1016/j.envpol.2025.127019	40850458	動物	-	1	1	1	不明	0	0.67mg BPA/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1313	M. García-Arévalo, E. Lorca-Gil, L. Cardoso, T. M. Batista, T. R. Rosa Jr, L. A. F. Ramos, M. A. Alves, A. Nadal, E. M. Carneiro and A. P. Daniel	2021	Ventricular Fibrosis and Coronary Remodeling Following Short-Term Exposure of Healthy and Malnourished Mice to Bisphenol A	Bisphenol A (BPA) is an endocrine disruptor associated with higher risk of insulin resistance, type 2 diabetes, and cardiovascular diseases, especially in susceptible populations. Because malnutrition is a nutritional disorder associated with high cardiovascular risk, we sought to compare the effects of short-term BPA exposure on cardiovascular parameters of healthy and protein-malnourished mice. Pancreatoxic male mice were fed a control- (n=10) or low-protein (LP; 6%) diet for 8 weeks and then exposed or not to BPA (50 μ kg/d, 5 days) for the last 3 days. Systolic blood pressure was higher in BPA-vs LP groups (control-like and low-protein groups). However, diastolic blood pressure was enhanced by BPA only in malnourished mice. Left ventricle (LV) and diastolic pressure (EDP), collagen deposition, and CTGF mRNA expression were higher in the control- vs LP-BPA groups. Conversely, LV systolic pressure, dP/dtmax, and dP/dtmin were lower in the control- vs LP-BPA group. Cardiac mRNA expression of Nox4 and Nox2 was higher in the control- vs LP-BPA group, while SOD1 was lower in the control- vs LP-BPA group. Nox2 tissue ratio and cross-sectional area of intramyocardial arteries were higher either in the LP or BPA group compared with the control mice. Taken together, our findings suggest that short-term BPA exposure results in LV diastolic dysfunction and fibrosis, and intramyocardial arteries hypertrophy, besides, potentiate protein malnutrition-induced hypertension and cardiovascular risk.	Front Physiol Vol.12 Pages 638506	10.3389/fphys.2021.638506	33912069	動物	-	1	0	1	1	0	50 μg kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1314	Z. Gao, S. Liu, L. Tan, X. Gao, W. Tan, C. Ding, M. Li, Z. Tang, X. Shi, Y. Luo and S. Song	2022	Testicular toxicity of bisphenol compounds: Homeostasis disruption of cholesterol/testosterone via PPARα activation	The widespread application of bisphenols (BPs) has made them ubiquitous in the environment. Although the side effects of bisphenol A (BPA) substitutes have received increasing attention, studies on their reproductive toxicity remain lacking. In this research, the effects of BPs and its substitutes, including bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF), on the male reproductive system were evaluated. Results showed that these BPs disturbed germ cell proliferation, induced germ cell apoptosis, and perturbed sperm physiologies and spermatogenesis, which resulted from the disruption of testosterone (T) biosynthesis in Leydig cells. Mechanistically, BPs activated peroxisome proliferator-activated receptor α (PPARα) and its downstream genes, including cytochrome P450 family 4 subfamily A member 11 (CYP4A11) and fatty acid binding protein 1 (FABP1). Conversely, administration of PPARα-antagonist GW6471 alleviated the BPs-induced testicular dysfunction. Overall, our studies indicated that BPF, BPS, and BPAF could induce testicular toxic effects similar to that of BPA, which were associated with the PPARα pathway.	Sci Total Environ. 2022 Aug 25:836:155628.	10.1016/j.scitotenv.2022.155628	35504394	動物、in vitro	精巣	1	1	1	1	0	0	-	-	-	不明	0	不明	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1315	T. Fujimoto	2020	Prenatal exposure to bisphenol A impairs predator odor-induced fear behavior in young rat offspring	OBJECTIVES: This study evaluated the changes in behaviors and the endocrine system in rat offspring at postnatal day 20 following prenatal exposure to bisphenol A (BPA), a major environmental endocrine disruptor. DESIGN: Using 3 predator vials (0.1 ml trimethylamine (TMT) as a mixture), I evaluated behavioral and endocrine responses to check whether the normal stress response is altered by BPA. SUBJECTS: 8-week-old female rats. METHODS: A low-dose group (BPA-L: 0.025 mg/kg/day) and a high-dose group (BPA-H: 0.25 mg/kg/day) were compared to a vehicle-dose (ethanol). The control group was not exposed to BPA. Spontaneous behaviors, such as locomotor activity and anxiety-like behaviors, were observed in an open field test. Fear-like behaviors were observed in response to predator odor (TMT) in a Y-maze test. RESULTS: In the BPA group, freezing was unchanged, but grooming behavior increased; however, increased freezing and grooming behaviors were observed following TMT odor exposure in the BPA groups. Additionally, blood corticosterone levels increased following TMT odor exposure in all three groups, but there was no difference between the BPA-exposure groups and the control group. Therefore, in the BPA-H group, despite the activation of the hypothalamus–pituitary–adrenal axis by TMT, freezing behavior did not increase, suggesting the absence of defensive behaviors. CONCLUSIONS: These findings suggest that prenatal exposure to high-dose BPA causes habituation to stress-induced by the predator odor and alters the normal stress response in young rat offspring.	Neuro Endocrinol Lett Vol.41 Issue 5 Pages 275-283	-	33315342	動物	-	1	不明	1	不明	0	0.025、 1.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1316	A. G. F. Filquer, F. D. N. Santos, D. B. Angeli, F. A. C. Silva, A. T. Dias, R. Alves, M. A. S. Leal, B. V. Nogueira, F. G. Amorim, B. P. Campagnaro, T. M. C. Pereira, M. Campos-Toimil, S. S. Meyrelles and E. C. Vasquez	2020	Bisphenol A contamination in infant rats: molecular, structural, and physiological cardiovascular changes and the protective role of kefir	The effects of bisphenol A (BPA) contamination on the cardiovascular function still are not clear. Here, we evaluated the vascular effects of BPA and the protective actions of kefir in infant rats. Animals (24 days old) were treated with BPA (100 μg/kg/day) for 60 days. BPA group, or administered with 0.2 mL (100 μ) in addition to BPA (BPA+kefir group), compared with non-treated rats (Control group). The vascular endothelial function was evaluated in aortic rings through the relaxation response to acetylcholine and specific blockers. The balance between reactive oxygen species (ROS) and nitric oxide (NO) was assessed through flow cytometry in the vascular tissue. The BPA group developed lipid deposition (↑10%) and the aorta (↑ vascular reactivity) showed an impaired ACh-induced relaxation (↓ 30%). The further studies by using NADPH, ROS and COX blockers revealed that the impaired vasorelaxation was due to increased ROS production (↑ 25%). NO bioavailability (↓ 22%) and increased vasoconstriction to prostanoids (↑ 26%) compared with the Control group. Besides, BPA increased the aortic wall thickness (↑ 20%) and the collagen deposition (↑ 30%). Kefir treatment prevented all BPA-induced vascular changes. Finally, the BPA group showed a lower body weight (↓ 20%) compared with the Control group (120.6 ± 5.86 and 177.1 ± 8.04 g, $P < 0.05$) and both received these values (139.6 ± 9 and 153.7 ± 7.4 g). Conclusion: Kefir by itself or in BPA-treated supported protective and endothelial dysfunction and it is one consequently a vascular ROS/NO imbalance, damage of endothelial layer and pro-apoptotic effects. The novelty is that the treatment using probiotic kefir was able to attenuate the progression the above BPA effects.	J Nutr Biochem Vol.75 Pages 108254	10.1016/j.jnutbio.2019.108254	31707283	動物	-	1	不明	1	1	0	100 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1317	K. Fouda and R. S. Mohamed	2025	Alginate Beads with Encapsulated Date Palm Pollen Extract: Development, Characterization and Their Potential Role in Hepato-Protection and Fertility-Stimulating Hormonal Improvement in Bisphenol A-Treated Rats	The goal of this study was to design polymeric beads with a core of date palm pollen (DPP; Phoenix dactylifera L.) extract using the ionic gelation method and then examine the effects of the extract in combination with alginate beads on bisphenol A (BPA)-induced hepatic damage and infertility in male rats. Methods: Alginate beads containing DPP extract were prepared and characterized for their morphology, encapsulation efficiency, and in vitro release behavior. Male rats were divided into six groups and treated orally for 30 days with BPA (50 mg/kg/day), DPP extract (200 mg/kg/day), or alginate beads containing DPP extract (equivalent to 200 mg/kg/day of DPP extract). The in vivo evaluation included assessments of liver enzymes, oxidative stress markers, histopathological examinations, and hormonal profiles. Results: The encapsulation efficiency (EE) was 76.27 ± 1.15%, and the loading capacity (LC) was 16.27 ± 0.25%. The study found that phenolic release was higher (98.83% ± 1.29%) in simulated intestinal fluid and lowest (58.63% ± 0.71%) in simulated stomach fluid after 2 h. This particular type of bead also exhibited significant antioxidant activity, phenolic component content, and flavonoid content. The estimated phenolic content was 56.08 mg GAE/g, with methyl gallate, gallic acid, and naringenin as the main components. In vivo evaluation findings revealed that both doses of alginate/DPP beads (BeDPx) significantly (p < 0.05) improved the liver, as demonstrated by downregulated liver function parameters, improved levels of male fertility-stimulating hormones, reduced oxidative stress parameters and inflammatory cytokines, and preserved both liver and testicular tissues from BPA-induced changes. Thus, the extract of alginate/DPP beads make them a promising choice for antioxidant, liver protecting, and male hormone-enhancing hydrogels.	Polymers (Basel) Vol.17 Issue 7	10.3390/polym17070912	40219302	動物	-	1	1	1	1	0	30 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1318	H. Fouad, E. M. Fawk, W. A. Alsamari, E. H. Nadaa and U. F. A. Ebrahim	2021	Structural and chemical role of mesenchymal stem cells and resveratrol in regulation of apoptotic -induced genes in Bisphenol-A induced uterine damage in adult female albino rats	The probable beneficial effects of mesenchymal stem cells (MSCs) and resveratrol were assessed in an experimental model of Bisphenol A (BPA)-induced uterine damage in rats. Thirty-five albino rats were involved and equally divided into five groups: Group I negative control rats received basal diet, Group II positive control rats received BPA by oral gavage for 21 days, Group III BPA treated rats received single oral gavage of resveratrol daily for two weeks, Group IV BPA treated rats received a single intravenous dose of MSCs, and Group V BPA treated rats received combined treatment of resveratrol and MSCs. Oxidative stress markers, apoptosis-related genes, and steroidal hormones were assessed. Histological and immunohistochemical examination of uterine tissue was conducted for TGF-β 1, Caspase-3, 8, and 9 (Cas3, Cas8, Cas9) genes were assessed. Results: Histological examination revealed that BPA induced severe uterine damage, while resveratrol and MSCs treatments showed significant improvement. BPA exposure caused a decrease in PON1 activity and increase in TOP. A 7-immunoreactivity. BPA also induced a significant increase in oxidative stress markers, malondialdehyde (MDA), SOD, CAT, and caspases activity genes. BPA induced a significant change in blood levels of gonadal hormones; a significant increase in FSH and a significant decrease in estradiol (E2) and progesterone (P). Treatment with either resveratrol, MSCs, or combination of them resulted in significant enhancement of histological findings, restoration of gonadal hormones to near-normal levels, and a significant decrease in oxidative stress markers and apoptotic genes. Combined treatment with resveratrol and MSCs demonstrated more significant therapeutic effects as regard to the studied parameters in association with all groups treated with either MSCs or resveratrol separately.	Tissue Cell Vol.70 Pages 101502	10.1016/j.tice.2021.101502	33582552	動物	-	1	1	1	1	0	20 mg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1319	C. Focaccetti, D. Nardozi, M. Benevento, V. Lucarini, V. Angiolini, R. Carraro, M. Scimeca, F. Servadei, A. Bonanno, F. Mancini, Z. M. Bashirat, M. Milella, S. Migliaccio, E. Ferretti, L. Cifaldi, L. Manuelli, C. Palumbo and R. Bei	2024	Bisphenol-A in Drinking Water Accelerates Mammary Cancerogenesis and Favors an Immunosuppressive Tumor Microenvironment in BALB-neuT Mice	Bisphenol A (BPA), a synthetic compound ubiquitously present in the environment, can act as an endocrine disruptor by binding to both canonical and non-canonical estrogen receptors (ERs). Exposure to BPA has been linked to various cancers, in particular, those arising in hormone-targeted tissues such as the breast. In this study, we evaluated the effect of BPA intake through drinking water on ErbB2/neu-driven cancerogenesis in BALB-neuT mice. Female mice were exposed to BPA (0.5 mg/L) in drinking water from 4 weeks of age, and mammary tumor development was monitored. BPA exposure did not affect the number of tumors per mouse and its concurrent decrease in tumor-free and overall survival. As assessed by immunohistochemistry, BALB-neuT tumors were ER negative, but parts of the alternative estrogen receptor GPR30, regardless of BPA exposure. On the other hand, BPA exposure resulted in a marked upregulation of progesterone receptors in perivascular tumors and of Ki67, CD31, and phosphorylated Akt in treated tumors. Moreover, based on several infiltration markers of immune cells, BPA favored an immunosuppressive tumor microenvironment. Finally, in vitro cell survival studies performed on a cell line established from a BALB-neuT breast carcinoma confirmed that BPA's impact on cancer progression can be particularly relevant after chronic, low-dose exposure.	Int J Mol Sci Vol.25 Issue 11	10.3390/ijms25116259	38892447	動物	-	1	1	1	BALB-neuT	0	25 μg/L（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1320	A. Flores, P. Moyano, E. Sola, J. M. García, J. García, M. T. Frejo, L. Guerra-Menéndez, E. Lobato, I. Lobo, L. Abascal and J. D. Pino	2023	Bisphenol-A Neurotoxic Effects on Basal Forebrain Cholinergic Neurons In Vitro and In Vivo	The widely used plasticizer bisphenol A (BPA) is well known for producing neurodegeneration and cognitive disorders, following acute and long-term exposure. Although some of the BPA actions, involved in these effects, have been unraveled, they are still incompletely known. Basal forebrain cholinergic neurons (BFCN) regulate memory and learning processes and their selective loss, as observed in Alzheimer's disease and other neurodegenerative disorders, leads to severe cognitive impairment. Here, we investigated the effects of BPA on BFCN in vitro and in vivo. Primary cultures of BFCN were established from embryonic rat basal forebrain and challenged with BPA for 7 days. Cholinergic neurons were identified by immunocytochemistry for choline acetyltransferase (ChAT). Cell viability was evaluated by the MTT assay. Cell death was assessed by flow cytometry and fluorescence microscopy. Cell cycle was analyzed by flow cytometry. Oxidative stress was evaluated by measuring reactive oxygen species (ROS) production and glutathione (GSH) levels. Mitochondrial membrane potential was measured by JC-1 staining. Intracellular calcium ([Ca2+]i) was measured by Fura-2 AM fluorescence. Adult male Wistar rats were used as a basal forebrain cholinergic neurodegeneration model. Acute treatment of rats with BPA (50 μg/kg) induced a severe cholinergic cholinergic cell loss from the basal forebrain (BFCN) 7 or 15 days, produced postsynaptic density protein 95 (PSD95), synaptophysin, synaptotagmin, and N-methyl-D-aspartate receptor subunit 1 (NMDAR1) synaptic proteins downregulation, an increase in glutamate content through an increase in glutaminase activity, a derangement in the vesicular glutamate transporter 2 (VGLUT2) and in the NR1/2 of Ca-sensor pathway, and death in GABA cells. These toxic effects observed in BFCN cells were mediated by overexpression of thioredoxin-interacting protein 2 (TXNIP2). These results may help to explain the synaptic plasticity, cognitive dysfunction, and neurodegeneration induced by the glutamate BPA, which could contribute to their prevention.	Biology (Basel) Vol.12 Issue 6	10.3390/biology12060782	37372067	動物	-	1	0	1	1	0	40 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1321	F. Fischer, T. Kretschmer, P. Seifert, I. Howaldt, C. Krieger, J. Rüdiger, B. Fink, Z. Yin, M. Bauer, M. L. Zenclussen, N. Weyer, A. Schumacher and A. C. Zenclussen	2024	Single and combined exposures to bisphenol A and benzophenone-3 during early mouse pregnancy have differential effects on fetal and placental development	Endocrine disrupting chemicals (EDCs) possess the capability to interfere with the endocrine system by binding to hormone receptors, for example on immune cells. Specific effects have already been described for individual substances, but the impact of exposure to chemical mixtures during pregnancy on maternal immune regulation, placentation and fetal development is not known. In this study, we aimed to investigate the consequences of exposure to bisphenol A (BPA) and benzophenone-3 (BP3) during early pregnancy in mice. Female mice were exposed to BPA, BP3 or a mixture of both (Mix) via drinking water from 2 weeks before mating until day 6.5 of pregnancy. Fetal and placental growth, fetal genetic sex (gPCR), female mice were exposed to 4 μg/kg BPA, 16 mg/kg BP3 or a BPA/BP3 mixture (Mix) from conception until day 6.5 of pregnancy. Fetal and placental growth, fetal genetic sex (qPCR), high-frequency ultrasound and Doppler measurements were used to determine alterations in maternal fetal development and hemodynamic parameters. Furthermore, uterine spiral artery remodeling and placental mRNA expression were studied via histology and ONT-OT-PCR, respectively. Effects of EDC exposure on maternal immune regulation were investigated via flow cytometry. BPA, BP3 and Mix exposure resulted in significantly smaller placentae and fetuses. Fetal sex ratio was not affected. Uterine spiral artery remodeling was impaired in all exposure groups, but BP3 and Mix showed the strongest effects. Placental gene transcription was altered after BPA exposure. Placental gene transcription was altered after exposure to BP3 and Mix, but to different extents. Flow cytometry analyses revealed an increase in uterine T cells and NK cells in BPA and BP3/MP-1 treated dams, at gd14. Doppler measurements revealed no effect on uterine hemodynamic parameters and spiral artery remodeling was not affected following EDC exposure. Our results provide evidence that exposure to BPA and BP3 during early gestation affects fetal development in a sex-dependent manner, placental function and immune cell frequencies at the feto-maternal interface. These results call for inclusion of studies addressing pregnancy in the risk assessment of environmental chemicals.	Sci Total Environ Vol.922 Pages 171386	10.1016/j.scitotenv.2024.171386	38431166	動物	-	1	1	1	1	0	4 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1322	L. S. Figueiredo, K. M. Oliveira, I. N. Freitas, J. A. Silva, Jr., I. N. Silva, B. C. Favero-Santos, M. L. Bonfleur, E. M. M. Carneiro and R. A. Ribeiro	2020	Bisphenol-A exposure worsens hepatic steatosis in ovariectomized mice fed on a high-fat diet: Role of endoplasmic reticulum stress and fibrogenic pathways	HIGHLIGHTS: Bisphenol (BP)-A exposure can impair glucose and lipid metabolism. However, it is unclear whether this endocrine disruptor (ED) modulates these processes in postmenopause, a period with organic changes that can increase the susceptibility to metabolic disorders. Here, we investigated the effects of BPA exposure on hepatic steatosis in ovariectomized mice fed on a high-fat diet. GRAPHICAL ABSTRACT. ABSTRACT: BACKGROUND: Adult female mice were OVX and submitted to a normocaloric diet or HFD and drinking water without (control [OVX-CT]) and BPA (BPA groups, respectively) or with 1 μg/mL BPA (OVX-CBPA and OVX-HBPA groups, respectively), for 2 months. KEY FINDINGS: OVX-HFD females displayed increased adiposity, glucose intolerance, insulin resistance and moderate hepatic steatosis. This effect was associated with a higher hepatic expression of genes involved in lipogenesis (Srebf1 and Scd1), β-oxidation (Cpt1a) and endoplasmic reticulum (ER) stress (Hspa5 and Hsp90b1). BPA did not affect adiposity or glucose homeostasis disruptions induced by HFD. However, this ED triggered worse steatosis, exacerbating hepatic fat and collagen deposition in OVX-HBPA. In association with a reduction in Wnt4 mRNA, and up-regulation of genes involved in β-catenin degradation (Axin2 and Gsk3b), BPA increased the expression of Tgfb1 and Col1a1, which are involved in fibrogenesis. BPA also increased the expression of genes involved in ER stress (Hspa5 and Hsp90b1), but not inflammation (Tnf and Il6). SIGNIFICANCE: BPA aggravated hepatic steatosis in OVX mice. Especially when combined to a HFD, BPA caused NAFLD progression, which was partly mediated by chronic ER stress and the TGF-β1 pathway.	Life Sci Vol.256 Pages 118012	10.1016/j.lfs.2020.118012	32593710	動物	-	1	1	不明	1	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　　通毒性評価（疫学）1：該当、0：該当しない　　通毒性評価（in vitro）1：該当、0：該当しない　　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で原著に基づき精査。　　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	保留性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1323	L. J. Ferreira, T. F. R. Ruiz, L. G. de Souza, G. E. Brito-Filho, S. I. Colleta, E. C. R. Leonel and S. R. Taboga	2025	Bisphenol A exposure alters hormonal modulation and responsivity in the prostate of aged female gerbils	The female prostate is a gland regulated by steroid hormones for homeostasis. Bisphenol A (BPA) is an endocrine disruptor related to the progression of malignant lesions in prostate. The aim of this study was to analyze the hormonal modulation and responsiveness of the prostate of aged female gerbils previously exposed to BPA. Females were exposed to 50 μg/kg/day during pregnancy and lactation, and the prostate was analyzed at 18 months of age. Histological analysis, immunohistochemistry for androgen receptor (AR), estrogen receptor alpha (ERα), progesterone receptor (PR), Ki-67 protein (PCNA), and apoptosis (TUNEL) and quantification (PAS) reactions, as well as morphological measures. For endurance and associated and the proliferation (PAAD) and apoptotic (CCSD) markers. Prostate quantification was also performed for the receptors and enzymes described, as well as morphological and morphometric analyses of the gland. The results showed an increase in the epithelial expression of AR and ERα, and a decrease in the expression of ERβ in this compartment. In addition, a decrease in epithelial expression was observed for the Ki-67 molecule and an increase in the prostate epithelial cell number in the expression of PAS and CDK2. By Bivariate test analyses, significant differences were observed in the protein quantification of the receptors and enzymes described. Thus, the current study showed the role of BPA in intraprostatic hormonal modulation, though alterations in the expression of hormone receptors and the occurrence of enzymes in the female prostate, which can lead to the progression of malignant lesions in this tissue.	Mol Cell Endocrinol. 2025 Apr 15:600:112507.	10.1016/j.mce.2025.112507	39988023	動物	前立腺	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1324	L. Feng, S. Chen, L. Zhang, W. Qu and Z. Chen	2019	Bisphenol A increases intestinal permeability through disrupting intestinal barrier function in mice	The an alteration of the intestinal permeability is associated with gut barrier function has been increasingly evident, which plays an important role in human and animal health. Bisphenol A (BPA), an industrial compound used worldwide, has recently been classified as an environmental pollutant. One of our earlier studies has demonstrated that BPA disrupts the intestinal barrier function by inducing apoptosis and inhibiting cell proliferation in the human colonic epithelial cells line. In this study, we investigate the effects of dietary BPA uptake on the colonic barrier function in mice, as well as the intestinal permeability. Dietary BPA uptake was observed to destroy the morphology of the colonic epithelium and increase the pathology score. The levels of endotoxin, diamine peroxidase, D-lactate, and secretin were found to have been significantly elevated in both serum and colonic tissue. BPA uptake was also found to significantly increase the FITC-dextran 4000 flux in the colon. Moreover, dietary BPA uptake was also found to have significantly reduced the expression of tight junction proteins ZO-1, occludin, and claudin-1 in colonic epithelium of BPA mice decreased significantly, and their gene abundance was also inhibited. Moreover, dietary BPA uptake was also found to have significantly reduced colonic microbial diversity and altered microbial structural composition. The functional profiles of colonic bacterial community exhibited adverse effects of dietary BPA intake on the endocrine and digestive systems, as well as the transport and catabolism functions. Collectively, our study highlighted that dietary BPA increased the colonic permeability, and this effect was closely related to the disruption of intestinal chemistry and physical and biological barrier functions.	Environ Pollut. 2019 Nov;254(Pt A):112960.	10.1016/j.envpol.2019.112960	31394344	動物	腸管バリア機能	1	1	1	1	0	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1325	D. Feng, H. Zhang, K. Jiang, J. Zou, Q. Li, H. Mai, D. Su, W. Ling and X. Feng	2020	Bisphenol A exposure induces gut microbiota dysbiosis and consequent activation of gut-liver axis leading to hepatic steatosis in CD-1 mice	Interactions between the intestine and the liver, the so-called 'gut-liver axis', play a crucial role in the onset of hepatic steatosis and non-alcoholic fatty liver disease. However, not much is known about the impact of bisphenol A (BPA) exposure on the gut-liver axis and consequent hepatic steatosis. The present study was designed to investigate the effects of BPA exposure on gut microbiota and hepatic steatosis. BPA induces hepatic steatosis by promoting gut microbiota dysbiosis and activating the gut-liver axis. In this study, male CD-1 mice were fed with diet containing BPA (50 μg/kg body weight/day) for 13 weeks. Dietary exposure to BPA increased lipid contents and fat accumulation in the liver. Analysis of 16 S rRNA gene sequencing revealed that the diversity of gut microbiota reduced and the composition of gut microbiota was altered by BPA fed mice. Further, the abundance of Proteobacteria, a marker of dysbiosis, increased, whereas the abundance of Bacteroidetes, a gut microbe associated with homeostasis, was reduced. Moreover, BPA-induced inflammation, markedly decreased. Expression levels of intestinal tight junction proteins (zona occludens 1 and occludin) also decreased drastically, leading to increased intestinal permeability and elevated levels of endotoxin. Furthermore, BPA up-regulated the expression of Toll-like receptor 4 (TLR4), the activation of which initiates the phosphorylation of nuclear factor kappa B (NF-κ B) in the liver and increased the production of inflammatory cytokines, including interleukin-1 β, interleukin-1 β, tumour necrosis factor- α, and interleukin-6. These findings in our work indicated that dietary intake of BPA induced hepatic steatosis, and this was closely related to dysbiosis of gut microbiota, elevated endotoxin levels, and increased liver inflammation through the TLR4/NF- κ B pathway.	Environ Pollut Vol.265 Issue Pt A Pages 114880	10.1016/j.envpol.2020.114880	32540565	動物	-	1	1	1	1	0	50 μg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1326	K. M. Faighar, D. Nasan and O. M. Kurnasch	2024	Gestational bisphenol A exposure alters energy homeostasis and adult hypothalamic neurogenesis in female mice	Regulation of physiological homeostasis, including energy balance, is thought to be modified by low levels of adult neurogenesis in the hypothalamus. Hormones such as oestradiol can influence both embryonic and adult hypothalamic neurogenic programmes, demonstrating a sensitivity of hypothalamic neural progenitor cells to endogenous hormones. Previously we showed that gestational exposure to environmental levels of the oestrogenic bisphenol A (BPA) changed neural progenitor cell behaviours in the embryo; however, we did not examine if these changes were permanent to affect adult neurogenesis. Here we investigated whether adult mice and/or progenies were altered in mice prenatally exposed to BPA and placed on a high-fat diet challenge. Gestationally exposed adult female mice on a standard diet gained less weight than non-BPA controls, but this was not observed in males or mice on a high-fat diet. Gestational BPA exposure did not affect the survival of adult-born cells in the hypothalamic arcuate nucleus (ARC). However, the number of neurogenesis was increased in the ARC, DMH, and PVH of adult female mice exposed to BPA or oestradiol-17β, suggesting that disrupted adult neurogenesis might perturb normal energy balance regulation in females. These results add to growing evidence that low-dose BPA exposure in utero causes changes to adult hypothalamic function.	Sci Rep Vol.14 Issue 1 Pages 16082	10.1038/s41598-024-66726-2	38992091	動物	-	1	1	1	1	0	50 μg/kg BPA (経口投与)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1327	R. Feng, S. Yang, X. Gu, C. Li, N. Bi and H. L. Wang	2022	Early-life exposure to bisphenol A induces dysregulation of lipid homeostasis by the upregulation of SCD1 in male mice	Exposure of Bisphenol A (BPA) is closely associated with an increased prevalence of obesity-related metabolic syndrome. However, the potential mechanism of BPA-induced adipogenesis remains to be fully elucidated. Herein, potential mechanisms of BPA-induced adipogenesis in 3T3-L1 preadipocytes were evaluated using RNA-Seq. Then, using an early-life BPA exposure model, we further evaluated the effects of BPA exposure on lipid and glucose homeostasis. The results showed that treatment of 3T3-L1 adipocytes was associated with 1,154 differentially expressed genes (DEGs). Of these DEGs, 1,154 were up-regulated and 1,154 were down-regulated. Pathway analysis revealed that BPA-induced adipogenesis was closely associated with the activation of the PPAR signaling pathway. Moreover, the expression of stearoyl-coenzyme A desaturase 1 (SCD1) was significantly increased in 3T3-L1 adipocytes exposed to BPA. Knockdown of SCD1 significantly decreased the BPA-induced lipid accumulation in 3T3-L1 adipocytes. Additionally, the expression of SCD1 was significantly increased in the liver of male mice exposed to BPA. Besides, the dysregulation of pro-inflammatory genes, TNF-α, IL-6 and CCR2 showed that BPA exposure promoted progression of hepatic inflammation. In conclusion, this study elucidated a novel mechanism in which obesity-associated with BPA exposure by targeting SCD1. Exposure to BPA should be carefully examined in the chronic liver metabolic diseases.	Environ Pollut. 2022 Jul 1:304:119201.	10.1016/j.envpol.2022.119201	35341816	動物、in vitro	-	1	1	1	1	0	500 μg/kg/日	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1328	S. Fallahmehdi, F. Ghorbani-Tahandeki, A. Sahebkar, A. Nadim, M. Kalhorizadeh, M. Kalashzadeh and M. Gorji-Valokola	2023	Potential neuroprotective effect of nanomicellar curcumin on learning and memory functions following subacute exposure to bisphenol A in adult male rats	Bisphenol A (BPA) is an endocrine-disrupting chemical commonly utilized in the manufacture of plastics, which may cause damage to brain tissue. Curcumin is a phytochemical with protective effects against neurological disorders. This study aimed to investigate the possible protective role of nanomicellar curcumin (NMC) against BPA-induced learning and memory impairments in male rats. Forty-eight male Wistar rats were randomly divided into 8 groups (6 rats in each group) receiving vehicle (1% DMSO), 1a, vehicle of NMC+Cur (5mL/kg/day), 1b, vehicle of NMC+Cur (5mL/kg/day), 2a, vehicle of BPA (50 mg/kg/day), 2b, vehicle of BPA (50 mg/kg/day)+Cur (5 mg/kg), 2c, vehicle of BPA (50 mg/kg/day)+Cur (10 mg/kg), and 2d, vehicle of BPA (50 mg/kg/day)+Cur (20 mg/kg) groups, respectively. Behavioral tests performed using passive avoidance training (PAT), open field (OF), and Morris water maze (MWM) tests. The expression of oxidative stress markers, proinflammatory cytokines, cellular stress responding enzymes, glutamate receptors, and BDNF/TrkB and memory-related proteins was measured in rat hippocampal tissue. BPA up-regulated ROS, MDA, TNF-α, IL-6, IL-1β, iNOS, GSK3, and p-TRB, and p-JNK levels; however, it down-regulated GSH, GPx, SIR, CAT, and T-, p-ERK1/2, p-NR2, p-NR2A, p-NR2B, p-GluA1, p-CREB, and BDNF levels. BPA decreased the discrimination index in the PAT and increased the escape latency in the MWM test. Co-administration of NMC and BPA significantly improved the memory impairment induced by BPA, but decreased the time spent in the target quadrant. The combination of BPA (50 mg/kg) and NMC+Cur (10 and 20 mg/kg) reversed all of BPA's adverse effects. Therefore, NMC+Cur exhibited neuroprotective effects against subacute BPA-caused learning and memory impairment.	Metab Brain Dis Vol.38 Issue 8 Pages 2691-2720	10.1007/s11011-023-01257-9	37843661	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1329	A. Fahrenkopf and C. K. Wagner	2020	Bisphenol A (BPA) induces progesterone receptor expression in an estrogen receptor α-dependent manner in perinatal brain	Bisphenol A (BPA) is a xenoestrogen that is prevalent in the environment of industrialized nations due its use in the production of many plastic household items. Virtually all adults in the U.S. have detectable levels of BPA in urine and it can be measured in fetal serum and in breastmilk, making developmental exposure a particular concern. The present study utilizes a progesterone receptor (PR) expression bioassay to assess the estrogenic activity of BPA in the developing brain. Pregnant Sprague Dawley rats were dosed orally with 0, 10, 50 μg/kg/d BPA from GD 15 to PND 1. Female offspring were sacrificed on PND 1 and PR immunoreactivity (PR-ir) in the medial preoptic nucleus (MPN) of females (Fuering, 1974) was measured. Increased MPN-ir in perinatal BPA is highly dependent on the activation of ERα, but not ERβ, via estrogenic, natural, hormones. While 10 μg/kg/d is nanomolar, here I provided that 2-5 (PO-2) significantly increased PR expression in the MPN of postnatal day 5 females compared to the MPN of females administered the oil vehicle. However, pretreatment with the ER antagonists, ICI 182,780 from PO-5 significantly attenuated the effects of BPA on PR expression, indicating an ERα dependent mechanism. The present results also demonstrate a non-monotonic effect of BPA on the direct expression of a transcription factor in developing brain.	Neurotoxicol Teratol Vol.78 Pages 106864	10.1016/j.ntt.2020.106864	31926947	動物	-	1	1	1	1	0	10、50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1330	N. M. Faheem, A. El Askary and A. F. Gharib	2021	Lycopene attenuates bisphenol A-induced lung injury in adult albino rats: a histological and biochemical study	Bisphenol A (BPA) leads to ROS production that considered the core of different inflammatory and chronic obstructive pulmonary diseases. As a natural antioxidant, lycopene plays a significant role in the prevention of many chronic diseases. This study aimed to investigate the possible protective role of lycopene against BPA-induced lung alterations using morphometric, histological, immunohistochemical and biochemical methods. Forty-eight adult male albino rats were divided into four groups (12 rats/group): group I (control) received 1 ml/kg/day corn oil by oral gavage, group II (lycopene) received lycopene (10 mg/kg/day) by oral gavage, group III (BPA) received BPA (50 mg/kg/day) by oral gavage, and group IV (BPA + lycopene) received BPA and lycopene in the same dose and route mentioned in groups II and III. All treatments were continued for 30 days and lycopene + BPA group, Ovcher BAH-Ang, blood and lung tissue samples were collected for biochemical, histological and immunohistochemical studies. Morphometrical and statistical analyses were performed. The BPA group revealed significantly elevated IL-1β, IL-6, MDA and NO, and it showed significantly reduced IL-10, SOD, CAT and GSH when compared to the control and lycopene + BPA groups. Histopathological and immunohistochemical examinations revealed that BPA induced severe alterations in the lung tissue in the form of congestion, cellular infiltration, lymphocytic infiltration, emphysema and fibrosis. The lycopene + BPA group showed significantly reduced mean percentage of H-SCAM3 immunoreaction and mean area percentage of Bax and caspase-3 immunoreaction with and significantly reduced mean area percentage of Bcl2 immunoreaction cells as compared with the BPA group. Lycopene is a protective agent against BPA-induced lung injury because of its anti-apoptotic, anti-inflammatory and antioxidant effects, as confirmed by biochemical and histological studies.	Environ Sci Pollut Res Int Vol.28 Issue 35 Pages 49139-49152	10.1007/s11356-021-14140-w	33932206	動物	-	1	1	1	不明	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1331	M. Fadishei, M. Ghasemzadeh Rahbardar, M. Imenshahidi, A. Mohajeri, B. M. Razavi and H. Hosseinzadeh	2021	Effects of Nigella sativa oil and thymoquinone against bisphenol A-induced metabolic disorder in rats	The underlying mechanisms of bisphenol A (BPA)-induced metabolic disorder and the protective impact of Nigella sativa oil (NSO) and thymoquinone (TQ) against BPA-induced metabolic disorder were investigated. Rats were treated as follows (Control, BPA (10 mg/kg), TQ (3 mg/kg), NSO (0.4 g/kg), BPA + TQ (10, 1, 3 mg/kg), and BPA + NSO (0.1, 0.2, 0.4 g/kg). BPA was administered by gavage for 4 weeks, TQ and NSO were injected intraperitoneally (daily, 30 days). The weight, blood pressure, serum parameters (glucose, lipid profile, hepatic enzymes, insulin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) levels, adiponectin), histopathological changes of liver and kidney, and hepatic oxidative stress were evaluated. BPA significantly increased the weight of liver, kidney, and abdominal fat, and induced hepatic steatosis. BPA also increased the blood pressure, MDA, lipid profile, hepatic enzymes, insulin, IL-6, TNF-α, and leptin, and decreased the GSH and phosphorylated forms of IRS. NSO, but not TQ, significantly reduced the liver and kidney weight, plasma IRS, AKT, and GSK-3β in the liver. Administration of NSO or TQ with BPA reduced the blood pressure, liver level of MDA, lipid profile, hepatic enzymes, insulin, IL-6, TNF-α, leptin, and increased the liver level of GSH and p-IRS, p-AKT, p-GSK. TQ and NSO are thought to be effective in controlling metabolic disorders induced by BPA.	Phytother Res Vol.35 Issue 4 Pages 2005-2024	10.1002/ptr.6944	33315269	動物	-	1	1	1	不明	0	10 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1332	C. H. Facine, S. G. P. Campos, T. F. R. Ruiz, R. M. Góes, P. S. L. Vilamaior and S. R. Taboga	2021	Protective effect of the association of curcumin with piperine on prostatic lesions: New perspectives on BPA-induced carcinogenesis	Bisphenol A (BPA) is a chemical agent which can exert detrimental effects on the male reproductive system, especially the prostate gland. In this study we described the efficacy of the dietary agent curcumin, alone or combined with piperine, to suppress the impact of BPA on the prostate. Adult gerbils were divided into nine experimental groups: (n = 7 each group), regarding control (water and oil), exposed to BPA (50 μg/kg/day in drinking water), curcumin (200 mg/kg/day), piperine (20 mg/kg/day), curcumin + piperine, BPA + curcumin, BPA + piperine, and BPA + curcumin + piperine, for 60 days. Ventral prostate was analyzed by histological, immunohistochemical, and ultrastructural methods. Curcumin + piperine (BPA-free) promoted prostatic inflammation and morphological lesions in normal and deoxycorticosterone pivalate-treated rats, associated with an increase in androgen receptor-positive cells and nuclear androgen receptor immunostaining in the stromal cells. Curcumin and piperine helped to minimize these effects. BPA plus piperine or curcumin stimulated a reduction in nuclear atypical phenotype, indicating a beneficial effect of phytochemicals. These three phytochemicals minimize the deleterious action of BPA in prostatic fibers, especially when administered in association. The protective action of curcumin and piperine consumption is associated with weight loss, anti-inflammatory potential, and control of prostate epithelial cell homeostasis.	Food Chem Toxicol Vol.158 Pages 112700	10.1016/j.fct.2021.112700	34838672	動物	-	1	1	1	不明	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1333	S. M. Eweda, A. S. A. Newairy, H. M. Abdou and A. S. Gaber	2020	Bisphenol A-induced oxidative damage in the hepatic and cardiac tissues of rats: The modulatory role of sesame lignans	Bisphenol A (BPA) is an environmental pollutant that is widely produced throughout the world. It is primarily used in the manufacture of polycarbonate plastics, epoxy resins, pastes and dental materials. BPA has been reported to worsen hepatotoxicity and cardiotoxicity. The antioxidant activity of sesame lignans is well established. The current study assessed the protective effects of sesame lignans against BPA-induced hepatotoxicity and cardiotoxicity. Rats were divided into 5 groups. A control group, a BPA-treated group, a sesame lignans -treated group and a sesame lignans and BPA-treated group. Rats were orally administered their respective doses daily (30 mg/kg body weight) BW) BPA and/or (6 mg/kg BW) sesame lignans) for 6 weeks. Liver function tests were performed using serum of all groups. Lipid profile and antioxidant status were also measured in liver tissue of the studied groups. The results were confirmed by histopathological examination of liver and heart tissues. The oral administration of BPA was revealed to elicit significant decreases in the body weight gain, serum albumin, total protein, high-density lipoprotein-cholesterol (HDL-C), hepatic glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) activities, glutathione-S-transferase (GST) accumulation, elevated activities of alanine aminotransferase, creatine kinase MB and lactate dehydrogenase, and histological changes of liver and heart tissues. However, the co-administration of sesame lignans with BPA attenuated hepatotoxicity, cardiotoxicity and BPA-induced histological changes. The results of the current study indicated that sesame lignans may be helpful in the development of novel natural drugs to treat hepatic and cardiovascular disorders.	Exp Ther Med Vol.19 Issue 1 Pages 33-44	10.3892/etm.2019.8193	31853270	動物	-	1	1	1	1	0	30 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1334	L. O. Esuola, O. O. Esan, A. S. Makinti, T. O. Ajibola, M. O. Adetuna, O. O. Aina, A. A. Oyagbemi, T. O. Omobowale, O. A. Oladele, E. Nwulia, M. A. Yakubu and O. O. Ogunti	2025	Therapeutic Effects of Naringin on Bisphenol A-Induced Oxidative Stress Damage in Nervous and Reproductive Systems of Cockerel Chickens	BACKGROUND: Bisphenol A (BPA) is an endocrine disrupting chemical, and it is mostly used in plastic industries. Naringin is a potent flavonoid that has been reported to possess several beneficial pharmacological properties such as antioxidant, anti-inflammatory, and antiapoptotic properties. OBJECTIVE: The aim of this study was to determine the protective effect of naringin against the damage induced by BPA in the brain and reproductive tissues of cockerels. METHODS: Twenty-four cockerels were randomly assigned into four groups of six birds each. Group 1 (control) was given feed and water only, group 2 (BPA) was given BPA at 100 mg/kg body weight (BW), group 3 (BPA and 100 mg/kg naringin) received 100 mg/kg BPA and/or 50 mg/kg BW naringin, and group 4 (200 mg/kg naringin treated) received 200 mg/kg naringin treated. BPA was administered via drinking water, while naringin was administered via oral gavage. Analyses, such as biochemical assays, hormonal assays, histopathology, and immunohistochemistry were done. RESULTS: The results showed a decrease in the level of LH, FSH, testosterone, and progesterone in the BPA-intoxicated group. Also, BPA induced a significant increase in the level of malondialdehyde (MDA) and nitric oxide (NO) in the brain and testes. Moreover, BPA-intoxicated cockerels had a significant decrease in the activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Furthermore, BPA induced a significant increase in the activities of acetylcholinesterase (AChE), monoamine oxidase (MAO), and butyrylcholinesterase (BuChE). Immunohistochemical evaluation revealed low expression of nephrilysin protein in the brain and increased expression of caspase-3 in the testes of the BPA-intoxicated group. CONCLUSIONS: Naringin reversed the neurotoxicity and reproductive toxicity of BPA by normalizing the values of the altered parameters. Hence, naringin ameliorated the deleterious effects caused by BPA in both the brain and testes by enhancing the antioxidant defense mechanism.	Vet Med Sci Vol.11 Issue 4 Pages e70322	10.1002/vms3.70322	40548488	動物	-	0	1	1	不明	0	100 ppm (飲水中濃度)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1335	A. E. Essawy, H. A. E. Abd Elhader, G. A. Khamiss, S. M. Eweda and H. M. Abdou	2023	Therapeutic effects of astragaloside IV and Astragalus spinosus saponins against bisphenol A-induced neurotoxicity and DNA damage in rats	BACKGROUND: Bisphenol A (BPA) is an endocrine disruptor to which humans are often subjected during daily life. This study aimed to investigate the ameliorative effect of astragaloside IV (AST) or saponins extracted from Astragalus spinosus (ASS) against BPA-induced neurotoxicity and DNA damage in rats. METHODS: Twenty-four male albino rats were randomly divided into four groups (six/group). Group I (control) received 1 ml/kg/day corn oil by oral gavage. Group II (BPA) received BPA (50 mg/kg/day). Group III (AST) and group IV (ASS) received BPA + A. spinosus saponins (ASS) (50 mg/kg/day) and BPA + AST (20 mg/kg/day) (oral gavage, age of 28 days) male Sprague Dawley rats were randomly and equally divided into four groups: control, BPA, BPA+ASS and BPA+A. spinosus saponins groups. Bisphenol A (BPA) (50 mg/kg/day) was administered orally to male rats from day 28 (BPA group) and along with ASS (50 mg/kg/day) (BPA+ASS group) or A. spinosus saponin (ASS) (50 mg/kg/day) (BPA+ A. spinosus saponins group) from day 28 to adult age (day 117 (W16.7)). Increased level of nitric oxide (NO) and decreased level of glutamine (Gln), glutamine (Glu), glutaminase (GLS) and glutamine synthetase (GS) were observed in the brain regions of BPA-treated rats compared with the control. On the other hand, co-administration of ASS or A. spinosus saponins with BPA considerably improved levels of these neurochemicals. The current study also revealed the ameliorative effect of ASS or A. spinosus saponins against BPA-induced DNA damage in the brain, testes, and liver tissues. RESULTS: Co-administration of ASS or A. spinosus saponins with BPA to rats for 4 weeks significantly reduced the values of comet parameters as well as the intensity of estrogen receptors (ERs) immunoreactive cells and improved the histological alterations induced by BPA in different brain regions. CONCLUSION: It could be concluded that ASS or A. spinosus saponins has a promising role in modulating the neurotoxicity and DNA damage elicited by BPA.	Pearl Vol.9 Pages a11930	10.7717/peerj.11930	34434659	動物	-	1	1	1	1	0	125 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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生殖性評価（動物）1：該当、0：該当しない　生殖性評価（疫学）1：該当、0：該当しない　生殖性評価（in vitro）1：該当、0：該当しない　生殖性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに生殖性基準不適合と判断されるものは作成段階で除外。当該性評価段階で原則として基づき除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1349	B. E. Ekgiatar, E. Adiwu and Z. N. Igwoe	2022	Glutamine Supplementation Attenuates Bisphenol A-Induced Testicular Toxicity in Rats	BACKGROUND: The induction of testicular toxicity by bisphenol A (BPA) may involve oxidative stress. Glutamine (Gln) is a rate limiter for the synthesis of glutathione (GSH), which inhibits oxidative stress. AIM: This study examined the potential of BPA to promote testicular structure and function in BPA-treated albino rats. STUDY DESIGN AND DESIGN: Thirty-two adult male albino rats (150-250 g) were randomly allocated to 8 (4-5) of 8 rats per group with the approval of the Research Ethics Committee. MATERIALS AND METHODS: Groups B–D were orally treated with Gln (28 mg/kg body weight). BPA (50 mg/kg body weight) and Gln (28 mg/kg body weight) + BPA (50 mg/kg body weight) were administered to groups C and D, respectively, for 28 days. Group A served as the control. On day 29, the rats were euthanized, and the testes were harvested and fixed in formalin, some underwent routine histological processing, and sections were collected and evaluated for graded hormones. The testes were weighed and evaluated for sperm parameters, oxidative stress markers and histology. STATISTICAL ANALYSIS: The data were analyzed using one-way analysis of variance and Bonferroni post hoc test. RESULTS: BPA caused a significant (P < 0.001) decrease in testis and body weights, sperm count, volume, motility and normal morphology when compared to the control. BPA significantly (P < 0.05) decreased serum testosterone, follicle-stimulating hormone, luteinizing hormone, testicular catalase, superoxide dismutase, GSH and GSH-peroxidase levels relative to control. Significantly (P < 0.001) increased serum prolactin, estradiol and testicular malondialdehyde levels occurred in BPA-treated rats relative to control. The toxins of BPA-treated rats showed sloughing and vacuolization of germ cells. However, Gln supplementation prevents BPA-induced testicular toxicity. Gln supplementation restored testis histology. CONCLUSION: Based on the observations in this study, Gln exerts effective against BPA-induced testicular toxicity.	J Hum Reprod Sci Vol.15 Issue 4 Pages 337-342	10.4103/jhrs.jhrs_54_22	37033138	動物	-	1	1	1	1	0	50 mg/kg 体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1350	C. Duman, N. Özkan Yenal and A. Mertaş	2022	How prenatal environmental factors affect rat molar enamel formation?	Amelogenin (AMELX) and ameloblastin (AMBN) are crucial for enamel formation, and interruptions in the production of these proteins may cause enamel defects. We investigated how prenatal environmental factors affect rat molar enamel formation. Pregnant Wistar albino rats were divided into four groups. Group I received no treatment, Group II received intraperitoneal (IP) lipopolysaccharide (LPS) (Escherichia coli O111:B4) on gestational day (GD) 9.5, Group III received oral bisphenol A (BPA) (50 mg/kg/day) from GD 6 until delivery, and Group IV received both LPS and BPA. Offspring were euthanized at 4 µg/kg BPA) daily from day GD 6 until delivery. LPS infection group rats were injected 125 µg/kg bacterial LPS once on day GD. Seven pups from the control group and ten pups from the experimental groups were euthanized on P10. Sections were stained with hematoxylin-eosin (H-E) and Gomori's one-step chrome staining (GT) and incubated with rabbit polyclonal antibodies to AMELX and AMBN to evaluate staining intensity at ameloblast stages. The surface morphology was evaluated in the stereomicroscope. ANOVA ($p = 0.008$, $p = 0.045$) and ANOVA ($p = 0.002$, $p = 0.001$, $p = 0.0001$) staining of all experimental groups. Yellowish coloration of the enamel/the group was observed in morphologic evaluation.	Odontology Vol.110 Issue 4 Pages 655-663	10.1007/s10266-022-00699-4	35262822	動物	-	1	1	1	1	0	5 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1351	M. Duan, Y. Wang, S. Chen, J. Lu, R. Dong, Q. Yu, J. Xia and Y. Chen	2025	Combined BPA and DIBP Exposure Induced Intestinal Mucosal Barrier Impairment Through the Notch Pathway and Gut Microbiota Dysbiosis in Mice	Bisphenol A (BPA) and diisobutyl (DIBP) phthalates are widely used as typical plasticizers in food packaging. Plasticizers can be released from containers, migrate into food, and be ingested by humans, leading to various health problems. However, little research has investigated the combined toxicity of BPA and DIBP, particularly their intestinal toxicity. Our goal is to analyze the combined toxicity of BPA (50 mg/kg) and DIBP (500 mg/kg) on the intestines of ICR mice. Additionally, we tried to find natural products that can inhibit or prevent the combined toxicity of BPA and DIBP. The results indicated that the combination of BPA and DIBP exposure results in a reduction of beneficial flora, an increase in IL-1 α levels (139.1 ± 12 μ mol/L), and a decrease in interleukin-4 levels (46.75 ± 5.5 μ mol/L). Furthermore, the Notch pathway was activated in the BD group compared to single-exposure sources. Nevertheless, Rubus chingii Hu pheno(Rc extract (RHPE) (150, 300, and 600 mg/kg) ameliorated the BPA and DIBP-induced intestinal microbiome disruption and intestinal mucosal barrier impairment by inhibiting the overactivation of the Notch pathway. The results of this study highlight the potential risks to human health posed by the combination of BPA and DIBP and may help explore the potential pathways of enterotoxicity caused by combined ingestion.	Foods Vol.14 Issue 2	10.3390/foods14020214	39856883	動物	-	1	1	1	KM	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1352	C. M. Dziewiecki, A. S. Birkric, E. P. Sellinger, A. D. Doshi, J. Y. Koh and J. M. Juraska	2023	Brief postnatal exposure to bisphenol A affects apoptosis and gene expression in the medial prefrontal cortex and social behavior in rats with sex specificity	Bisphenol A (BPA) is an endocrine disruptor found in polycarbonate plastics and exposure in humans is nearly ubiquitous and it has widespread effects on cognitive, emotional, and reproductive behaviors in both human and animal models. In our laboratory we previously found that perinatal BPA exposure results in a higher number of neurons in the adult medial prefrontal cortex (mPFC) and testes play in adolescents of both sexes. Here we examine changes in the rate of postnatal apoptosis in the rat prefrontal cortex and its timing with brief BPA exposure. Because an increased number of neurons in the mPFC is a characteristic of a subtype of autism spectrum disorder, we tested social preference following brief BPA exposure and also expression of a small group of genes. Males and females were exposed to BPA from postnatal days (P) 4 through 8 or from P10 through 14 by oral gavage. Apoptosis was measured in the mPFC at P5 and P15 using activated caspase-3 immunohistochemistry. At P21 or P22, social preference was tested in a three-chamber apparatus. Juvenile preference and decreased social exposure of Sprague Dawley and Fischer 1, two synaptic scaffolding genes that have been implicated in social deficits. There were no significant effects of BPA in the female subjects. These results draw attention to the negative consequences following brief exposure to BPA during early development.	Neurotoxicology Vol.94 Pages 126-134	10.1016/j.neuro.2022.11.011	36442689	動物	-	1	1	1	1	0	40, 400 µg BPA/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1353	J. F. Dou, M. Puttabyatappa, V. Padmanabhan and K. M. Bakulski	2020	Developmental programming: Transcriptional regulation of visceral and subcutaneous adipose by prenatal bisphenol-A in female sheep	BACKGROUND: Bisphenol-A (BPA) exposure is widespread and early life exposure is associated with metabolic syndrome. White visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) are implicated in the development of metabolic syndrome. We adipose depot-specific effects of prenatal BPA treatment are poorly understood. OBJECTIVE: To determine the impact of prenatal BPA exposure on genome-wide gene expression in VAT and SAT. We hypothesized that prenatal BPA exposure would alter the transcriptome in VAT and SAT, and that the effects would be different between VAT and SAT. Development and immune response pathways were upregulated in VAT, while metabolic pathways were upregulated in SAT. These adipose depot-specific genes and pathways were consistent with prenatal BPA treatment in SAT. BPA treatment resulted in differential expression of 108 genes (TEK upregulated and BPIFB1 and altered pathways (immune response downregulated). BPA processing upregulated). In contrast to VAT, BPA treatment differentially expressed 3 genes and upregulated chromatin and RNA processing pathways. CONCLUSION: Prenatal BPA treatment induces adult depot-specific alterations in RNA metabolism in the mitochondria, RNA processing, and chromatin structure, reflecting the diverse roles of VAT and SAT in regulating lipid storage and insulin sensitivity. These adipose tissue transcriptional dysregulations may contribute to the metabolic disorders observed in prenatal BPA-treated female sheep.	Chemosphere Vol.255 Pages 127000	10.1016/j.chemosphere.2020.127000	32417515	動物	-	1	0	1	不明	0	0.5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1354	J. Dou, S. V. Thangaraj, M. Puttabyatappa, V. R. Elangovan, K. Bakulski and V. Padmanabhan	2021	Developmental programming: Adipose depot-specific regulation of non-coding RNAs and their relation to coding RNA expression in prenatal testosterone and prenatal bisphenol-A -treated female sheep	Inappropriate developmental exposure to steroids is linked to metabolic disorders. Prenatal testosterone excess or bisphenol A (BPA, an environmental estrogen-mimic) leads to insulin resistance and adipocyte disruptions in female lambs. Adipocytes are key regulators of insulin sensitivity. Metabolic tissue-specific differences in insulin sensitivity coupled with adipose depot-specific changes in key mRNAs, were previously reported. We hypothesized that prenatal testosterone and BPA treatment would alter adipose depot-specific non-coding RNA (ncRNA) expression and their relation to coding RNA (mRNA). mRNA, ncRNA, and RNA-Seq was performed on visceral (VAT) and subcutaneous (SAT) adipose depots of prenatal testosterone and BPA treated animals were sequenced. Adipose depot-specific changes in the mRNA that are consistent with the depot-specific mRNA expression in terms of directionality of changes and functional implications in insulin resistance, adipocyte differentiation and cardiac hypertrophy were found. Importantly, the adipose depot-specific mRNA changes were model-specific and mutually exclusive, suggestive of different regulatory entry points in this regulation.	Mol Cell Endocrinol Vol.564 Pages 111868	10.1016/j.mce.2023.111868	36708980	動物	-	1	0	1	不明	0	0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1355	Y. Dong, Z. Zhang, H. Liu, L. Jia, M. Qin and X. Wang	2020	Exacerbating lupus nephritis following BPA exposure is associated with abnormal autophagy in MRL/lpr mice	For the development of Lupus nephritis, environmental factors are reasoned to be one of the risk factors. In recent years, the role of bisphenol A (BPA) in kidney injury has attracted wide attention. In this study, we investigated the effects of BPA exposure on the development of lupus nephritis in MRL/lpr mice. Female MRL/lpr mice were exposed to 0.2 µg/mL BPA in drinking water from 4 weeks of age. Urine protein, urine occult blood and pathological injury in MRL/lpr mice. BPA increased the expression of IFN-γ in serum and activated the inflammatory response in both MRL/lpr and C57 mice. Unlike C57 mice, BPA-treated rapidly activated autophagy associated proteins, but the autophagy signaling pathway lacked the regulation of Beclin1 and LC3 associated phagocytosis deficiency, and decreased Nrf2 protein expression to meet tissue of MRL/lpr mice. Therefore, exacerbating lupus nephritis induced by BPA exposure was associated with the activation of inflammation, abnormal autophagy and decreased antioxidant ability.	Am J Transl Res Vol.12 Issue 2 Pages 649-659		32194912	動物	-	1	1	1	MRL/lpr, C57/BL6	0	0.2, 0.2 µg/mL（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1356	Y. Dong, L. Gao, Q. Sun, L. Jia and D. Liu	2023	Increased levels of IL-17 and autoantibodies following Bisphenol A exposure were associated with activation of PI3K/AKT/mTOR pathway and abnormal autophagy in MRL/lpr mice	Bisphenol A (BPA) is a common environmental endocrine disruptor which mimic the effect of estrogen. The immunotoxicity of BPA has attracted widespread attention in recent years. However, the effects and mechanism of BPA on autoimmune disease were rarely reported. Systemic lupus erythematosus (SLE) is a typical autoimmune disease, and its etiology and mechanism are complex and unclear. Currently, inflammation and the abnormal autophagy are considered to be the important pathogenesis of SLE. In this study, we investigated the effects of BPA exposure on the development of SLE in MRL/lpr mice. Female MRL/lpr mice were exposed to 0.2 µg/mL BPA in drinking water from 4 weeks of age. Urine protein, urine occult blood and pathological injury in MRL/lpr mice. We found that BPA exposure increased the concentration of serum anti-dsDNA antibody and IL-17, and the level of ROR γ t protein (the transcription factor of Th17 cells). Moreover, there were higher expression of p-PI3K, p-AKT, p-mTOR, ULK1, Rubicon, PI3KC3, Beclin1, LC3 and lower expression of P62 in MRL/lpr mice compared with the control. However, there were no significant changes in the expression of IL-17, RORγt or mTOR in C57 mice exposed to BPA for the same dose. Our study implied that BPA exposure induced the overactivation of SLE, which might be related to the up-regulation of PI3K-AKT-mTOR signaling pathway and abnormal autophagy. Our study indicated that lupus mice were more susceptible to BPA, and provided a new insight into the mechanism by which BPA exacerbated SLE. Therefore, our study suggested that autoimmune patients and susceptible population should be considered when setting thresholds for environmental BPA exposure.	Ecotoxicol Environ Saf Vol.255 Pages 114788	10.1016/j.ecoenv.2023.114788	36948005	動物	-	1	1	1	MRL/lpr, C57/BL6	0	0.2, 0.2 µg/mL（飲水中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1357	W. Dong, J. Hu, J. Wang, W. Sun, Y. Sun and J. Yu	2022	Bisphenol A exposure advances puberty onset by changing Kiss1 expression firstly in arcuate nucleus at juvenile period in female rats	Bisphenol A (BPA) is ubiquitous. In the environment and its adverse effects on precocious puberty have been reported. But its mechanism is not clear. In the present study, the potential effects of BPA on endocrine functions of hypothalamus, especially in the arcuate (ARC) nucleus, and environmental pertinent dose (50 mg/kg/day) of BPA on female rats were studied from postnatal day (P) PND21 to PND35 in female Sprague Dawley (SD) rats. Normally rats were exposed to 0.5 mg/kg/day (1/day) (1 BPA in corn oil vehicle from PND21 to PND35 via intramuscular injection. From PND35 to PND 39, BPA caused enrichment of H3K9me2 and H3K9me3 at Kiss1 promoter, consistent with elevated gene expression of Kiss1 and ERα's (ERα and Kiss1) increased even 72 hours in BPA groups from PND35. Until PND39, BPA induced obviously overexpression of Kiss1 and ERα(ARC) in BPA nuclies. Subsequently, the vagina opening and first ovulation had occurred earlier in rats with BPA exposure in respect to vehicle by PND35. In this study, it is suggested that the effects of BPA on precocious puberty may be due to its actions to activate Kiss1 gene in ARC during the juvenile period from PND21 to PND35 firstly, subsequently to make the ERα recess, resulting in precocious puberty in the rest.	Reprod Toxicol Vol.110 Pages 141-149	10.1016/j.reprotox.2022.04.005	35429613	動物	-	1	0	1	0	0	0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1358	A. H. Dikmeci, İ. Karabağ, S. Gizel, Z. F. Erbağ a and A. Yılmaz	2022	Toxicological assessment of low-dose bisphenol A, lead and endosulfan combination: chronic toxicity study in male rats	In the present study, toxic effects, both alone and combined, of bisphenol A (BPA), lead (Pb) and endosulfan (ED) in the low doses were investigated in rat liver and kidney functions. In the study, bisphenol A (BPA), lead (Pb) and endosulfan (ED) were chosen because although they are the chemicals that are most frequently exposed to, as combined toxic effect studies were unknown in these chemicals. Sixty four male Wistar albino rats were used in the study, and they were randomly divided into eight groups (n = 8 per group); control, BPA (5 mg/kg), Pb (100 ppm), ED (0.01 mg/kg), BPA+Pb, BPA+ED, Pb+ED and BPA+Pb+ED. The rats were exposed to BPA, Pb and ED by oral gavage for 90 days. Biochemical analyses of liver and kidney tissues, and histopathological examinations of liver and kidney tissues were performed. Biochemical results revealed that the treatment with the BPA+Pb+ED in the low doses induced severe liver and kidney damage. Moreover, when combined groups, it was found that the toxic effects of BPA, Pb and ED were increased in the liver and kidney tissues. The results of the present study suggested that the BPA, Pb and ED caused more dramatic changes in both histological architecture and cell apoptosis in the liver and kidney tissues when there was a combined exposure.	Environ Sci Pollut Res Int Vol.29 Issue 7 Pages 10558-10574	10.1007/s11356-021-16407-8	34523106	動物	-	1	不明	1	1	0	5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1359	D. Dixit, A. Roy, A. Shukla, P. Sharma and M. Mandal	2024	The Effects of Short- and Long-Term Ingestion of Plastic Toxin Bisphenol A on Gastrointestinal Transit Time in Rats	Introduction Exposure to bisphenol A (BPA), a toxic chemical released from plastic, affects various body functions, including reproduction, metabolism, and development. The most common route of exposure to BPA is oral, and the gastrointestinal (GI) tract is, therefore, the first body system to be exposed to BPA. BPA has been well documented to impair gut contractility in vitro, in vivo, it may therefore be hypothesized that BPA may adversely affect GI motility and hence also deter the movement of food, resulting in the increased transit of food bolus. In the GI tract. There are no reports so far on the effects of BPA on GI transit time. Objectives The present study was designed to investigate the effects of short- and long-term ingestion of BPA on GI transit time in rats. Methods Male albino rats were randomly divided into three groups (n = 6 each) and received vehicle (1% Tween 80), BPA (5 mg/kg), or BPA (50 mg/kg) orally for 7 days and 28 days, respectively. At the end of each time point, rats were fasted overnight and administered a charcoal meal (5% charcoal suspension in 10% gum acacia) at a dose of 10 mL/kg orally. Thirty minutes later, rats were euthanized, and the distance traveled by the charcoal meal was measured. The results were analyzed using one-way ANOVA followed by Dunnett's post hoc test. Results Short-term ingestion of BPA (5 mg/kg) did not affect GI transit time, whereas long-term ingestion of BPA (50 mg/kg) significantly ($p < 0.05$) increased GI transit time by 20% compared to the vehicle-treated group. Conclusion Both short- and long-term ingestion of BPA at the doses used in this study did not affect GI transit time in rats. Considering the fact that BPA is a ubiquitous chemical, the present study has important implications for human health. Since short-term and long-term (28 days) oral exposure to BPA containing food harmed GI transit, Since GI transit may lead to metabolic disorders, such as constipation.	Curious Vol.16 Issue 2 Pages e53694	10.7759/cureus.53694	38455775	動物	-	1	1	1	1	0	2、50 µg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1360	R. K. Dirkes, R. J. Welty, J. Mao, J. Kinkade, V. J. Vieira-Potter, C. S. Rosenfeld and P. S. Bivona	2021	Gestational and lactational exposure to BPA, but not BPS, negatively impacts trabecular microarchitecture and cortical geometry in adult male offspring	Bisphenol A (BPA) and bisphenol S (BPS) are endocrine disrupting chemicals (EDCs) found primarily in plastics. Estrogen is a primary hormonal regulator of skeletal growth and development; however, the impact of gestational BPS or BPS exposure on skeletal health of offspring remains relatively unknown. Here, adult female mice were randomized into three treatment groups: 250 µg BPA/kg BW (BPA), 300 µg BPS/kg BW (BPS), or vehicle control (CON). Animals in each group were further randomized to exercise treatment (EX) or sedentary (SED) control, resulting in six overall groups. BPA, BPS or CON treatment was administered 5 days/week via oral gavage for 3 weeks prior to mating and continued through mating, gestation, and lactation. One female offspring from each dam ($n = 6$/group) was euthanized at 21 weeks of age to evaluate effects of EDC exposure on the adult skeleton. Cortical geometry of the mid-diaphysis and trabecular microarchitecture of the distal femur were assessed via micro-computed tomography. Biomechanical strength and mineral apposition rate of the femoral diaphysis were assessed via three-point bending and dynamic histomorphometry, respectively. Osteocalcin expression was measured using immunohistochemistry. Two-factor ANOVA or ANCOVA were used to determine the effects of maternal EX and BPA or BPS on trabecular and cortical bone outcomes. Maternal EX led to a significant decrease in body fat percentage and bone stiffness, independent of EDC exposure. Offspring exposed to BPA had significantly lower trabecular bone volume, trabecular number, connectivity density, cortical thickness, and greater trabecular spacing compared to BPS or CON animals. In conclusion, gestational BPA, but not BPS, exposure negatively impacted trabecular microarchitecture and cortical geometry in adult male offspring. If these findings translate to humans, this could have significant public health impacts on expecting women in those seeking to become pregnant.	Bone Rep Vol.15 Pages 101147	10.1016/j.bonr.2021.101147	34820485	動物	-	1	1	1	1	0	200 µg BPA/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1361	R. K. Dirkes, R. J. Welty, J. Mao, J. Kinkade, V. J. Vieira-Potter, C. S. Rosenfeld and P. S. Bivona	2021	Gestational and lactational exposure to BPA or BPS has minimal effects on skeletal outcomes in adult female mice	Bisphenol A (BPA) and bisphenol S (BPS) are estrogen-disrupting chemicals (EDCs) found in the environment and common household items. Estrogen is a primary hormonal regulator of bone growth and development; however, the impact of gestational BPS or BPS exposure on skeletal health of offspring remains relatively unknown. Here, adult female mice were randomized into three treatment groups: 250 µg BPA/kg BW (BPA), 300 µg BPS/kg BW (BPS), or vehicle control (CON). Animals in each group were further randomized to exercise treatment (EX) or sedentary (SED) control, resulting in six overall groups. BPA, BPS or CON treatment was initiated prior to mating and continued through mating, gestation, and lactation. One female offspring from each dam ($n = 6$/group) was euthanized at 21 weeks of age to evaluate effects of EDC exposure on the adult skeleton. Cortical geometry of the mid-diaphysis and trabecular microarchitecture of the distal femur were assessed via micro-computed tomography. Biomechanical strength and mineral apposition rate of the femoral diaphysis were assessed via three-point bending and dynamic histomorphometry, respectively. Osteocalcin expression was measured using immunohistochemistry. Two-factor ANOVA or ANCOVA were used to determine the effects of maternal EX and BPA or BPS on trabecular and cortical bone outcomes. Maternal EX led to a significant decrease in body fat percentage, independent of EDC exposure. Offspring exposed to BPA had significantly lower trabecular bone volume, trabecular number, connectivity density, cortical thickness, and greater trabecular spacing compared to BPS or CON animals. In conclusion, gestational BPA or BPS exposure at maternal exercise have minimal impact on skeletal outcomes in female adult offspring.	Bone Rep Vol.15 Pages 101136	10.1016/j.bonr.2021.101136	34632005	動物	-	1	1	1	1	0	200 µg BPA/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階で除外。当該物質評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物飼及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1362	V. Dirca, A. O. Docea, A. I. Dracea, T. K. Nikolaussakis, P. D. Sivanikolaiu, D. Nikolouz, K. S. Golokhvast, A. F. Hernandez, D. Calina and A. Tsatsakis	2023	A mixture of 13 pesticides, contaminants, and food additives below individual NOAELs produces histopathological and organ weight changes in rats	The current approach for the risk assessment of chemicals does not account for the complex human real-life exposure scenarios. Exposure to chemical mixtures is everyday life has raised scientific, regulatory, and societal concerns. In recent years. Several studies aiming to identify the safety limits of chemical mixtures determined hazardous levels lower than those of separate chemicals. Following these observations, this study aimed to investigate the effects of a mixture of 13 pesticides, contaminants, and food additives, at doses below their individual no-observed-adverse-effect-levels (NOAELs), namely, methyl parathion, aspartame, sodium benzoate, EDTA, ethylparaben, butylparaben, propylparaben, bisphenol A and acesulfame K in adult rats. Animals were divided into four dosing groups (GROUP1: Control; GROUP2:MIX1: One-third LOD; GROUP3: Medium dose-MD1 and GROUP4:MIX1: High dose-HD) 5mg/kg BW/day). After 14 months of exposure, all animals were sacrificed, and their organs were harvested, weighed, and pathologically examined. The results showed that the mixture induced significant changes in the relative weights of the liver, kidneys, and lungs in the MIX1 group. Moreover, the MIX1 group exhibited more severe exposure to the chemical mixture compared to the study, several histopathological changes in all examined organs. The main organs that contribute to chemical tolerance formation and clearance (liver, kidneys, and lungs) consistently presented histopathological changes following exposure to the chemical mixture. In conclusion, exposure to very low doses. Below the NOAELs of the tested mixture for 18 months induced histopathological lesions and systemic effects in a dose-and tissue-dependent manner.	Arch Toxicol Vol.97 Issue 5 Pages 1285-1298	10.1007/s00204-023-03455-x	36892595	動物	-	1	不明	0	1	1	–	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1363	G. Diamanto, I. Coly, Z. Zamos, J. Ding, M. Blencowe, J. Lang, A. Bline, M. Singh, A. I. Lucio and X. Yang	2021	Systems toxicogenomics of prenatal low-dose BPA exposure on liver metabolic pathways, gut microbiota, and metabolic health in mice	Bisphenol A (BPA) is an industrial plasticizer widely found in consumer products, and exposure to BPA during early development has been associated with the prevalence of various cardiometabolic diseases including obesity, metabolic syndrome, type 2 diabetes, and cardiovascular diseases. To elucidate the underlying mechanisms of BPA-induced adverse effects, we conducted a multi-dimensional systems biology study assessing the liver transcriptome, gut microbial community, and diverse metabolic phenotypes in both male and female mouse offspring exposed to 0, 4 μg/kg/day BPA (human tolerable daily intake), or 40 μg/kg/day BPA from mating through weaning. Our results revealed that BPA induced significant sex-dependent changes in the liver transcriptome in a dose- and sex-dependent manner. Bacteria such as those belonging to the S24-7 and Lachnospiraceae families were predominant and affected by BPA exposure. Interestingly, BPA significantly altered the composition in an age

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1375	J. Ciavelli, S. V. Thangaraj, H. Sur, S. Dumke, B. Akintaifo, A. K. Vyas, B. Gregg, R. M. Sargis and V. Padmanabhan	2024	Developmental programming: An exploratory analysis of pancreatic islet compromise in female sheep resulting from gestational BPA exposure	Developmental exposure to endocrine disrupters like bisphenol A (BPA) are implicated to later life metabolic dysfunction. Leveraging a unique sheep model of developmental programming, we conducted an exploratory analysis of pancreatic islets from 6 month old female offspring exposed to BPA during gestation days 30-90 (term ~147 days). Pregnant ewes were fed a control diet or the control diet supplemented with 4 mg/kg/day BPA and offspring were evaluated. Prenatal BPA exposure reduced α-cell area and increased α-cell proximity to β-cells. Increased glucagon staining and α-cell number, and increased α- and β-cell nuclei. Findings were most consistent in fetal pancreata assessed at GD90 and in adult offspring exposed to the lowest BPA dose. While islet assessed in fetuses, adult islet fibrosis was increased. Collectively, these data provide further evidence that early life BPA exposure is a likely threat to human metabolic health. Future studies should corroborate these findings and decipher the molecular mechanisms of BPA's developmental endocrine toxicity.	Mol Cell Endocrinol Vol.588 Pages 112202	10.1016/j.mce.2024.112202	38552943	動物	-	1	0	1	不明	1	0.05, 0.5, 5 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1376	S. Christiansen, M. Axelstad, M. Scholze, H. K. L. Johansson, U. Hass, K. Mandrup, H. L. Frandsen, H. Frederiksen, L. K. Isling and J. Boberg	2020	Grouping of endocrine disrupting chemicals for mixture risk assessment - Evidence from a rat study	Exposure to mixtures of endocrine disrupting chemicals may contribute to the rising incidence of human-related diseases in humans. Real life mixtures are complex, comprised of chemicals with mixed modes of action, and risk assessment of mixtures is challenging. Here we investigated whether mixtures of chemicals with similar mode of action (MoA) could be grouped for risk assessment. We tested mixtures of chemicals with diverse endocrine modes of action (sex steroid synthesis inhibition, androgen receptor antagonism, thyroid hormone synthesis inhibition) and with different potencies. Pregnant rats and/or their male offspring were exposed during pregnancy and lactation simultaneously to either bisphenol A and butylparaben (low), diethylhexyl phthalate and propylparaben (low), or a mixture of all four substances (Treatment). In male offspring, the anogenital distance was significantly reduced and nipple retention in male offspring was increased in animals exposed to low and Treatment, with the mixture effects in one cell supplemented by the dose additive model. The combination of data and the expanded multi-more marked changes on tissue and other endocrine-sensitive endpoints than each binary mixture on its own. Sperm counts were reduced by all exposures. These experimental outcomes suggest that the dose additive model is a reasonable assumption for risk assessment of mixtures of chemicals with diverse modes of action, and that grouping of chemicals can be based on their effects on the Adverse Outcome Pathway. AOP's can provide important guidance if both the information on observed organ tissues and the information on observed mode/mechanism of action are taken into account.	Environ Int Vol.142 Pages 105870	10.1016/j.envint.2020.105870	32593051	動物	-	1	1	0	1	不明	–	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1377	T. Chioccarelli, M. Migliaccio, A. Suglia, F. Manfrevola, V. Porreca, N. Diano, S. Errico, S. Fasano and G. Cobellis	2021	Characterization of Estrogenic Activity and Site-Specific Accumulation of Bisphenol-A in Epididymal Fat Pad: Interfering Effects on the Endocannabinoid System and Temporal Progression of Germ Cells	The objective of this work has been to characterize the estrogenic activity of bisphenol A (BPA) and the adverse effects on the endocannabinoid system (ECS) in modulating germ cell progression. Male offspring exposed to BPA during the lactal perinatal period at doses below the no-observed-adverse-effect-level were used to investigate the exposure effects in adulthood. Results showed that BPA accumulates specifically in epididymal fat rather than in abdominal fat and targets testicular expression of 3β- hydroxysteroid dehydrogenase and cytochrome P450 aromatase, thus promoting sustained increase of estrogens and a decrease of testosterone. BPA exposure affects the ECS tone, altering the expression of CB1, CB2, FAAH, and NAPE-PLD in the testis and epididymal fat. Moreover, BPA exposure induces the premature expression of germ cells markers to the meiotic to ECS, and promotes epithelial germ cell exfoliation. In particular, the presence of cell-related (i.e. spermatogonia and spermatocytes) accelerates progression of spermatocytes and spermatids, promotes epithelial detachment of round and condensed spermatids and interferes with expression of cell-cell junction genes (i.e., zonula occludens protein-1, cinnectin and β-catenin). Altogether, our study provides evidence that early exposure to BPA produces in adulthood accelerated and site-specific BPA accumulation in epididymal fat, becoming a risk factor for the reproductive endocrine pathways associated to ECS.	Int J Mol Sci Vol.22 Issue 5	10.3390/ijms22052540	33802611	動物	-	1	1	1	0	0.4 μg/mL BPA 溶かす水設定	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1378	T. Chioccarelli, F. Manfrevola, M. Migliaccio, L. Altucci, V. Porreca, S. Fasano and G. Cobellis	2020	Fetal-Perinatal Exposure to Bisphenol-A Affects Quality of Spermatozoa in Adulthood Mouse	Bisphenol A (BPA) is considered an endocrine disruptor with estrogenic activity. It is described as an environment polluting industrial chemical whose adverse effects on the male reproductive system depend on the period of exposure (i.e., fetal, perinatal, or adult life). We exposed male mice to BPA during the fetal-perinatal period (from 0 days post coitum to 10 days post partum) and investigated the impact of this early life exposure on gamete health in adulthood animals at 70 days of age. Both in control and BPA-exposed mice, viability and motility of spermatozoa, as well as sperm motility, acquisition and chromatin condensation of spermatozoa, were evaluated. Our results showed that BPA exposure affects the quality of spermatozoa, inducing a significant reduction of viability and motility and an alteration of spermatozoa, in particular, BPA exposure interferes with biochemical mechanism useful to stabilize sperm chromatin condensation, as it interferes with oxidation of thiol groups associated to chromatin.	Int J Endocrinol Vol.2020 Pages 2750501	10.1155/2020/2750501	32256569	動物	-	1	1	1	1	0	0.4 μg/mL BPA 溶かす水設定	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1379	S. V. Chiginets, G. V. Bryukhin and S. N. Zavyalov	2020	Characterization of Sperm of White Rats at Exposure of Bisphenol A and Triclosan	We studied the effect of unstable dioxolone endocrine disrupters bisphenol A and triclosan on the reproductive function of mature male Wistar rats. Animals of both experimental groups received bisphenol A and triclosan homogenously (PVC in a dose of 200 mg/kg) for 2 months with free access to water and food. Analyses were measured directly in the testicular tissue by gas chromatography mass spectrometry (GC-MS). In both experimental groups, the concentrations of bisphenol A and triclosan in the testicular tissue significantly differed from the control (intact animals). Animals exposed to bisphenol A significantly differed by sperm parameters (total number, motility, and sperm morphology) from control rats. Animals receiving triclosan significantly differed from control rats only by the number of actively motile spermatozoa and the weight of the testicles.	Bull Exp Biol Med Vol.168 Issue 6 Pages 753-756	10.1007/s10517-020-04795-9	32328937	動物	-	1	1	不明	1	0	200 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1380	L. K. Chi, Q. Yuan, M. Y. Wang, C. R. Guo, X. D. Zhu, H. B. Jiang, Q. H. Zhang, Y. Zhao, L. Li and H. Yan	2024	Metabolomics reveals that ferroptosis participates in bisphenol A-induced testicular injury	OBJECTIVE: Bisphenol A (BPA) is a common environmental endocrine disruptor that negatively impairs male reproductive ability. This study aimed to explore the alterations in serum metabolomics that occur following BPA exposure and the mechanism via which BPA induces the death of testicular cells in a male mouse model. METHODS: The mice were classified into two groups: BPA-exposed and control groups, and samples were collected for metabolomic determination, screen quality analysis, electron microscopy, enzyme-linked immunosorbent assay, quantitative real-time PCR, pathological staining, and Western blot analysis. RESULTS: BPA exposure caused testicular damage and significantly decreased sperm quality in mice. Combined with non-target metabolomics analysis, this was closely related to ferroptosis. Indicators of abnormal metabolites of arachidonic acid and phosphatidylcholine, and the expression of its related genes, and Cu2 synthetase, β-glutathione peroxidase 4, lysophosphatidylcholine acyltransferase 3, and phosphatidylethanolamine-binding protein 1 were significantly altered. CONCLUSIONS: BPA can induce testicular damage, and reduced fertility, by affecting lipid metabolism in male mice. Inhibiting ferroptosis may potentially function as a therapeutic strategy to mitigate the male reproductive toxicity induced by BPA.	Heliyon Vol.10 Issue 11 Pages e31667	10.1016/j.heliyon.2024.e31667	38882385	動物	-	1	1	1	ICR	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1381	M. D. Cheng, C. L. Li, X. Y. Pei, Y. F. Zhang, D. D. Jia, Y. B. Zuo, S. L. Cai, P. F. Li, H. Xin and Y. F. Zhang	2023	Integrative analysis of DNA methylome and transcriptome reveals epigenetic regulation of bisphenols-induced cardiomyocyte hypertrophy	Cardiac hypertrophy, a kind of cardiomyopathic abnormality, might trigger heart contractile and diastolic dysfunction, and even heart failure. Currently, bisphenols (BPs) including bisphenol A (BPA) and its alternatives, bisphenol AF (BPAF), bisphenol F (BPF) and bisphenol S (BPS), are ubiquitously applied in various products, and potentially possess high cardiovascular risks for humans. However, the substantial experimental evidences of BPs on heart function, and their structure-related effects on cardiomyocyte hypertrophy are still cogently needed. DNA methylation, a typical epigenetics, plays key roles in BPs-induced transcription dysregulation, thereby affecting human health including cardiovascular system. Thus, in this study, we performed RNA-seq and reduced representation bisulfite sequencing (RRBS) to profile the roles of BPs-induced cardiotoxicity and to determine the key roles of DNA methylation in the toxic action. Further, the capabilities of three BPA analogues, together with BPA, in impacting heart function and changing DNA methylation and transcription were also comparatively investigated. Results showed that BPA and its analogues induced cardiomyocyte hypertrophy and dysfunction in zebrafish larvae. Integrative analysis revealed that BPA-like risks in both transcription and methylated hierarchies. Moreover, we validated the expression levels of four cardiomyocyte hypertrophy related candidate genes, Pnn-l, Pdlim3, Dlx6 and Gsx2b, which were up-upregulated and with DNA hypomethylation. The findings on the induction of BPA analogues on cardiomyocyte hypertrophy and DNA methylation revealed their potential detrimental risks in heart function of humans.	Ecotoxicol Environ Saf Vol.263 Pages 115391	10.1016/j.ecoenv.2023.115391	37611474	動物	-	1	1	1	1	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1382	Z. Chen, Z. Chen, J. Ma, Y. Chen, L. Chen and C. Deng	2025	m6A RNA methylation modulates autophagy by targeting Map1lc3b in bisphenol A induced Leydig cell dysfunction	Bisphenol A (BPA) exposure can affect testicular Leydig cells (LCs), potentially causing male infertility. Research suggests that RNA epigenetic response environmental exposure may impact LCs functional maintenance. However, the role of N6-methyladenosine (m6A) RNA methylation in BPA-induced LC dysfunction remains unclear. This study found that BPA exposure (50 μg/kg/day) for 28 days significantly reduces testosterone biosynthesis and upregulates m6A modification in LCs, using both in vivo and in vitro models. The involvement of the m6A "writer" Mettl3, "eraser" Alkbh5, and "reader" Ythdf2 in BPA-impacting LCs. m6A levels during BPA exposure was discovered, highlighting their central role. Manipulating these factors to reduce m6A methylation levels demonstrated potential for alleviating BPA-induced damage to LCs. Furthermore, integrated analysis of transcriptomic and MeRIP-sequencing data reveals that the upregulation of m6A levels induced by BPA specifically targets the Map1lc3b mRNA, a pivotal regulator of autophagy, thereby exerting suppressive effects on autophagic processes. In conclusion, our findings suggest that targeting m6A RNA methylation could be a potential therapeutic approach to mitigate BPA-induced reproductive toxicity, offering novel insights into the epigenetic regulation of male reproductive health.	J Hazard Mater. 2025 Mar 5:485:136748.	10.1016/j.jhazmat.2024.136748	39662354	動物、in vitro	精巣	1	1	1	0	0	-	-	-	不明	不明	不明	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1383	W. Chen, Q. E. B. Sun, P. Zhang, N. Li, S. Fei, Y. Wang, S. Liu, X. Liu and X. Zhang	2023	PARP1-catalyzed PARylation of YY1 mediates endoplasmic reticulum stress in granulosa cells to determine primordial follicle activation	Although only a small number of primordial follicles are known to be selectively activated during female reproductive cycles, the mechanisms that trigger this recruitment remain largely uncharacterized. Mitoregulated activation of primordial follicles may lead to the exhaustion of the non-renewable pool of primordial follicles, resulting in premature ovarian insufficiency. Here, we found that poly(ADP-ribose) polymerase 1 (PARP1) enzymatic activity in the surrounding granulosa cells (GCs) in follicles determines the subpopulation of the dormant primordial follicles to be activated. Conversely, specifically inhibiting PARP1 in oocytes in vivo or in vitro has no significant effect on primordial follicle activation. Mechanistically, PARP1 catalyzes the PARylation of YY1 and thereby induces endoplasmic reticulum (ER) stress in GCs. Moreover, we identified a new mechanism in which ER stress promotes a key molecular chaperone of endoplasmic reticulum stress, ERP29, and promotes Ca2+ homeostasis in GCs, which is required for GCs maintaining proper ER during primordial follicle activation. Inhibiting PARP1 prevents the loss of primordial follicle pool by attenuating the excessive ERS in GCs under fetal bisphenol A exposure. Together, we demonstrate that PARP1 in GCs acts as a pivotal mediator to determine the fate of the primordial follicles and may represent a novel therapeutic target for the retention of primordial follicles pool in females.	Cell Death Dis Vol.14 Issue 8 Pages 524	10.1038/s41419-023-05984-w	37582914	動物	-	1	0	1	不明	0	10 μg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1384	J. Chen, S. I. Ikeda, L. Kang, K. Nagishi, K. Tsubota and T. Kurihara	2023	Bisphenol A exposure triggers endoplasmic reticulum stress pathway leading to ocular axial elongation in mice	MACHADO-JOSEPH: Ocular axial elongation is one of the features of myopia progression. Endoplasmic reticulum (ER) stress-associated scleral remodeling plays an important role in ocular axial elongation. Bisphenol A (BPA) is one of the most common environmental pollutants and is known to affect various human organs through ER stress. However, whether BPA exerts an effect on scleral remodeling remains unknown. The purpose of this study was to investigate the effect of BPA exposure on ocular axial elongation in mice. Methods: Four-week-old male C57BL/6J mice were administered BPA (0.05 mg/kg/day) or vehicle by oral gavage. Another group of mice was administered BPA (0.05 mg/kg/day) and 4-phenylbutyric acid (4-PBA, 100 mg/kg/day), a chemical chaperone and inhibitor of ER stress, by oral gavage. Refractive error and axial length were measured by retinoscopy and SD-OCT system. Western blot was performed to detect the expression level of ER stress-related proteins. RESULTS: BPA administered mice exhibit axial elongation and myopic refractive shift with endoplasmic reticulum stress in the sclera. BPA administration activated scleral PERK and ATF6 pathways, and 4-PBA eye drops attenuated ER stress response and subsequent myopia progression. CONCLUSIONS: BPA-exacerbated axial elongation during myopia development in a mouse model by inducing scleral ER stress and activation of the PERK-ATF6 pathway. 4-PBA eye drops are ER stress inhibitor suppressed BPA-induced myopia development.	Front Med (Lausanne) Vol.10 Pages 1255121	10.3389/fmed.2023.1255121	37746069	動物	-	1	0	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1385	F. Chen, H. Zhang, H. Huang, J. Liu, W. Zhu, L. Lu, Y. Xie, H. Li, S. Pi, J. Zhong, S. Ding, K. Zhang, F. Wu, B. Zhang and Y. He	2025	Early-Life Exposure to Bisphenol A Damaged Pancreas That May Increase Offspring Sensitivity to High-Fat Diets	Previous studies have identified early life as a sensitive window for BPA exposure that may increase the risk of metabolic disease in adulthood. However, less attention has been paid to the effects of early-life BPA exposure on the pancreas and its relationship to the development of metabolic diseases. In this study, we exposed females to 50 μg/kg/d BPA in drinking water from 5 days of gestation to weaning of offspring mice and found that early-life BPA exposure induced pancreatic damage, including islet fibrosis, β-cell dysfunction, and acinar cell damage, in male offspring at 3 weeks of age. Moreover, at 7 weeks, and resulted in abnormalities in glucose tolerance and insulin tolerance, whereas no significant abnormalities were observed in females. Lipidomics analysis of the pancreas revealed a strong high-fat-metabolism sensitivity. Single-cell transcriptomic showed that early-life BPA exposure significantly altered the pancreas of offspring males. Lipid profiles of mouse pancreatic assemblase gene mRNA expression were upregulated, enzyme activity was reduced, and pancreatic steatosis, especially lipo-chotic ameloles, were increased in abundance, the latter of which was closely correlated with the increased pancreatic SEEL content as well as the decreased SEEL enzyme activity. Taken together, our results suggest that early-life BPA exposure may increase the susceptibility of mice to a high-fat diet by altering pancreatic lipid metabolism in mice and that there are significant sex differences in its effect.	J Toxicol Vol.2025 Pages 6189790	10.1155/jt/6189790	40842956	動物	-	1	1	1	1	0	50 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1386	D. Chen, K. Zhao, F. Huang, X. Guan, J. Tan, M. A. K. Wee, J. Shao, J. Xie, J. Wang and H. Chen	2022	Pubertal Bisphenol A exposure increases adult rat serum testosterone by resetting pituitary homeostasis	Bisphenol A (BPA) is widely used by manufacturers and in consumer products. Its release in the environment may affect male reproductive function. In this study, we examined the effect of low dose (0.1 mg/kg BW, short-term BPA exposure during puberty on the adult male rat pituitary-testis axis and explored the underlying mechanisms. Short-term BPA exposure during puberty affected the adult male rat pituitary-testis axis. BPA significantly increased serum testosterone levels without affecting serum luteinizing hormone (LH) and decreased pituitary estrogen receptor (ER) α and increased ERβ mRNA levels. Correlation analysis showed that BPA significantly altered the pituitary gene profiles of multiple steroidogenic pathways, including steroidogenic acute regulatory protein, cytochrome P450 11A1, cytochrome P450 17A, and low-density lipoprotein receptor. RNA-Seq analysis of testicular DNAs showed that BPA significantly affected the gene profiles of multiple testicular steroidogenic pathways without affecting germ cells. Also, GO- and KEGG analysis suggested that GPCR-related PI3K/AKT signaling was activated, which was confirmed by the increased phosphorylation of PI3Cδ, AKT1 and CREB. The results indicated that a low dose, short-term BPA exposure during puberty affected the adult male rat pituitary (ER-α/ ERβ) and testis (testosterone) homeostasis.	Environ Pollut Vol.298 Pages 118764	10.1016/j.envpol.2021.118764	34973380	動物	-	1	不明	不明	1	0	0.1 mg/kg BW	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1387	A. Chaneya, C. Sahu, S. Singla and G. Jora	2023	Zinc Deficiency Exacerbates Bisphenol A-Induced Hepatic and Renal Damage: Delineation of Molecular Mechanisms	Zinc (Zn) plays an important role in the maintenance of redox status in the biological system. Zn deficiency has been found to be associated with negative effects on the functioning of many organ systems, including hepatic and renal systems. Bisphenol A (BPA) can alter Zn homeostasis and perturb the physiological systems by provoking oxidative stress, which can lead to damage of different organs such as reproductive, immune, neurendocrine, hepatic and renal systems. The present study aims to investigate the toxicity of BPA in Zn-deficient condition in the liver and kidney of rat and to correlate its synergistic action. Zn deficiency was induced by feeding Zn-deficient diet (ZDD), and BPA was administered orally (100 mg/kg) till 30th. Male Sprague-Dawley rats were divided into four groups: NPC + Vehicle (normal feed and water); NPC + BPA (100 mg/kg) (ZDD + Vehicle (fed with Zn-deficient diet only) and ZDD + BPA (Zn-deficient diet + BPA, 100 mg/kg) for 5 weeks. Biochemical, histopathological, TUNEL assay and protein expression profiles were determined to assess the hepatic and renal damage. Zn deficiency exacerbated BPA-induced hepatic and renal damage, as indicated by increased serum markers, tumor antigen, birth Bax-ECG-associated protein-1, superoxide dismutase-1, metallothionein and apoptosis. Incidence showed that ZDD and BPA have a synergistic exacerbation effect on the liver and kidney of rat.	Biol Trace Elem Res Vol.201 Issue 6 Pages 2879-2894	10.1007/s12011-022-03392-3	36076144	動物	-	1	1	1	1	0	100 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1388	Y. S. Çatin, F. Ahıntaş and M. Berkiz	2023	Protective role of resveratrol and apigenin against toxic effects of bisphenol a in rat salivary gland	OBJECTIVES: The aim of this study was to investigate the cellular changes caused by Bisphenol A (BPA) exposure in salivary gland cells and to examine the protective role of resveratrol (RSV) and apigenin (APG) molecules against the negative effects of BPA. MATERIALS AND METHODS: Forty-two rats were randomly divided into 6 groups, as: (1) control, (2) BPA (130 mg/kg), (3) BPA + RSV (50 mg/kg), (4) BPA + APG (20 mg/kg), (5) RSV (50 mg/kg), and (6) APG (20 mg/kg). BPA, RSV, and APG were administered by oral gavage for 30 days. RESULTS: BPA significantly increased the number of mast cells and the level of tissue malondialdehyde (MDA) ($p < 0.05$). The BPA administration did not cause a significant change in tissue prostaglandin E2 (PGE2) and nitric oxide levels, whereas two-dose RSV significantly reduced the tissue PGE2 levels compared to BPA ($p < 0.05$). BPA caused cytopathological changes and apoptosis in salivary gland cells. In the BPA group, edema, nuclear pleomorphism, and aplastic nuclei were observed. Moreover, both RSV and APG were found to provide a protective against BPA-induced cellular damage, while RSV provided better cellular protection than APG. The control group had a normal histological structure. CONCLUSION: BPA caused cytopathological changes and oxidants in salivary gland cells. As a result, it was observed that these phytochemicals probably have a protective effects in BPA intoxication.	Drug Chem Toxicol Vol.46 Issue 1 Pages 88-96	10.1080/01480545.2021.2011310	34875952	動物	-	1	1	1	不明	0	130 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1389	T. Cavalieri Sousa, C. B. de Oliveira, M. L. Silva Ricardo, A. Muce de Aquino, W. R. Soares, A. S. Cruz Veras, M. E. Almeida Tavares, G. R. Teixeira, A. C. D. Castilho, F. L. Pacagnelli, I. Zalaiti Brandt and L. de Oliveira Mendes	2024	Prostate histological investigation in rats exposed to bisphenol a and phytochemicals during the perinatal period and subjected to hormonal stimulus in adulthood	Bisphenol A (BPA) is an environmentally dispersed chemical associated with tumor development. Phytochemicals such as indole-3-carbinol (I3C) and genistein (GEN) have chemoprotective effects on tumor cells. Thus, this study aimed to evaluate the prostatic morphological aspects of rats exposed to BPA, GEN, and I3C during the perinatal period and submitted to hormonal stimulus in adulthood. Blood was collected to obtain hormone measurements, and the prostate was collected for histological analysis. Hormonal stimulation increased the prostate weight in all groups. Perinatal exposure to BPA, GEN, and I3C and hormonal stimulation in adulthood increased the glandular and stromal volumes. Although BPA did not alter the prostate morphology, the phytochemicals provided beneficial effects for the prostate histological organization in adult animals subjected to hormonal stimulus.	Int J Environ Health Res. 2024 Jan;34(1):201-212.	10.1080/09603123.2022.2140127	36319067	動物	内分泌/前立腺	1	1	1	1	0	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1390	L. Y. Castillo, J. Rios-Carrillo, J. C. González-Orozco, I. Camacho-Arroyo, J. P. Morin, R. C. Zepeda and G. Roldán-Roldán	2022	Juvenile Exposure to BPA Alters the Estrous Cycle and Differentially Increases Anxiety-like Behavior and Brain Gene Expression in Adult Male and Female Rats	Perinatal exposure to bisphenol A (BPA) in murine models has been reported to affect social behavior and increase anxiety. However, there is little information about the effects of BPA exposure during puberty, a period in which sex hormones influence the maturation and differentiation of the brain. In this work, we evaluated the effects of BPA administration during the juvenile stage (PND 21-35) on anxiety in male and female rats. Newly weaned Wistar rats were treated with BPA (0, 50, or 500 µg/kg/day) for 15 days. To compare the time- and inter-sex-behavioral profiles, rats were evaluated using four different anxiety models: the Open Field test (OFT), the Elevated plus-maze (EPM), the Light-dark box test (LDB), and the Defensive burying test (DBT). Rodents exhibited a low level of anxiety, which was similarly distributed in our estrous profile at both doses. In all the tests, BPA-induced changes in the anxiety-like behavioral effects of BPA exposure was observed in female rats. The latter showed an altered estrous cycle that initiated earlier in life and had a shorter duration, with the estrous phase predominating. Moreover, the expression of ESR1, ESR2, GABRA1, GPER1, GR, NR3C1, and NR3C2 genes increased in the hippocampus and hypothalamus of male rats treated with 50 µg/kg, but not in females. Our results indicate that BPA consistently induces a higher anxiety profile in male than in female rats, as evidenced predominantly by an increase in passive-coping behaviors and changes in brain gene expression, highlighting the importance of sex in peripubertal behavioral toxicology studies.	Toxics Vol.10 Issue 9	10.3390/toxics10090513	36136478	動物	-	1	1	1	1	0	50、500 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1391	D. Caserta, M. P. De Marco, A. R. Bednarz and F. Costanzi	2022	Endocrine Disruptors and Endometrial Cancer: Molecular Mechanisms of Action and Clinical Implications, a Systematic Review	It has been widely demonstrated that endocrine disruptors play a central role in various physiopathological processes of human health. In the literature, various carcinogenic processes have been associated with endocrine disruptors (EDCs) exposure, including endometrial cancer. The aim of this systematic review is to summarize the molecular mechanisms of action and clinical implications of EDCs. PubMed/MEDLINE, Ovid and ISI Web of Science databases were searched. Numerous endocrine disruptors were analyzed. The most relevant results showed how Bisphenol A (BPA) shows to act like carcinogenesis, enzymes, as several levels. It has been demonstrated how BPA can interact with hormonal receptors and with different transcription proliferation and antiproliferative factors. Furthermore, the effect of Polycyclic aromatic hydrocarbons on thyl hydrocarbon receptors was investigated, and the role of flame retardants in promoting proliferation and metastasis was confirmed. The results obtained demonstrate how the mechanisms of action of endocrine disruptors are manifold in the pathophysiology of endometrial cancer, acting on different levels of the carcinogenesis process.	Int J Mol Sci Vol.23 Issue 6	10.3390/ijms23062956	35328379	動物	-	不明	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1392	D. Caserta, F. Costanzi, M. P. De Marco, L. Di Benedetto, E. Matteucci, C. Assogni, M. C. Pacilli, A. R. Bednarz, F. Bellati and I. Ruscito	2021	Effects of Endocrine-Disrupting Chemicals on Endometrial Receptivity and Embryo Implantation: A Systematic Review of 34 Mouse Model Studies	Several available studies have already analyzed the systemic effects of endocrine-disrupting chemicals (EDCs) on fertility women and neonatal outcomes, but little is still known in humans about the precise mechanisms of interference of these compounds with the endometrial receptivity. There is consistent evidence that continuous and prolonged exposure to EDCs, is a risk factor for reduced fertility and fecundity in women. Preliminary studies on mammalian models provide robust evidence about this issue and could help gynecologists and fertility experts to prevent long-term injury caused by EDCs on human fertility. To address this review, we aimed to systematically summarize all available data about EDC effects on blastocyst endometrial implantation. We performed a systematic review using PubMed/MEDLINE/Ovid/Web of Science all to-date studies, carried out on mouse models, which have investigated the effects of EDCs on blastocyst implantation. Thirty-four studies were included in the review. Our results showed that EDCs can affect implantation in a number of implantation sites and pregnancy rates, particularly after BPA and phthalate exposure. Furthermore, the endometrial expression of estrogen ERα and progesterone receptor (PR), as well as their activation pathways, is compromised after EDC exposure. Finally, the expression of the primary endometrial markers of receptivity (such as MUC1, HOXA10, leukemia inhibitory factor (LIF), osteopontin (OPN), and integrin β3) was altered after EDC contact was analyzed. In conclusion EDC-mediated alterations of blastocyst implantation in mouse model. Several players of the implantation mechanism are strongly influenced by the exposure to different categories of EDC.	Int J Environ Res Public Health Vol.18 Issue 13	10.3390/ijerph18136840	34202247	動物	-	不明	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1393	Y. Cao, J. Xu, J. Liu, Y. Liang, F. An, S. Wang, Z. Wei and L. Wang	2023	Bisphenol A exposure decreases sperm production and male fertility through inhibition PCBP2 expression	Growing evidence suggests that the exposure of bisphenol A (BPA), an endocrine disruptor that commonly present in the environment, can impair reproduction. However, conflicting results have been reported, and the underlying mechanism has not been fully understood. In this study, 3 week-old male mice were used and exposed to 50 mg/kg/d BPA or equivalent corn oil for 28 days. Then male reproductive parameters were then collected for morphology examination by HE stains. The number of sperm was counted, and the morphology was analyzed by PAS (periodic acid-schiff) and eosin staining. Fertilization capacity and successful rate were analyzed after in vitro fertilization (IVF). The expression of poly(rC)-binding protein 2 (PCBP2) in the testis was detected by immunohistochemistry and immunofluorescence. Our results showed that BPA exposure significantly reduced the testicular tissue of mice exposed to BPA. BPA interference was used to verify the regulatory mechanism of BPA exposure on germ exposure to GC-2 cells. Our data showed that the number of sperm was decreased, and the morphology was impaired in BPA-exposed mice. In addition, the serum testosterone level and fertilization efficiency were also reduced. Mechanistic studies showed that BPA could suppress the expression of PCBP2, a key regulatory gene in spermatid development, by activating the ERK/JNK/Cmaf. In conclusion, we found that BPA exposure can impair spermatid development via affecting key gene expression that is at least partially due to epigenetic modification.	Environ Sci Pollut Res Int Vol.30 Issue 59 Pages 123309-123323	10.1007/s11356-023-30815-y	37985585	動物	-	1	1	1	不明	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1394	Y. Cao, S. Chen, J. Lu, M. Zhang, L. Shi, J. Qie, J. Lu, D. Li, L. Ma and Y. Zhang	2022	BPA induces placental trophoblast proliferation inhibition and fetal growth restriction by inhibiting the expression of SRB1	Bisphenol A (BPA) is a common environmental toxicant that is known to be associated with fetal growth restriction (FGR). However, the mechanisms of low BPA-induced FGR is poorly characterized. We conducted animal tests to identify the abnormal expression of SRB1 in female placental tissues with high BPA-induced FGR and further verified its decreased expression in human placenta and BeWo cells. Next, the effect of BPA on the proliferation of BeWo cells was investigated. Our results showed that BPA exposure significantly reduced the number of proliferating trophoblast cells in placental tissues of FGR rats. Cell-based BeWo cells treated with PCBA, and BPA exposure markedly reduced the expression of PCNA and cyclin-dependent kinase 2 (CDK2), which inhibited placental proliferation. In vitro studies showed that BPA also induced the expression of CDK1, CDK2, cyclin B and phosphorylated Rb in placental trophoblast cells, indicating cell cycle arrest after exposure to BPA. In addition, the expression of c-JUN and phosphorylated ATM was upregulated in BPA-exposed trophoblasts, indicating increased DNA damage. Our results indicate that BPA-induced FGR is achieved by reducing the expression of SRB1, inhibiting placental proliferation and increasing DNA damage. Our findings not only explain the mechanism of BPA-associated developmental toxicity but also shed light upon developing novel therapeutic targets.	Environ Sci Pollut Res Int. 2023 May;30(21):60805-60819.	10.1007/s11356-023-26850-4	37037937	動物、in vitro	生殖発生毒性	1	1	1	1	1	0	-	-	-	-	1	不明	不明	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1395	J. X. Cai, Z. Li, J. Dai, X. L. Wang, H. Zhang and J. X. Cheng	2022	[4-nonylphenol combined with bisphenol A induces testicular autophagy and spermatogenic impairment by inhibiting the Akt/mTOR pathway in F1 male offspring rats]	OBJECTIVE: To study the impacts of exposure of F0 generation rats to 4-nonylphenol (4-NP) and bisphenol A (BPA) on the autophagy of testicular cells and key gene expressions of the Akt/mTOR pathway in the F1 generation offspring rats. METHODS: Using a 2×2 factorial design, 192 female and male rats were randomly assigned to receive intragastrically 4-gavage solution of 0.5 mg/kg 4-NP, 50 mg/kg BPA+0.5 mg/kg 4-NP, 50 mg/kg BPA, or 0.9% NaCl (0.2 ml/100 g) for 30 days. Then the rats in each group were mated at a ratio of 1:2. After pregnancy, the female rats continued the above intragastrical administration till delivery. The testicular tissues of the male offspring rats were collected for observation of the ultrastructure of the testicular cells and detection of the autophagy-related protein LC3 and mRNA expression levels of Akt, mTOR, RIPTOR and RHEB. RESULTS: The sperm count of the F1 generation male offspring rats was markedly decreased in the 4-NP and BPA+4-NP groups compared with that in the control group ($P < 0.05$) but no significant interaction effect was observed between BPA and 4-NP ($P > 0.05$). The ratio of LC3-II / LC3-I was remarkably increased in the 4-NP, BPA and BPA+4-NP groups ($P < 0.01$), and a significant interaction effect was observed between BPA and 4-NP ($P < 0.01$). The mRNA expressions of Akt, mTOR, RIPTOR and RHEB in the 4-NP and BPA+4-NP groves were lowered, and the decreased count of sperm and increased number of autophagic vacuoles, TgH2A and their regulatory gene mRNA expressions of ZZW3 in the 4-NP group, as well as in that of mTOR in the BPA group and Akt in the BPA+4-NP group (all $P < 0.05$). It eventually up-regulated expression of BCAP1 mRNA was found in all the three intervention groups ($P < 0.05$), and a significant interaction effect between BPA and 4-NP on the expressions of Akt and BCAP1 mRNA ($P < 0.05$). CONCLUSIONS: Long-term exposure to low-concentration BPA and 4-NP impairs the testicular function of the F1 generation male offspring rats, which is closely related to the autophagy of testicular cells and changes of the Akt/mTOR pathway.	Zhonghua Nan Ke Xue Vol.28 Issue 3 Pages 195-202	-	37462956	動物	-	1	1	1	不明	0	0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1396	C. Cagliyan, F. M. Kandemir, A. Aya, G. C. Gür, S. Küçükler and E. Darendelioğlu	2022	Neuroprotective effects of 18β-glycyrrhetinic acid against bisphenol A-induced neurotoxicity in rats: Involvement of neuronal apoptosis, endoplasmic reticulum stress and JAK1/STAT1 signaling pathway	The exposure to bisphenol A (BPA) is inevitable owing to its common use in the production of polycarbonate plastics. Studies to reduce side effects are getting importance since BPA causes severe toxicities in important organs. Therefore, in this study, we aimed to investigate the neuroprotective effects of 18β-glycyrrhetinic acid (18β-GA) against BPA-induced neurotoxicity in rats. Male Wistar albino rats were divided into five equal groups as follows: (1) Control group, (2) 18β-GA group (100 mg/kg), (3) BPA group (250 mg/kg), (4) 250 mg/kg BPA + 50 mg/kg 18β-GA group, (5) 250 mg/kg BPA + 100 mg/kg 18β-GA group. BPA treatment was associated with increased MDA level while reduced GSH concentration, activities of glutathione peroxidase, superoxide dismutase, and catalase. BPA supplementation caused apoptosis in the brain by up-regulating caspase-3 and Bax levels and down-regulating Bcl-2. BPA also caused endoplasmic reticulum (ER) stress by increasing mRNA transcript levels of PERK, IRE1, ATF-6 and GRP78. Additionally, in rats observed that BPA administration activated JAK1/STAT1 signaling pathway and levels of TNF-α, NF-κB, p38 MAPK and JNK in the brain. However, co-treatment with 18β-GA at a dose of 50 and 100 mg/kg considerably ameliorated oxidative stress, inflammation, apoptosis, ER stress and JAK1/STAT1 signaling pathway in brain tissue. Overall, the data of this study indicate that brain damage associated with BPA toxicity could be ameliorated by 18β-GA administration.	Metab Brain Dis Vol.37 Issue 6 Pages 1931-1940	10.1007/s11011-022-01027-z	35699857	動物	-	1	1	1	0	250 mg/kg（雌中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1397	M. C. Butler, C. N. Long, J. A. Kinkead, M. T. Green, R. E. Martin, B. L. Marshall, T. E. Willeman, A. K. Schenk, J. Mao and C. S. Rosenfeld	2020	Endocrine disruption of gene expression and microRNA profiles in hippocampus and hypothalamus of California mice: Association of gene expression changes with behavioural outcomes	The hypothalamus and hippocampus are sensitive to early exposure to endocrine-disrupting chemicals (EDCs). Two EDCs that have raised particular concerns are bisphenol A (BPA), a widely prevalent chemical in many common household items, and genistein (GEN), a phyto-oestrogen present in soy and other plants. We hypothesized that early exposure to BPA or GEN may lead to permanent effects on gene expression profiles for leading RNAs (mRNAs and microRNAs; miRs), which can affect the translation of mRNAs. Dunn-ESID induced behavioural alterations changes may affect behavioural and metabolic patterns. California mice (Peromyscus californicus) were exposed to environmentally relevant concentrations of BPA (2.5 μg/kg bw/day), GEN (5 mg/kg bw/day), BPA + GEN, or vehicle (sesame oil) from PND 2 to PND 21. Offspring were fed high-fat diet (HFD) or lean control diet (LFD) at weaning. Behavioural and metabolic tests were performed at 300 days of age. A quantitative polymerase chain reaction analysis was performed to correlate mRNAs and miRs in the hypothalamus and hippocampus. 10 BPA and GEN-exposed California mice offspring showed social communication impairments. Hypothalamic Xpo, Ern1, Klhl3 and Lrpr were increased in 10 BPA offspring; miR-124 was elevated but miR-30b-5p was reduced in 5 GEN offspring; miR-9 and miR-153 were increased in the hippocampus of 10 BPA offspring, whereas GEN decreased hippocampal miR-9a and miR-153 expression. Correlation analysis revealed that increased expression of miR-30b and miR-185a was associated with social communication deficits in 10 BPA individuals. The findings reveal a cause for concern such that developmental exposure of BPA or GEN in California mice (and potentially by translation in humans) can lead to long-lasting neurobehavioural consequences.	J Neuroendocrinol Vol.32 Issue 5 Pages e12847	10.1111/jne.12847	32297422	動物	-	1	1	1	1	0	5 mg/kg（雌中濃度）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1398	F. Bujalance-Reyes, A. M. Mollina-López, N. Ayala-Soldado, A. Lora-Benítez, R. Mora-Medina and R. Moyano-Salvago	2022	Analysis of Indirect Biomarkers of Effect after Exposure to Low Doses of Bisphenol A in a Study of Successive Generations of Mice	Bisphenol A (BPA) is considered as being an emerging pollutant, to which both animal and human populations are continuously and inadvertently exposed. The identification of indirect biomarkers of effect could be a key factor in determining early adverse outcomes from exposure to low doses of BPA. Thus, this study aimed to find new ones, to evaluate and identify indirect biomarkers of effect through the analysis of their blood biochemistry, and of certain reproductive parameters, after exposure to different BPA concentrations (0.5, 2, 5, 50, and 100 µg/kg BW/day) in drinking water over generations. Our results showed that there were no modifications in the reproductive parameters analyzed. No estrous cycle disturbances, litter size, or the percentage of live pups were affected by the exposure to BPA. However, the exposure to BPA markedly modified the concentrations in the biochemical parameters, e.g., alterations in the glucose levels, that increased significantly ($p < 0.05$) in the breeders at the higher exposure doses (50 and 100 µg/kg BW/day in F1; 50 µg/kg BW/day in F2 and 100 µg/kg BW/day in F3). Moreover, the glucose levels in the offspring (F1, F2, and F3) were significantly altered ($p < 0.05$) by the exposure to BPA, with the most significant changes observed in the highest dose in F1 and F3, inferring possible hepatic alterations. Further, body anomalies showed a distinction in their values in F1 and F3 (except the groups exposed to 100 µg/kg BW/day, whereas in F2 the values of this parameter increased with respect to the control group, this aspect likely being related to a possible hepatic and renal alteration. Based on these results, glucose, albumin, and total proteins could initially be considered as early indicators of indirect effect after prolonged exposure to low BPA doses over generations.	Animals (Basel). 2022 Jan 26;12(3):300.	10.3390/ani12030300	35158624	動物	一般毒性(繁殖、生化)	1	1	1	C57BL/6:1	1	0.5,2,5,50,100 µg/kg/day	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1399	G. V. Ryukhin, D. S. Lankov, N. V. Gribachyova and O. B. Selyaninova	2025	Sexual Behavior of the Offspring of Female Rats Exposed to Bisphenol A	We studied the effect of bisphenol A orally administered to female rats on sexual behavior of their offspring. The males of the experimental group demonstrated significantly decreased number of approaches to a partner, repeating them from a receptive female; the copulatory rate during direct interaction with the female was also reduced. In females of the experimental group, the lordosis quotient and lordosis intensity were decreased. The revealed changes indicate that bisphenol A intoxication of female rats leads to significant disturbance of sexual behavior in their offspring of both sexes.	Bull Exp Biol Med. 2025 May;179(1):10-13.	10.1007/s10517-025-06423-w	40679519	動物	発達神経毒性	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_1400	K. A. Bruno, L. P. Macomb, A. C. Morales-Lara, J. E. Mathews, J. A. Folaranmi, A. L. Yang, D. N. Di Florio, B. H. Eisenfeld, E. B. Whelan, G. R. Solomon, A. R. Hill, C. C. Hewa-Rahinduwage, A. J. Scott, H. D. Gmeyner, F. A. Mollica, M. S. Greenaway, G. M. Cooper and D. Fairweather	2021	Sex-Specific Effects of Plastic Caging in Murine Viral Myocarditis	MICROBIANS: Myocarditis is an inflammatory heart disease caused by viral infections that can lead to heart failure, and occurs more often in men than women. Since animal studies have shown that myocarditis is influenced by sex hormones, we hypothesized that endocrine disruptors, which interfere with natural hormones, may play a role in the progression of the disease. The human population is exposed to the endocrine disruptor bisphenol A (BPA) through the use of polycarbonate plastics. Mice housed in BPA-containing plastic cages have altered immune responses to viral infection. METHODS: Male and female A/J mice were housed in polycarbonate cages with BPA or in cages with BPA-free plastic. Mice were infected with coxsackievirus B3 and some mice were treated with some serious control water. Myocarditis was induced with coxsackievirus B3 on day 21 and the endpoints were assessed on day 28 post-infection. RESULTS: We found that male BALB/c mice that were exposed to plastic cages had increased myocarditis due to complement activation and elevated numbers of neutrophils and macrophages, whereas females had enhanced mast cell activation and fibrosis. CONCLUSIONS: These findings show that housing mice in traditional plastic caging increases viral myocarditis in males and females, but using sex-specific immune mechanisms.	Int J Mol Sci. 2021 Aug 17;22(16):8834.	10.3390/ijms22168834	34445539	動物	免疫	1	1	1	1	0	不明	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性影響等不適合と判断されるものは作成段階評価へ進め、当該物評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1401	A. Bruyère, D. Valman, E. Bou-Mansur, M. C. Chagnon and L. L. Corre	2020	Hepatic transcriptome and DNA methylation patterns following perinatal and chronic BPS exposure in male mice	BACKGROUND: Bisphenol S (BPS) is a monosubstituted bisphenol A (BPA) substitute, since BPA is virtually banned worldwide. However, BPS and BPA have both endocrine disrupting properties. Their effects appear mostly in metabolic disorders and reproductive dysfunctions. Epigenetic mechanisms, such as DNA methylation, are involved in the effects of BPA. Nevertheless, the epigenetic methylome of the liver in CD-1 males and CD1®(ICR) male mice (NEOLTD, The, Indianapolis, IN, USA) was studied. Male mice were exposed to BPA (50 µg/kg bw/day) or BPS (50 µg/kg bw/day) via their diet as a model of chronic exposure (CTD: cumulative dose) and their livers were collected at 70 days. The histological analysis and the quantification of the gene expression of toxicity-related markers by RT-qPCR confirmed the complete spermatogenesis in all groups for both periods of exposure. However, our results suggest a deleterious effect of BPS on the blood-testis barrier in adults after perinatal exposure as BPS and BPA CD-1 treatments induced a decrease in cadherin-2 and connexin-43 gene expression, which are proteins of the junctional complexes. As none of these effects were found after a prepubertal exposure, these results suggested the reversibility of BPA's effects. Caution must be taken when transposing this study to humans, and additional studies are needed in this regard. However, from a regulatory perspective, this study emphasizes the importance of taking into account different periods of exposure, as they uncover different sensitivities to BPA exposure.	BMC Genomics Vol.21 Issue 1 Pages 881	10.1186/s12864-020-07294-3	33297965	動物	-	1	1	1	1	0	1.5 µg/kg 体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1402	V. Brouard, M. Driouach, N. Ella, I. Guérin, V. Hanoux, H. Bourdine-Lelong and C. Delalande	2022	Effects of bisphenol A and estradiol in adult rat testis after prepubertal and pubertal exposure	Over the past few decades, male fertility has been decreasing worldwide. Many studies attribute this outcome to endocrine disruptors, exposure such as bisphenol A (BPA), which is a chemical compound used in plastics. Our previous study showed that BPA exposure during the prepubertal period altered the expression of genes involved in the blood-testis barrier (BTB) in rats. Estradiol (E2), which is also a hormone to which we are constantly exposed, is a contributing factor in testicular dysfunction. Therefore, the aim of this study was to investigate the effects of BPA, E2, and their mixture, on the BTB in adult rats. For both periods, male rats were sacrificed at 70 days. The histological analysis and the quantification of the gene expression of testis cell markers by RT-qPCR confirmed the complete spermatogenesis in all groups for both periods of exposure. However, our results suggest a deleterious effect of BPA on the blood-testis barrier in adults after pubertal exposure as BPA and BPA+E2 treatments induced a decrease in cadherin-2 and connexin-43 gene expression, which are proteins of the junctional complexes. As none of these effects were found after a prepubertal exposure, these results suggested the reversibility of BPA's effects. Caution must be taken when transposing this study to humans, and additional studies are needed in this regard. However, from a regulatory perspective, this study emphasizes the importance of taking into account different periods of exposure, as they uncover different sensitivities to BPA exposure.	Reprod Toxicol Vol.111 Pages 211-224	10.1016/j.reprotox.2022.06.004	35700937	動物	-	1	不明	1	1	0	50 µg/kg bw/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1403	G. E. Brito Filha, T. F. R. Ruiz, L. G. de Souza, L. J. Farado, F. C. A. Dos Santos, P. S. L. Villanueva, E. C. R. Loanes and S. R. Taboga	2025	Mammary Gland Reactive Stroma Characterization at Aging After Bisphenol A Exposure During Hormonal Susceptibility Windows	Mammary gland development is influenced by endocrine signaling, which remodels epithelial and stromal compartments. Reactive stroma phenotype is observed when stromal disturbances occur, leading to changes in extracellular matrix composition and occurrence of reactive cell types. One of the main targets of these alterations is endocrine-disrupting chemical exposure, such as bisphenol A (BPA). Studies suggest that BPA acts on receptor binding sites of survival hormones, interfering the endocrine response. The aim of this study was to investigate the reactive stroma features, on mammary glands of aged female gerbils (Meriones unguiculatus) exposed to BPA during hormonal susceptibility windows. Animals were exposed to 25 µg/kg/day BPA during pregnancy and lactation (PND1-21) and sacrificed at 540 days old. Histological analysis revealed an increase of myofibroblasts (Lowered L/I = 0.1866) and active fibroblasts (FAP+) in Normal Fibroblasts (Lowered L/I = 0.1926). These results showed newly associated cells in BPA exposure, which can be an indicator of Fibroblastic polarization. CD163 (+) stromal cells were also identified and detected among epithelial cells after BPA endocrine disruption. Angiogenesis was supported by VEGF increasing in the gland tissue, which promoted an increase in blood vessel density. Thus, our results demonstrated that reactive stroma was raised in the mammary gland after BPA exposure. This profile was supported by changes in the fibroblastic population due to an imbalance in synthetic phenotypes and the expression of FGF-10, as well as the angiogenic activity that could corroborate with the malignancy and aggressiveness induced by BPA exposure.	Cell Biol Int. 2025 Apr;49(4):397-406.	10.1002/cbin.12280	39873202	動物	発がん性	1	1	1	ラットおよびゲルビル（ジャービル）	1	-	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1404	J. Brankovič, J. Leskovec, S. Škurm, V. Čarkovnik-Flajs, S. Šterpin, J. Osredkar, E. Pogorevc, D. Antolinc and M. Vrezl	2022	Experimental Exposure to Bisphenol A Has Minimal Effects on Bone Tissue in Growing Rams-A Preliminary Study	Bisphenol A (BPA) is a well-known synthetic compound that belongs to the group of endocrine-disrupting chemicals. Although bone tissue is a target for these compounds, studies on BPA-related effects on bone morphology in farm animals are limited. In this preliminary study, we investigated the effects of short-term dietary BPA exposure on femoral morphology, metabolism, mineral content, and biomechanical behavior in rams aged 5–6 months. Fourteen rams of the Istrian Pramenka breed were randomly divided into a BPA group and a control group (seven rams/group) and exposed to 25 µg BPA/kg bw for 52 days. Femoral was collected for determination of bone turnover markers (procollagen-I-terminal propeptide, C-terminal telopeptide), and femurs were processed via computed tomography, histomorphometry, three-point bending test, and mineral analysis. The BPA group showed a higher bone formation rate (mineralizing surface/bone surface, MS/BS) and mineral apposition rate (MAR) than the control group ($p < 0.05$). However, the exposure to BPA exposed rams. These results suggest that a 2-month, low-dose exposure to BPA in growing rams did not affect the histomorphology, metabolism, and biomechanical behavior of femurs; however, it influenced the composition of microelements, which could affect the ferromatrix and histological properties of bone in the long term.	Animals (Basel) Vol.12 Issue 17	10.3390/ani12172179	36077899	動物	-	1	1	1	不明	0	25 µg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1405	M. C. Borland, M. J. Schlicht, N. Acweda, A. M. Soto and G. Prins	2021	Effects of perinatal exposure to bisphenol A on induction of prostate cancer in Sprague Dawley rats by MNU and testosterone	Perinatal and neonatal exposure to bisphenol A (BPA) has been linked to enhancement of prostate cancinogenesis. In rats induced by combined treatment with estradiol and testosterone, but human data are lacking. This study aimed to determine the effects of perinatal BPA exposure on induction of prostate cancer in rats by sequential treatment with N-methyl-N-nitrosurea (MNU) and continuous low dose administration of testosterone. Pregnant Sprague Dawley rats were exposed to 0 (control), 2.5, 25 or 250 µg BPA/kg/day via drinking water from gestation day 6 to weaning of the male offspring. Male pups were treated postnatal day 90 with MNU (50 mg/kg) and continuous testosterone (2.5 mg/kg/day) via subcutaneous implants. All rats were euthanized 26 weeks after MNU injection. The perinatal BPA exposure did not significantly affect the incidence of prostatic carcinoma (adenocarcinoma) in the dorsolateral prostate (DLP) and ventral prostate (VP). The incidence of malignant tumors at any site in the body was significantly lower in exposed rats (81-90 %) than in controls (93 %). In conclusion, perinatal BPA exposure did not significantly modify prostate cancer induction by MNU plus testosterone in rats, unlike the enhancement of prostate carcinogenesis induced by treatments involving estradiol administration. Which of the two models of prostate carcinogenesis is more relevant for the human situation is unclear at present.	Toxicology Vol.484 Pages 153394	10.1016/j.tox.2022.153394	36521576	動物	-	1	0	1	1	0	2.5, 25 µg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1406	T. Bonnet-Belda, H. Fenies, R. Al-Abdulla, I. Quesada, J. A. Gustafsson, A. Nadal and P. Alonso-Magdalena	2020	Bisphenol-A exposure during pregnancy alters pancreatic β-cell division and mass in male mice offspring: A role for ERβ	Bisphenol-A (BPA) is a widespread endocrine-disrupting chemical that constitutes a risk factor for type 2 diabetes mellitus (T2DM). Data from animal and human studies have demonstrated that early exposure to BPA results in adverse metabolic outcomes in adult life. In the present work, we exposed pregnant heterozygous estrogen receptor β (ERβ) knock-out (BERKO) mice to 10 µg/kg bw BPA during days 9–16 of pregnancy, and measured β-cell mass and proliferation in wildtype (WT) and BERKO male offspring at postnatal day 30. We observed increased pancreatic β-cell proliferation and mass in WT, an in vitro effect was produced in BERKO mice. Dispersed islet cells, to primary culture treated with 1 nM BPA showed unaltered parameters. β-cell replication rate, which was blunted in pancreatic β-cells from BERKO mice and reinstated by the selective ERβ agonist WAY-200070. This increased β-cell proliferation was found in male adult as well as in neonate pancreatic β-cells, suggesting that BPA directly impacts β-cell division at earliest stages of life. These findings support the hypothesis that BPA during pregnancy upregulates pancreatic β-cell division and mass in an ERβ-dependent manner. Thus, other natural or artificial chemicals may use this ERβ-mediated pathway to promote similar effects.	Food Chem Toxicol Vol.145 Pages 111681	10.1016/j.fct.2020.111681	32805339	動物	-	1	不明	1	----------	0	10 µg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1407	H. Bordbar, S. S. Yahyaei, A. Noorafshan, E. Aliabadi and M. Nasehi	2023	Resveratrol ameliorates bisphenol A-induced testicular toxicity in adult male rats: a stereological and functional study	BACKGROUND: Bisphenol A (BPA) is one of the most widely used synthetic chemicals worldwide. BPA as an endocrine disruptor affects the reproductive systems through mutagenic and antiandrogenic properties. Resveratrol (RES) as a natural polyphenol and potent antioxidant exhibits protective effects against reproductive toxicity by inhibiting of oxidative stress. All male rats were divided into eight groups (n=6), including CONTROL, OLIVE OIL (0.1 ml/ day), Carboxy methylcellulose (CMC) (1 ml of 1/5 g CL RES (100mg/kg/day), low dose of BPA (25 mg/kg/day), high dose of BPA (50 mg/kg/day), low dose of BPA + RES, and high dose of BPA + RES groups. Treatments were performed by oral gavage for 60 consecutive days. Then, the rats were anesthetized and their testes were removed for stereological study. RESULTS: We observed a significant BWG, the rat's testes symmetry in the low and high doses of BPA groups compared to control groups (P< 0.05). The volume of testicular components as well as the diameter and length of seminiferous tubules significantly reduced (1-16 %), and the total number of the testicular cell types decreased (14-57 %) on average in the low and high doses of BPA groups. Moreover, serum follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone hormone concentration showed a significant reduction in both doses of BPA groups (P< 0.05). Nevertheless, treatment with RES could ameliorate all the above-mentioned changes in the low and high doses of BPA groups (P< 0.05). CONCLUSION: RES could prevent BPA-induced testicular structural changes and sperm quality via improving gonadotropin hormones and testosterone levels.	Basic Clin Androl Vol.33 Issue 1 Pages 1	10.1186/s12610-022-00174-8	36604652	動物	-	1	1	1	1	0	25, 50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1408	H. Bordbar, F. Soleymani, E. Nadimi, S. S. Yahyaei and K. Fazelian-Dehkordi	2021	A Quantitative Study on the Protective Effects of Resveratrol against Bisphenol A-induced Hepatotoxicity in Rats: A Stereological Study	BACKGROUND: Bisphenol A (BPA) is a widely used chemical with toxic effects on the liver. Resveratrol (RES) is an herbal compound with protective properties. This study aimed to investigate the protective effects of RES on the liver in rats exposed to BPA. METHODS: This study was conducted in 2018 in Shiraz, Iran. Thirty Sprague-Dawley male rats were divided into five groups: a control group (distilled water), a sham group (olive oil 0.1 ml/day), BPA (50 mg/kg/day), BPA + RES (50 mg/kg/day + 100 mg/kg/day), and RES (100 mg/kg/day) groups. Treatments were performed by oral gavage for 60 consecutive days. At the end of study, the animals' livers were removed, and stereological measurements were made to obtain the total liver volume, portal triad volume, hepatocyte nucleus and cytoplasm volumes, sinusoidal space volumes and length, and Kupffer cell (KC) numbers. The data were analyzed using the one-way analysis of variance test. RESULTS: The hepatocyte number, the total liver volume, and hepatocyte nucleus and cytoplasm volumes were significantly reduced in the BPA group ($P < 0.05$). The number of KCs and the height of sinusoids in the BPA group were increased ($P < 0.05$). Nevertheless, treatment with RES could ameliorate all the above-mentioned changes in the low and high doses of BPA groups ($P < 0.05$). CONCLUSION: RES could prevent BPA-induced testicular structural changes and sperm quality via improving gonadotropin hormones and testosterone levels.	Iran J Med Sci Vol.46 Issue 3 Pages 218-227	10.30476/ijms.2020.83308.1233	34083854	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1409	B. Bordás, L. Gioiosa, G. Parolaz and M. Mamaudino	2023	Exposure to either Bisphenol A or S Represents a Risk for Crucial Behaviors for Pup Survival, Such as Spontaneous Maternal Behavior in Mice	INTRODUCTION: Maternal behavior depends on a multitude of factors, including environmental ones, such as Endocrine Disrupting Chemicals (EDCs), which are increasingly attracting attention. Bisphenol A (BPA), an EDC present in plastic, is known to exert negative effects on maternal behavior. Bisphenol S (BPS), a BPA substitute, seems to share some endocrine-disrupting properties. In this study, we focused on the analysis of the effects of perinatal exposure to BPA or BPS on maternal behavior. METHODS: Female mice were exposed to BPA or BPS (0.04 mg/kg/day) from 5 weeks of age to the end of lactation. Maternal behavior was observed during lactation (PND1-PND10). On PND11, the mothers were sacrificed, and their brains were collected for immunohistochemical analysis. We assessed the number of pups at birth, the sex ratio, and the percentage of dead pups to evaluate, indirectly, the quality of maternal care. In the hypothalamic-preoptic-septal circuit, we quantified the density of cells expressing oxytocin receptor (OTR) and vasopressin 1a receptor (V1aR). RESULTS: We observed that BPA- and BPS-exposed dams exhibited a reduction in maternal care, along with the treatment itself, way often, later in life, the offspring's physiology and behavior. Exposure to BPA during critical developmental periods represents a risk for both dams and offspring, even at low environmentally relevant doses, through the functional alteration of neural circuits controlling fundamental behaviors for pup survival, such as maternal behaviors.	Neuroendocrinology Vol.113 Issue 12 Pages 1283-1297	10.1159/000526074	35850097	動物	-	1	1	1	1	0	4µg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1410	B. Bordás, A. Caslle, M. T. Ostuni, M. Bettarelli, S. Nasini, M. Mamaudino, G. Parolaz and S. Gotti	2024	Perinatal exposure to bisphenol A or S: Effects on anxiety-related behaviors and serotonergic system	Bisphenols, synthetic organic compounds used in the production of plastics, are an extremely abundant class of Endocrine Disrupting Chemicals, i.e., exogenous chemicals or mixtures of chemicals that can interfere with the endocrine system and produce adverse effects. Bisphenol A (BPA), the most widely used bisphenol, is known to exert negative effects on the reproductive system and on behavior. Bisphenol S (BPS) is a BPA substitute (BPS), so it is considered safe, as it is not yet regulated. In this study, we investigated the effects on anxiety-related behaviors, and the serotonergic system, which is highly involved in controlling these behaviors, in adult mice. We treated CD1® dams orally with a dose of 4 µg/kg body weight/day (i.e., EFSA TDI) of BPA or BPS dissolved in corn oil or with vehicle alone, at the onset of mating and continued treatment until the offspring were weaned. Adult offspring of both sexes underwent behavioral tests (Open Field, Elevated Plus Maze, Novelty Suppressed Feeding) and immunohistochemical analysis of the serotonergic system. Our results showed that perinatal exposure to BPA and BPS induced anxiety-related behaviors in males, females, and both sexes (ambiguous). The analysis of the serotonergic system highlighted a sex dimorphism in the DR only, with ventral females showing higher values of serotonin immunoreactivity (5-HT+) than control males. BPA-treated males displayed a significant increase of 5-HT+ in all analyzed nuclei, whereas BPS-treated males showed an increase in ventral DR only. In females, both bisphenols treated groups showed a significant increase of 5-HT+ in ventral DR compared to the controls, and BPA-treated females also showed a significant increase in VmPC These results provide evidence that exposure during the early phases of life to BPA or BPS alters anxiety and the raphe serotonergic neurons, in a sex-dependent manner.	Chemosphere Vol.349 Pages 140827	10.1016/j.chemosphere.2023.140827	38042429	動物	-	1	1	1	1	0	4 µg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1411	B. Bordás, A. Caslle, F. Mortarolo, M. Bettarelli, F. Napoli, S. Gotti, G. Parolaz and M. Mamaudino	2023	Effects of perinatal exposure to bisphenol A or S in EAE model of multiple sclerosis	Epidemiological studies support the idea that multiple sclerosis (MS) is a multifactorial disease, overlapping genetic, epigenetic, and environmental factors. A better definition of environmental risks is critical to understand both etiology and the sex-related differences of MS. Exposure to endocrine disrupting compounds (EDCs) fully represents one of these risks. EDCs are natural or synthetic exogenous substances (or mixtures of substances) that can interfere with the endocrine system and produce adverse effects. Bisphenol A (BPA), the most widely used bisphenol, is known to exert negative effects on the reproductive system and on behavior. Bisphenol S (BPS), one of the most widely used substitutes for BPA, its treatment in bisphenols is still not adequately investigated. It is necessary to clarify their role also in the pathological context to define a risk. In disease onset and course in both sexes. In this study, we examined, in both sexes, the effects of perinatal exposure to BPA and BPS in one of the most widely used mouse models of MS, experimental autoimmune encephalomyelitis (EAE). Exposure to bisphenols seemed to be particularly deleterious in males. In fact, both BPA- and BPS-treated males showed anticipation of the disease onset and more substantial motor loss in the spinal cord. Overall, BPA-treated males also displayed an exacerbation of EAE course and an increase in inflammation markers in the spinal cord. Analyzing the consequences of bisphenol exposure on EAE will help us better understand the role of both xenoestrogens and endogenous estrogens on the sexually dimorphic characteristics of MS.	Cell Tissue Res Vol.392 Issue 2 Pages 467-480	10.1007/s00441-023-03746-w	36750500	動物	-	1	1	1	1	0	4 µg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1412	B. Bordás, A. Caslle, M. Bettarelli, M. Mamaudino and S. Gotti	2025	Perinatal exposure to bisphenol A or S alters differently sexual behavior and kisspeptin system in mice	The effects of bisphenol A (BPA), a highly diffused endocrine disrupting chemical found mainly in plastics, on neural circuits and behaviors are well known. However, the effects of its substitutes have not been fully investigated yet. Bisphenol S (BPS) is considered safe, as it is not yet regulated. In this study, we investigated the effects on sexual behaviors and the kisspeptin system. CD1® dams were orally treated with 4 µg/kg body weight/day of BPA, BPS, or vehicle from mating until the end of weaning of the offspring. In the adult offspring, we performed the two-bottle "3 flavors test, and we observed the spontaneous sexual behavior. Exposure to BPA caused a delay in puberty onset in females, while BPS caused early ejection in males, and both altered the estrous cycle in females. The sexual and sexual-related behaviors were partially altered, with BPA-treated males showing a lack of preference for sweet solutions and BPS-treated females showing an anticipation of sexual receptivity. In the AVPV, an BPA-treated females showed a significant increase in kisspeptin-immunoreactive neurons, while BPS led to a decrease in the same population. In the arcuate nucleus, and BPS induced a reduction compared to control females. Among males, we observed a significant increase in the cases number of BPA-treated males and a significant decrease in the perioral kisspeptin nucleus of BPS-treated ones. These results support the idea that perinatal exposure to low doses of either BPA or BPS is altering, in a sexually differentiated way, some reproductive-relevant parameters, sexual behaviors, and kisspeptin hypothalamic nuclei.	Environ Res Vol.269 Pages 120888	10.1016/j.envres.2025.120888	39828186	動物	-	1	1	1	1	0	4 µg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1413	B. Bordás, A. Caslle, M. Bettarelli, S. Gotti, G. Parolaz and M. Mamaudino	2021	Effects of chronic exposure to bisphenol A in adult female mice on social behavior, vasopressin system, and estrogen membrane receptor (GPER1)	Bisphenol A (BPA), an organic synthetic compound found in some plastics and epoxy resins, is classified as an endocrine-disrupting chemical. Exposure to BPA is especially dangerous if it occurs during specific "critical windows" of development, such as pregnancy and lactation. Recently, BPA substitutes, such as bisphenol S (BPS), have been introduced in the market, but their safety is questionable. In this study, we exposed CD1® female mice to BPA or BPS during pregnancy. Three months old CD1® females were orally exposed to BPA or to vehicle (corn oil). The treatment (5 µg/kg body weight/day) started the day 0 of pregnancy and continued throughout pregnancy, lactation, and lasted for a total of 120 weeks. BPA-treated dams did not show differences in body weight or food intake, but they showed accelerated estrous cycle compared to the controls. In order to evidence alterations in social and sociosexual behaviors, we performed the Three-Chamber test for sociability, and sexual and non-Spontaneous circulate (such known targets of endocrine-disruptors) particularly involved in the control of social behavior like vasopressin and the oxytocin systems. The test revealed some alterations in the displaying of social behavior. BPA-treated dams have higher locomotor activity compared to the control dams. Immunohistochemistry for vasopressin revealed that BPA-treated dams have a significantly higher number of vasopressin-immunoreactive cells in the bed nucleus of the stria terminalis (BNST), but not in the paraventricular and supraoptic nuclei (PVN and SON). Immunoreactivity (ir) in the paraventricular and supraoptic nuclei (PVN treated females, while we did not find any alteration of the oxytocin system. In parallel, we have also observed, in the same hypothalamic nuclei, a significant reduction of the membrane estrogen receptor GPER1 expression.	Eur J Histochem Vol.65 Issue s1	10.4081/ejh.2021.3272	34755506	動物	-	1	1	1	1	0	4 µg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1414	N. Bi, X. Gu, A. Fan, D. Li, M. Wang, R. Zhou, Q. C. Sun and H. L. Wang	2022	Bisphenol-A exposure leads to neurotoxicity through upregulating the expression of histone deacetylase 2 in vivo and in vitro	Bisphenol A (BPA), an environmental endocrine disruptor, is toxic to the central nervous system. Although recent studies have shown BPA-induced neurotoxicity, it is far from clear what precisely epigenetic mechanisms are involved in BPA-induced neurotoxicity. In this study, we found that BPA exposure (0.5 mg/kg/day) for 30 days impaired the spatial memory of male mice in the Morris water maze test and Y-maze test at 12 weeks. The results showed that 1 μM BPA exposure for 36 h impaired neurite outgrowth of PC12 cells through decreasing the primary and secondary branches. Besides, BPA exposure decreased the level of its HDAC isoform HDAC2 both in the Golgi-Cox staining of hippocampal neurons in BPA-exposed Thy1-Cre mice. Mice lacking HDAC2 in forebrain excitatory neurons (HDAC2 cKO) were markedly rescued the spine density impairments in the hippocampus and prevent the cognitive impairment caused by BPA exposure in vivo. Collectively, HDAC2 plays an essential role in BPA-induced neurotoxicity, which provides a potential molecular target for medical intervention.	Toxicology Vol.465 Pages 153052	10.1016/j.tox.2021.153052	34838597	動物、in vitro	-	1	不明	1	1	0	1mg/kg/日	-	-	-	1	0	1 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1415	N. Bi, J. Ding, R. Zou, X. Gu, Z. H. Liu and H. L. Wang	2021	Developmental exposure of bisphenol A induces spatial memory deficits by weakening the excitatory neural circuits of CA3-CA1 and EC-CA1 in mice	Bisphenol A (BPA) is an environmental endocrine disruptor and impairs learning and memory. However, the direct evidence for BPA exposure affecting neural circuits has been limited. In this study, a virus tracing assay was used to investigate the neural circuits of CA3-CA1 and EC-CA1 in the hippocampus of mice exposed to BPA (0.5 mg/kg/day) from conception to 12 weeks of age. Then, the Morris water maze and Y-maze tests were used to assess the spatial memory of mice. Three transgenic mice were used to respond

別添-2　統合文献リスト

内分泌かく乱性評価（動物）1：該当、0：該当しない　内分泌かく乱性評価（疫学）1：該当、0：該当しない　内分泌かく乱性評価（in vitro）1：該当、0：該当しない　透明性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに透明性基準不適合と判断されるもの以外を透明性評価へ進め、当該時点評価段階で原則に基づき判定。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	透明性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1427	K. Barašić, K. Živančević, D. Jasovac, A. Buha Djordjevic, M. Ačkar, D. Jovgovski, E. Antonijević Miljaković, M. Ćurčić, Z. Bulat, B. Antonijević and D. Đukić-Ćosić	2020	Multi-strain probiotic ameliorated toxic effects of phthalates and bisphenol A mixture in Wistar rats	Phthalates and bisphenol A, to which people are mainly exposed through food, interfere with the body's endocrine system, along with various other toxic effects. Literature data suggest that probiotic cultures might be effective in the prevention and treatment of these disorders. The aim of this study was to examine the ameliorative effects of multi-strain probiotic culture on the toxicity induced by a phthalate and bisphenol A mixture in Wistar rats. Animals were divided into four experimental groups (n = 8): (1) Control (corn oil); (2) P (probiotic; 0.76 * 10(8) CFU/kg/day); Saccharomyces boulardii + Lactobacillus rhamnosus + Lactobacillus plantarum LP 01(R)) + Lactobacillus plantarum HEALOS; (3) MIX (50 mg/kg b.w./day DEHP + 50 mg/kg b.w./day DBP + 25 mg/kg b.w./day BPA); (4) MIX + P. Animals were euthanized after 28 days of daily oral gavage treatment. blood and organs were collected for further analysis. Probiotic reduced systemic inflammation and had protective effects on liver, kidneys, spleen, testicles and severe glucose level. It almost completely remedied the changes in biochemical, hematological and hormonal parameters, and mitigated changes in relative liver size, food consumption and organ histology. These results suggest consuming multi-strained probiotics as a dietary therapeutic strategy against toxicity of the investigated mixture.	Food Chem Toxicol Vol.143 Pages 111540	10.1016/j.fct.2020.111540	32645469	動物	-	1	1	0	1	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1428	K. Barašić, A. Pavić, D. Jasovac, K. Živančević, D. Božić, N. Radaković, E. Antonijević Miljaković, A. Buha Djordjevic, M. Ćurčić, Z. Bulat, B. Antonijević and D. Đukić-Ćosić	2023	Comprehensive investigation of hepatotoxicity of the mixture containing phthalates and bisphenol A	Connections between the mixture containing bis(2- ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP) and bisphenol A (BPA) and liver injury were explored through in silico investigation and in vivo models. Comparative Toxicogenomics Database (CTD), ToxDL, ToppGene and Cytoscape were used for bioinformatic analysis. In vivo subacute study was performed on female rats (n = 8): (1) Control (corn oil); (2) DEHP, 50 mg/kg b.w./day; (3) DBP, 50 mg/kg b.w./day; (4) BPA, 25 mg/kg b.w./day; (5) MIX: DEHP + DBP + BPA. Zebrafish embryo were exposed to the investigated substances in different doses, singularly and in mixture, to assess developmental toxicity. Bioinformatic analysis revealed 1,4-dihydropyridine, phthalic acid, and bisphenol A as the most significant chemicals. Pathway analysis pointed to endocrine disruption, cell cycle, and metabolism as the most affected processes. Histopathology revealed severe vacuolar degeneration in MIX and bisphenol A-affected livers. Zebrafish embryo toxicity study showed that DEHP (~ 2 mg/mL) and MIX (~ 1 mg/mL) induced 72 hpf lethality, while their higher doses increased 24 h lethality. The effect of DBP in binary mixtures led to a lethal outcome at the two highest concentrations, while the hepatotoxicity of DEHP/DBP/BPA mixture was dictated by BPA (confirmed by the benchmark dose analysis).	J Hazard Mater Vol.445 Pages 130404	10.1016/j.jhazmat.2022.130404	36455319	動物	-	1	不明	1	1	0	25 mg/kg bw/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1429	K. Barašić, D. Jovgovski, K. Živančević, A. Buha Djordjević, E. Antonijević Miljaković, M. Milković, J. Kolur-Stanojević, B. Antonijević and D. Đukić-Ćosić	2021	Combining in vivo pathohistological and redox status analysis with in silico toxicogenomic study to explore the phthalates and bisphenol A mixture-induced testicular toxicity	The aim of this study was to: (1) determine and compare the capacity of bis (2- ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), bisphenol A (BPA), and their mixture to produce testicular toxicity after the subacute exposure of female rats (n = 8): (1) Control (corn oil); (2) DEHP, 50 mg/kg b.w./day; (3) DBP, 50 mg/kg b.w./day; (4) BPA, 25 mg/kg b.w./day; (5) MIX: DEHP + DBP + BPA, 50 mg/kg b.w./day DEHP + 50 mg/kg b.w./day DBP + 25 mg/kg b.w./day BPA; (6) MIX + P: MIX + probiotic (0.76 * 10(8) CFU/kg/day); Saccharomyces boulardii + Lactobacillus rhamnosus + Lactobacillus plantarum LP 01(R)) + Lactobacillus plantarum HEALOS, and (2) to explore the underlying mechanisms using in silico toxicogenomic approach. Testes were extracted and prepared for histological assessments under the light microscope (hematoxylin and eosin staining) and redox status analysis. The Comparative Toxicogenomics Database (CTD; http://CTD.mddr.org), Cytoscape software (https://cytoscape.org/) and ToppGene Suite (https://toppgene.cchmc.org/) were used for data mining. Present pathohistological study has demonstrated severe testicular toxicity of the BPA group (desquamated germinal epithelium cells, enlarged cells with hyperchromatic nuclei, multinucleated cell forms and intraepithelial vacuoles) in comparison with the single substances, while effects on redox status parameters were either more prominent, or present only in the MIX group. In silico investigation revealed 19 genes linked to male reproductive disorders, affected by all three investigated substances. Effects on metabolism, ERK pathway, apoptosis and oxidative stress could be singled out as the most probable mechanisms involved in the subacute DEHP, DBP and BPA-induced testicular toxicity, while the effect on oxidative stress parameters was confirmed by in vivo experiment.	Chemosphere Vol.267 Pages 129296	10.1016/j.chemosphere.2020.129296	33348264	動物	-	1	不明	1	1	0	25 mg/kg bw/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1430	K. Barašić, A. Buha Djordjevic, K. Živančević, E. Antonijević, M. Anđelković, D. Jovanac, M. Ćurčić, Z. Bulat, B. Antonijević and D. Đukić-Ćosić	2020	Toxic Effects of the Mixture of Phthalates and Bisphenol A-Subacute Oral Toxicity Study in Wistar Rats	Phthalates and bisphenol A, classified as endocrine disruptors, have weak mutagenic, and endogenic properties, and affect thyroid hormone regulation. The aim of this study on male rats was to compare the subacute toxic effects of low doses of single compounds (bis (2- ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and bisphenol A (BPA)) with the effects of their mixture through different biochemical, hormonal, and hematological parameters. Rats were divided into five experimental groups: Control (corn oil); DEHP (50 mg/kg b.w./day); DBP (50 mg/kg b.w./day); BPA (25 mg/kg b.w./day); MIX (DEHP + DBP + BPA in the same ratio and dose). Blood was collected from the retroorbital plexus of rats (n = 8) after 28 days of oral gavage treatment, and prepared for redox status and essential metals analysis. By conducting additional in vivo experiment, probiotic (Rhamnosus GG) administration was applied. There were 24 DEHP, DBP and BPA-positive related genes, indicating the three most probable mechanisms—apoptosis, inflammation and oxidative stress. In vivo experiment confirmed that significant changes in redox status/essential metal parameters were either prominent, or only present in the MIX group, indicating possible additive effects. In vivo experiment confirmed the ability of the multy-strain probiotic to bind DEHP/DBP/BPA mixture, while probiotic administration ameliorated mixture-induced changes in rat tissue.	Int J Environ Res Public Health Vol.17 Issue 3	10.3390/ijerph17030746	31979393	動物	-	1	1	1	1	0	25 mg/kg bw/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1431	K. Barašić, D. Božić, K. Živančević, M. Milenković, D. Jasovac, B. Marić, E. Antonijević Miljaković, A. Buha Djordjević, P. Vukomanović, M. Ćurčić, Z. Bulat, B. Antonijević and D. Đukić-Ćosić	2021	Integrating in silico with in vivo approach to investigate phthalate and bisphenol A mixture-linked asthma development: Positive probiotic intervention	The aim of this study was to explore the mechanisms of bis(2- ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP) and bisphenol A (BPA) mixture-induced asthma development and test probiotic as a potential positive modulator of these processes. Female rats were divided into five groups (n = 8): (1) Control (corn oil); (2) DEHP (50 mg/kg b.w./day); (3) DBP (50 mg/kg b.w./day); (4) BPA (25 mg/kg b.w./day); (5) MIX (DEHP + DBP + BPA in the same ratio and dose as in (2), (3) and (4)); (6) MIX + P (probiotic (0.76 * 10(8) CFU/kg/day); Saccharomyces boulardii + Lactobacillus rhamnosus + Lactobacillus plantarum LP 01(R)) + Lactobacillus plantarum HEALOS). Blood was collected from the retroorbital plexus of rats (n = 8) after 28 days of oral gavage treatment, and prepared for redox status and essential metals analysis. By conducting additional in vivo experiment, probiotic (Rhamnosus GG) administration was applied. There were 24 DEHP, DBP and BPA-positive related genes, indicating the three most probable mechanisms—apoptosis, inflammation and oxidative stress. In vivo experiment confirmed that significant changes in redox status/essential metal parameters were either prominent, or only present in the MIX group, indicating possible additive effects. In vivo experiment confirmed the ability of the multy-strain probiotic to bind DEHP/DBP/BPA mixture, while probiotic administration ameliorated mixture-induced changes in rat tissue.	Food Chem Toxicol Vol.158 Pages 112671	10.1016/j.fct.2021.112671	34793900	動物	-	1	1	1	1	0	25 mg/kg bw/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1432	L. Bao, C. Zhao, L. Feng, Y. Zhao, S. Duan, M. Qiu, K. Wu, N. Zhang, X. Hu and Y. Fu	2022	Ferritinophagy is involved in Bisphenol A-induced ferroptosis of renal tubular epithelial cells through the activation of the AMPK-mTOR-ULK1 pathway	Bisphenol A (BPA) is a common environmental contaminant, whose exposure is associated with the progression of various kidney diseases. BPA exposure has turned out to be associated with cytotoxicity to renal tubular epithelial cells, but its underlying mechanism remains unknown. Herein, we found that BPA exposure induced ferroptosis in kidney and renal epithelial cells, as indicated by increased intracellular iron accumulation, lipid peroxidation and cells death upon BPA exposure. Additionally, utilization of ferrostatin-1 and desferrioxamine, typical ferroptosis inhibitors, can fundamentally diminish cells death. Intriguingly, our discoveries demonstrated that BPA exposure induced ferritinophagy, a selective autophagy process that degrades ferritin to release free iron, which was validated by the following findings: BPA-induced cells death was aggravated after autophagy promotion with rapamycin treatment, occurred after BPA treatment and reversible iron presented ferroptosis through Fenton reaction. We next demonstrated that BPA activated the AMPK-mTOR-ULK1 signaling pathway in vivo. AMPK-mTOR- and ULK1 knockdown dramatically mitigated BPA-induced TCMK-1 cells death, and decreased MDA and LC3 levels, but increased FTH protein content. These results indicate that activation of the AMPK-mTOR-ULK1 signaling is involved in BPA-induced ferritinophagy. In conclusion, renal dysfunction and renal tubular epithelial damage induced by BPA are linked to ferroptosis, which depends on the activation of ferritinophagy through AMPK-mTOR-ULK1 axis.	Food Chem Toxicol. 2022 May:163:112909.	10.1016/j.fct.2022.112909	35292335	動物	腎尿細管上皮細胞	1	不明	単独	Balb/c mice	0	10, 100 μg/kg.1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1433	O. Banerjee, S. Singh, S. K. Prasad, A. Bhattacharjee, T. Seal, J. Mandal, S. Sinha, A. Banerjee, B. K. Maji and S. Mukherjee	2023	Exploring aryl hydrocarbon receptor (AhR) as a target for Bisphenol-A (BPA)-induced pancreatic islet toxicity and impaired glucose homeostasis: Protective efficacy of ethanol extract of Centella asiatica	The estrogenic impact of Bisphenol-A (BPA), a widely recognized endocrine disruptor, causes disruption of pancreatic β-cell function through estrogen receptors (ERs). While BPA's binding affinity for ERs is significantly lower than that of its natural counterpart, estrogen, recent observations of BPA's affinity for aryl hydrocarbon receptor (AhR) is especially noteworthy, as AhR is also a key role in BPA's toxicological effects within the endocrine pancreas. To explore this, oxo-investigated BPA's (10 and 100 μg/ kg/body weight/day for 21 days) potential to activate AhR within pancreatic islets and assessed the protective role of ethanolic extract of Centella asiatica (CA) (200 and 400 mg/kg body weight/day for 21 days) against BPA-mediated toxicity in mouse model. Our results indicate that BPA-driven activation triggers the activation of AhR and modulates its target genes, which pancreatic islets. In contrast, CA activates AhR but diverts downstream pathways differentially and excludes NrF2. Additionally, CA was observed to counteract the disruptive effects of BPA on glucose homeostasis, oxidative stress, and inflammatory markers in pancreatic islets. Furthermore, molecular docking studies suggested that CA's phytochemicals could bind to AhR, supporting its role as a potential AhR antagonist. Overall, our findings suggest that CA's antioxidant and anti-inflammatory properties, combined with its ability to counteract BPA-induced AhR activation, may underlie its protective effects on pancreatic islets. Moreover, our research provides valuable insights into the mechanisms involved in the diabetogenic actions of BPA.	Toxicology. 2023 Dec:500:153693.	10.1016/j.tox.2023.153693	38042274	動物	代謝	1	0 (ip)	1	1	0	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1434	O. Banerjee, S. Singh, T. Paul, B. K. Maji and S. Mukherjee	2024	Centella asiatica mitigates the detrimental effects of Bisphenol-A (BPA) on pancreatic islets	Bisphenol A (BPA), a widely used in food packaging and household products, leadings to daily human exposure and potential health risks by fueling metabolic diseases like type 2 diabetes mellitus (T2DM). Understanding BPA's endocrine disruption mechanisms is crucial for developing effective therapeutic strategies. Centella asiatica (CA), a traditional medicinal herb, is known for its antioxidant and anti-inflammatory properties, utilized for centuries in Ayurvedic therapy. We investigated the effects of Centella asiatica (CA) ethanol extract on BPA-induced pancreatic islet toxicity in male Swiss albino mice. BPA administration (10 and 100 μg/kg body weight, twice daily) for 21 days caused glucose homeostasis disturbances, insulin resistance, and islet dysfunction, which were partially mitigated by CA supplementation (200 and 400 mg/kg body weight). Additionally, heightened oxidative stress, elevated levels of proinflammatory cytokines, loss of mitochondrial membrane potential (MMP), abnormal cell cycle, and mitochondria-mediated apoptosis were observed in BPA-exposed islets. However, our study suggests that CA enhanced AhR signaling to mitigate the disrupted pancreatic endocrine function in BPA-exposed mice. By creating light on how BPA interacts with AhR, our research provides valuable insights into the mechanisms involved in the diabetogenic actions of BPA.	Sci Rep Vol.14 Issue 1 Pages 8043	10.1038/s41598-024-58545-2	38580733	動物	-	1	0	1	1	0	10、100 μg/kg体重	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1435	O. Banerjee, T. Paul, S. Singh, B. K. Maji and S. Mukherjee	2025	Individual and combined antagonism of aryl hydrocarbon receptor (AhR) and estrogen receptors (ERs) offers distinct level of protection against Bisphenol A (BPA)-induced pancreatic islet cell toxicity in mice	Bisphenol A (BPA), a pervasive endocrine-disrupting chemical, is known to convey harmful impact on pancreatic islets through estrogen receptors (ERs). Conversely, BPA can activate aryl hydrocarbon receptor (AhR) as well, but the combined role of AhR and ERs in mediating BPA's toxicity remains unclear. Therefore, we investigated the individual and combined role of AhR and ERs in BPA-induced pancreatic islet toxicity in male Swiss albino mice. BPA administration (10 and 100 μg/kg body weight, twice daily) for 21 days caused glucose homeostasis disturbances, insulin resistance, and islet dysfunction, which were partially mitigated by CA-supplementation (200 and 400 mg/kg body weight). Additionally, heightened oxidative stress, elevated levels of proinflammatory cytokines, loss of mitochondrial membrane potential (MMP), abnormal cell cycle, and mitochondria-mediated apoptosis were observed in BPA-exposed islets. However, our study suggests that CA enhanced AhR signaling to mitigate the disrupted pancreatic endocrine function in BPA-exposed mice. By creating light on how BPA interacts with AhR, our research provides valuable insights into the mechanisms involved in the diabetogenic actions of BPA.	Naunyn Schmiedebergs Arch Pharmacol.	10.1007/s00210-024-03506-9	39377923	動物、in vitro	-	1	0	1	不明	0	10、100 μg/kg体重/日	-	-	-	1	0	1 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1436	A. Balci, G. Ozkemahli, P. Erkekoglu, D. Zeybek, N. Yersal and B. Kocer-Gumusel	2023	Effects of prenatal and lactational bisphenol a and/or di(2-ethylhexyl) phthalate exposure on male reproductive system	Bisphenol A (BPA) and phthalates are abundantly used endocrine disrupting chemicals (EDCs). The aim of this study was to evaluate the effects of single and combined exposures to BPA and/or di(2-ethylhexyl) phthalate (DEHP) on male reproductive system during prenatal and lactational periods. Female Wistar albino rats were randomly divided into four groups (n = 8-10 rats/group): Control (corn oil), BPA (50 mg/kg/day), DEHP (50 mg/kg/day), and BPA+DEHP (50 mg/kg/day DEHP and 50 mg/kg/day BPA). Dosages exposed to EDCs, through oral 0-21 gestational days and lactation period by stomach gauge. Male offspring (n = 5/group) from each mother were fed till adulthood and were then euthanized. Later, reproductive hormones, sperm parameters, and oxidative stress parameters were determined. In conclusion, we can suggest that prenatal and lactational exposure to BPA and DEHP may cause adverse effects in male reproductive system in later stages of life especially after combined exposure.	Int J Environ Health Res Vol.32 Issue 4 Pages 902-915	10.1080/09603123.2020.1805416	32787440	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1437	A. Balci, G. Ozkemahli, P. Erkekoglu, N. D. Zeybek, N. Yersal and B. Kocer-Gumusel	2020	Histopathologic, apoptotic and autophagic, effects of prenatal bisphenol A and/or di(2-ethylhexyl) phthalate exposure on prepubertal rat testis	Bisphenol A (BPA) and di(2-ethylhexyl) phthalate (DEHP) are endocrine disrupting chemicals (EDCs) used in a wide variety of industrial products as plasticizers. Exposure to EDCs, particularly in mixtures, in prenatal and early postnatal periods may lead to unwanted effects and can cause both developmental and reproductive problems. In this study, we aimed to determine the individual and combined effects of prenatal and lactational exposure to BPA and/or DEHP on testicular histology, apoptosis, and autophagic proteins. Pregnant Sprague-Dawley rats (n = 5-6 rats/group) were exposed to: Control (corn oil), BPA (50 mg/kg/day), DEHP (50 mg/kg/day), and BPA (50 mg/kg/day) + DEHP (50 mg/kg/day) via oral gavage during pregnancy and lactation. The male offspring (n = 5) from each group were chosen randomly, and their testicular examinations were performed at the 35th postnatal day. Histopathological changes in testes were evaluated by Johnsen's testicular histology scoring system. Immunohistochemical staining was performed to evaluate the apoptotic and autophagic proteins. Histopathological changes in testes revealed that exposure to BPA and DEHP mixture in combination caused a significant increase in testicular histology score when compared to the control group. Moreover, exposure to BPA and DEHP mixture increased Bax/Bcl-2 ratio, increased TUNEL-positive spermatogonia and TUNEL-positive testicular apoptotic cells, and autophagic proteins. As evidenced by increased LC3 puncta/cells counts and decreased p62 levels) in testicular tissue. We can suggest that EDCs cause more dramatic changes in both testicular structure and cell death when there is combined exposure.	Environ Sci Pollut Res Int Vol.27 Issue 16 Pages 20104-20116	10.1007/s11356-020-08274-6	32239407	動物	-	1	1	1	1	0	50 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1438	M. M. Badawy, M. M. Elsherbiny, G. E. Elshopakey, A. E. Elzayyat, M. Abd -El-Samie, El-Kattan, M. G. Hamama, F. H. Abdelraouf and A. Fahdi	2022	Potential Effects of Bisphenol A on the Heart and Coronary Artery of Adult Male Rats and the Possible Role of L-Carnitine	Bisphenol A (BPA) is an environmental toxin utilized for the production of polycarbonate plastics and epoxy resins. Due to BPA's extensive production and environmental contamination, human exposure is unavoidable. The effects of low-dose of BPA on various body tissues and organs, remain controversial. Our study investigated the potential of BPA to induce biochemical, histopathological, and immunohistochemical changes in the coronary arteries of adult male rats and the possible role of L-carnitine (LC). Forty adult male rats were divided into four equal groups (n = 10): control group, LC group (received 200 mg/kg/day LC), BPA group (received 50 mg/kg/day of BPA) and 200 mg/kg/day LC + BPA group (n = 10). Coronary artery samples were collected for histopathological, immunohistochemical, and biochemical analyses. BPA induced abnormal histological alterations in the coronary arteries in the form of necrosis in the tunica media, vacuolation in cells in the media and detachment of the endothelium of the intima. Congestion of blood vessels and infiltration by polymorphonuclear cells were observed in the myocardium. There was an enhanced collagen deposition in both tissues indicating fibrosis. Immunohistochemical changes included enhanced eNOS and caspase-3 expression in the coronary artery and myocardium indicating vascular damage and apoptosis, respectively. Oxidative damage was evident in the coronary artery and the myocardium of BPA-treated rats, which was indicated by the reduced level of glutathione (GSH) and elevated malondialdehyde (MDA) levels. The coadministration of LC significantly improved BPA-induced structural alterations and oxidative stress. In conclusion, BPA could potentially cause pathologic changes and oxidative damage in the coronary artery and myocardium, which could be improved by LC coadministration.	J Toxicol Vol.2022 Pages 7760594	10.1155/2022/7760594	36601412	動物	-	1	1	1	1	0	40 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1439	I. Babiloni-Chust, R. S. Dos Santos, R. M. Medina-Gali, A. A. Perez-Serna, J. A. Encinar, J. Martinez-Pinna, J. A. Gustafsson, L. Marcuquia and A. Nadal	2022	G protein-coupled estrogen receptor activation by bisphenol-A disrupts the protection from apoptosis conferred by the estrogen receptors ERα and ERβ in pancreatic beta cells	17-β -estradiol protects pancreatic β -cells from apoptosis via the estrogen receptors ERα, ERβ and GPER. Conversely, the endocrine disruptor bisphenol A (BPA), which exerts multiple effects in beta cell type via the same estrogen receptors, increased basal apoptosis. The molecular initiated events that trigger these opposite actions have yet to be identified. We demonstrated that combined genetic-decrepitation and pharmacological blockade of each estrogen receptor increased apoptosis to a different extent. The increase in apoptosis induced by BPA was diminished by the pharmacological blockade or the genetic silencing of GPER, but not by the blockade of ERα or ERβ. Moreover, BPA, but not 17-β -estradiol, increased the activity of the ERK1/2 pathway via GPER. The activation of GPER by BPA was confirmed in a proximity ligation assay in mice. However, the ERα and ERβ agonists PPT and DPN, respectively, had no effects on basal cell viability. To exert their biological actions, ERα and ERβ form homodimers and heterodimers. Molecular dynamics simulations together with proximity ligand assays and coimmunoprecipitation experiments indicated that the interaction of BPA with ERα and ERβ, as well as GPER activation by β1 decreased ERα-β1 heterodimers. We propose that ERα-β1 heterodimers play an antiapoptotic role in beta cells, and that BPA- and β1-induced decreases in ERα-β1 heterodimers lead to beta cell apoptosis. Unveiling how different estrogenic chemicals affect the crosstalk among estrogen receptors should help to identify diabetogenic endocrine disruptors.	Environ Int Vol.164 Pages 107250	10.1016/j.envint.2022.107250	35461094	動物	-	1	不明	不明	0	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1440	L. F. Azevedo, C. R. Porto Dechandt, C. Cristina de Souza Rocha, M. F. Homo re Carneiro, L. C. Albadó ere F. Barbosa, Jr.	2019	Long-term exposure to bisphenol A or S promotes glucose intolerance and changes hepatic mitochondrial metabolism in male Wistar rats	The present study evaluates the effects of low-level long-term exposure to bisphenol A (BPA) and bisphenol S (BPS) on serum biochemical markers, glucose homeostasis, mitochondrial energy metabolism, biogenesis and dynamics, and oxidative stress in the liver of male Wistar rats. Animals were exposed to BPA or BPS (0.5 mg/kg bw/day) for 90 days, starting at 30 days of age. Results showed that BPA and BPS induced glucose intolerance. Regarding mitochondrial metabolism, both bisphenols augment the electron entry by complex II relative to complex I in the mitochondrial respiratory chain (MRC), and reduce mitochondrial coupled (MP) reduces (OXPHOS) capacity and uncouples respiration (relative to maximal capacity of MRC) but promotes a significant increase in fatty acid oxidation. Either exposure to BPA or BPS leads to an increase in mitochondrial derived reactive oxygen species, mainly at complex I. Additionally, BPA and BPS significantly upregulate the expression levels of dynamin-related protein 1 related to mitochondrial fission, while BPA downregulates the expression of profission-activated receptor gamma coactivator 1 alpha, a known regulator of mitochondrial biogenesis. In summary, our data shows that exposure to both compounds alters metabolic homeostasis and mitochondrial energy metabolism, providing new mechanisms by which BPA and BPS impair the mitochondrial metabolism.	Food Chem Toxicol Vol.132 Pages 110694	10.1016/j.fct.2019.110694	31344369	動物	-	1	1	1	1	0	50 μg/kg bw	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1441	L. F. Azevedo, M. F. Homoc Carneiro, C. R. P. Dechandt, J. S. Cassoli, L. C. Alberici and F. Barbosa, Jr.	2020	Global liver proteomic analysis of Wistar rats chronically exposed to low-levels of bisphenol A and S	Exposure to bisphenol A (BPA) and bisphenol S (BPS) has been associated with the development of metabolic disorders, such as obesity, dyslipidemias, and nonalcoholic fatty liver disease. Nonetheless, the associated mechanisms are still not fully understood. BPS is being used with no restrictions to replace BPA, which increases the concern regarding its safety and claims for further investigation on its potential mechanisms of toxicity. Therefore, we performed a global liver proteomic analysis of male Wistar rats exposed to BPA or BPS (0.5 mg/kg bw/day) for 90 days. Biochemical and morphometric parameters were measured in male Wistar rats chronically exposed to 50 or 500 μg/kg bw of BPA or BPS, unlike endocrine mechanisms of liver proteome expression. Our results revealed that exposure to 50 μg/kg/day of both compounds. Exposure to the lowest dose of BPA led to the development of hyperglycemia and hypercholesterolemia, while the BPS dose led to the development of hypertriglyceridemia. Besides, exposure to 500 μg/kg/day of BPS significantly increased body weight gain and LDL cholesterol levels. Hepatic proteins differentially expressed in BPS and BPS exposed groups compared to the control group were mostly related to lipid metabolism and synthesis, with upregulation of glutathione activity related to exposure 2 (LDI fold in BPA and 2.5 fold in BPS), which is involved in glycerol triglycerides synthesis, and butyrobetaine/glutaryl CoA dioxygenase (BBOX1), which is involved in fatty acid oxidation. Besides, BPA and BPS induced oxidative stress in the liver, as demonstrated by the increase in the activity of SOD and GPX1 and BPS-dysregulated expression of liver antioxidant enzymes, which are involved in cellular reactive oxygen species detoxification. Altogether, the results of the present study contribute to expand the scientific understanding of how BPA and BPS lead to the development of metabolic disorders and reinforce the risks associated with exposure to these contaminants.	Environ Res Vol.182 Pages 109080	10.1016/j.envres.2019.109080	31901629	動物	-	1	不明	1	1	0	50, 500 μg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1442	S. Aydemir, C. Öztoy, O. Özkan, Ş. Kum and M. Tuğlu	2020	Investigation of the effects of bisphenol-A exposure on lymphoid system in prenatal stage	Bisphenol-A (BPA) used in the production of plastic materials is a omnipresent volatile agent. It also has a steroid hormone-like activity therefore, it poses a danger to human health. In our study, we aimed to investigate the effects of BPA on lymph node and spleen in male rats exposed to this agent during prenatal stage. The pregnant female rats were divided into four groups; control, olive (corn oil), low dose (100 μg/kg BPA), and high dose (1000 μg/kg BPA). BPA was dissolved in 1 mL of corn oil and administered to the pregnant rats every day during pregnancy. On the 21st and 45th day after the birth, male rats' lymph node and spleen samples were taken and histopathological examinations were performed. Samples were stained with hematoxylin and eosin to determine the histological changes. Apoptotic cells were detected by immunohistochemistry. The results of staining were evaluated by H-score, and statistical analysis was performed. In the samples, BPA applications were not found to cause significant tissue damage. But there was a significant decrease in the immunoreactivities of CD3 and CD20 after BPA applications in both 21st and 45th day samples. When high dose BPA administration, decreased CD3 immunoreactivity was statistically significant. It is thought that BPA does not cause histologically significant tissue damage, but it may impair organ function at cellular level. The investigation of molecules involved in organ function will be useful in revealing the mechanisms that will cause dysfunction.	Toxicol Ind Health Vol.36 Issue 7 Pages 502-513	10.1177/0748233720941759	32696725	動物	-	1	不明	1	不明	0	200, 600 μg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1443	B. Attema, O. Kummu, S. Pihlajen, J. Weisell, T. Vuoisi, E. Penonen, M. Vorinn, J. Rysä, S. Kersten, A. L. Leonen and J. Hakkola	2024	Metabolic effects of nuclear receptor activation in vivo after 28-day oral exposure to three endocrine-disrupting chemicals	Environmental exposure to endocrine-disrupting chemicals (EDCs) can lead to metabolic disruption, resulting in metabolic complications including adiposity, dyslipidemia, hepatic lipid accumulation, and glucose intolerance. Hepatic nuclear receptor activation is one of the mechanisms mediating metabolic effects of EDCs. Here, we investigated the potential to use a repeated dose 28-day oral toxicity test for identification of metabolic effects of EDCs. Female Wistar Han RCC rats were exposed to 3 EDCs, tributyltin (TBT), bisphenol A (BPA), and 17α-ethinylestradiol (EE), for 28 days by gavage. BPA had no significant metabolic effects. TBT and EE induced hepatic expression of lipid anabolic genes and reduced circulating triglycerides. TBT exposure increased serum TG, BG and HDL-c at 100 μg/kg/d and 300 μg/kg/d, HDL-C at 1000, and 300, 600 μg/kg/d of TBT and EE, respectively. TBT and EE also induced hepatic steatosis. TBT and EE also induced hepatic expression of typical prototypic X receptor (PXR) and peroxisome proliferator-activated receptor (PPAR)α target genes, respectively. Exposure to BPA resulted in limited gene expression changes. In conclusion, the observed changes in metabolic health parameters were modest, suggesting that a standard repeated dose 28-day oral toxicity test is not a sensitive method for the detection of the metabolic effects of EDCs.	Arch Toxicol. 2024 Mar;98(3):911-928.	10.1007/s00204-023-03658-2	38182912	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-	-
統合_1444	A. Aslantuk and M. Uzunhisarcikli	2020	Protective potential of curcumin or taurine on nephrotoxicity caused by bisphenol A	Bisphenol A (BPA) received heightened attention in the recent years due to humans continuously being exposed to it. This study explores the effect of taurine or curcumin on subacute BPA treatment-induced nephrotoxicity in rats. Wistar albino rats (n=24) were exposed to BPA (130 mg/kg/day) for 28 days by gavage. Curcumin (200 mg/kg/day) and taurine (200 mg/kg/day) were administered to BPA-treated rats. Antioxidant enzyme activities like catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione S-transferase (GST), BPA exposure also induced histopathological changes like tubular and glomerular degeneration, vascular congestion, and interstitial cell infiltration in kidney tissue. Concurrent with taurine (200 mg/kg/day daily) or curcumin (200 mg/kg/day) administered the lipid peroxidation level and antioxidant enzyme activities and histological alterations brought about by BPA. In this study, curcumin and taurine application provided protection against renal toxicity caused by BPA but did not prevent toxic effect completely.	Environ Sci Pollut Res Int Vol.27 Issue 19 Pages 23994-24003	10.1007/s11356-020-08716-1	32304054	動物	-	1	1	1	1	0	130 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1445	Y. Asadi-Fard, M. Z. Soleimani, M. J. Khodayar, L. Khorsandi, M. Shirazi and A. Samimi	2023	Morin improves Bisphenol-A-induced toxicity in the rat testicular mitochondria and sperms	OBJECTIVE: The present study aimed to examine the ameliorative effects of Morin (MRN) on Bisphenol A (BPA)-induced oxidative stress in testicular mitochondria and sperm quality of rats. METHODS: BPA and MRN (50 and 100 μM) were given to the spermatozoa and testicular tissue mitochondria. The sperm quality, mitochondrial stability, and MMP (mitochondrial membrane potential) were examined. Superoxide dismutase, CAT activity, and MDA level were measured in the testicular tissue mitochondria. Besides, 35 male rats were divided into five groups and received BPA and MRN (50 and 100 mg/kg/day) for 35 days. RESULTS: BPA significantly lowered the MMP, sperm viability, and motility of the sperms. MRN (four dependently) has a small stabilization activity of the mitochondria, around MMP, as well as it improved the percentage of abnormality, motility, and viability of the sperms. CONCLUSIONS: These data demonstrated that MRN dose-dependently attenuated BPA-induced mitochondrial damage and improved sperm quality by preventing oxidative stress.	IBRA Assist Reprod Vol.27 Issue 2 Pages 174-179	10.5935/1518-0557.20220010	36356172	ex vivo	-	-	-	-	-	-	-	-	-	-	-	1	0	25, 50, 100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1446	Z. Y. An, T. Zhang, G. J. Lu, X. Xu, X. Fang, S. Z. Han, S. Y. Chang, X. J. Yin, L. H. Quan and J. D. Kang	2025	Chenodeoxycholic acid improves oocyte maturation and embryo quality during bisphenol A exposure by activating the EGFR-ERK1/2 signaling pathway	Chenodeoxycholic acid (CDCA) is a fetoxific acid present in the follicular fluid surrounding growing oocytes. In this study, we demonstrate that supplementation with CDCA activates the EGFR signaling in cumulus-oocyte complexes (COCs) to improve oocyte quality. Bisphenol A (BPA), a well-documented environmental toxicant, disrupts female reproductive function. We found that BPA exposure suppressed EGFR signaling in porcine COCs, leading to meiotic arrest, increased the concentration of cGMP and cAMP. However, supplementation with CDCA improves oocyte maturation and embryo quality during BPA exposure. Cumulus cells, as essential support cells for oocytes, regulate oocyte meiotic resumption and maintenance mainly by providing energy substrates and energy. Notably, CDCA treatment of granulosa cells (GCs) significantly increased glycolysis-related enzymes (GFAs) did not significantly affect the oocyte maturation rate. These findings indicate that the influence of CDCA on oocyte development may be mediated via its action on the surrounding cumulus cells. In addition, we knocked down EGFR in cumulus cells using siRNA and found that the beneficial effects of CDCA on oocyte maturation and embryo development were eliminated. These findings demonstrate that CDCA effects oocyte quality by activating the EGFR signaling in cumulus cells. In summary, the present study reveals that CDCA promotes oocyte meiotic recovery and improves oocyte quality by activating EGFR signaling in cumulus cells, thereby enhancing the developmental potential of embryos.	Ecotoxicol Environ Saf Vol.302 Pages 118725	10.1016/j.ecoenv.2025.118725	40712544	ex vivo	-	-	-	-	-	-	-	-	-	-	-	1	0	25 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1447	M. A. S. Amin, H. M. A. Sorpol, R. H. E. Gouda and A. M. Abomgela	2023	Bisphenol A enhances apoptosis, fibrosis, and biochemical fluctuations in the liver of adult male rats with possible regression after recovery	Bisphenol A (BPA) is an environmental contaminant that might be harmful. Human exposure to BPA rate occur during the fetal and postnatal periods and extends throughout life. This study aimed to estimate the effects of oral administration of BPA on rat liver and assess the possibility of recovery after cessation. Adult male albino rats were orally administered with BPA 150 mg/kg body weight/ for 8 weeks, and then one group was left to recover for 8 weeks. Liver specimens were collected at the end of the experimental period and after the recovery period. Histological, immunohistochemical, and biochemical examinations as well as cellular apoptosis, fat accumulation, and collagenic and elastic fiber deposition were performed. Results revealed that BPA induced hepatic inflammation, ballooned hepatocytes, and necrosis with apoptosis and fibrosis. After the administration of BPA, serum levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, and bilirubin increased, while albumin and total protein decreased. Additionally, total protein, albumin, and high-density lipoproteins decreased. After a recovery for 8 weeks, hepatic cellular and vascular pathologies returned to normal, except for some inflammatory infiltration. Regarding biochemical alterations, most of the parameters were deviated toward normal during recovery. However, most of them were still significantly different from controls. This explored BPA hepatotoxicity from structural and functional aspects, and the possible spontaneous reversibility was confirmed. However, the precise mechanisms underlying hepatotoxicity or recovery need more in-depth investigations.	Anat Rec (Hoboken) Vol.306 Issue 1 Pages 213-225	10.1002/ar.25032	35773941	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1448	S. Ambreen, T. Akhtar, N. Hameed, I. Ashfaq and N. Sheikh	2019	In Vivo Evaluation of Histopathological Alterations and Trace Metals Estimation of the Small Intestine in Bisphenol A-Intoxicated Rats	BPA, a ubiquitously used plasticizer, has become one of the contaminants of emerging concern and causes many serious health implications in humans due to multiple exposure pathways. The current study was aimed at investigating the deteriorities of structures that arise by exposure of the small intestine to BPA through trace elements estimation of tissues as well as the study of serum profile. Two major groups of Wistar rats were established: one control group and the other experimental group, which was further divided into four groups based on dose (20 mg/kg bodyweight and 35 mg/kg bodyweight, respectively) and duration of exposure (3 and 12 weeks, respectively). Histological study of the small intestine showed the disordered structures in the experimental groups. The special staining performed illustrated the accumulation of calcium deposits in the small intestine and the presence of collagen fibers in the lamina propria and submucosa of the small intestine in the experimental groups. Estimation of trace elements in the tissues of the small intestine by the profiling illustrated an increase in total iron binding capacity and glucose levels and a decrease in the serum total iron level (p≤0.05). An increased expression of a proinflammatory cytokine (IFN-γ) was observed in the liver. From all these findings, it was inferred that BPA caused many structural alterations in the small intestinal tissues, which further affected its functioning. The calcium deposits seen through special staining affected the motility of the small intestine and caused its dysfunction. It was also reduced from serum profiling that BPA affected the homeostasis of iron and glucose and caused its imbalance. Also, as BPA got absorbed from the small intestine and reached the liver via the blood stream, it caused hepatocytic in the liver and led to increased inflammatory response by IFN-γ against the toxicant.	Can J Gastroenterol Hepatol Vol.2019 Pages 9292316	10.1155/2019/9292316	31886155	動物	-	1	1	1	1	0	10、25 mg/kg/体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1449	M. Alol, K. Rehman, M. S. H. Akash , A. Yaqoob and S. M. Shoaib	2022	Determination of Metabolomics Profiling in BPA-Induced Impaired Metabolism	Exposure to bisphenol A (BPA) is unavoidable and it has far-reaching negative effects on living systems. This study aimed to explore the toxic effects of BPA in an experimental animal model through a metabolomics approach. Male Sprague Dawley rats were randomly divided into two groups ($n=6$). The experimental group was orally administered BPA (50 mg/kg/day) dissolved in corn oil, while the control group received corn oil. The study was conducted for 28 days, and the results showed that BPA-treated rats showed an impairment in amino acid metabolism, taking place in the mitochondria by significantly ($p \leq 0.05$) decreasing the levels of certain amino acids, i.e., lysine, threonine, asparagine, leucine, tachycine, and glycerin acid in the urine plasma. However, the administration of 150 did prove effective against the BPA-induced intoxication and significantly ($p \leq 0.05$) increased the levels of the above-mentioned amino acids. Moreover, BPA also induced oxidative stress in the liver, as indicated by the increased activity of superoxide dismutase (SOD), superoxide dismutase (SOD), glutathione, and catalase levels and an reduction in malondialdehyde level in the BPA group confirmed the generation of oxidative stress and hepatotoxicity in the experimental mice exposed to BPA. The expression of Carnitine palmitoyltransferase I (CPT-1), carnitine palmitoyltransferase II (CPT-II), lecithin–cholesterol acyltransferase (LCAT), carnitine O-octanoyltransferase (CROT), carnitine acylcarnitine translocase (CACT), and 3-methylglutaconyl/enoyl-thioesterase methylcrotonase (HTR) genes was significantly upregulated in the liver tissue homogenates of experimental mice exposed to BPA, although HSD regulated the expression of these genes when compared with BPA-treated experimental mice. CPT-I, CPT-II, and CACT genes are located in the mitochondria and are involved in the metabolism and transportation of carnitine. Hence, this study confirms that BPA exposure induced oxidative stress, upregulated gene expression, and impaired lipid and amino acid metabolism in experimental mice.	Pharmaceutics Vol.14 Issue 11	10.3390/pharmaceutics14112496	36432690	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1450	T. F. A. Almeida, S. R. Oliveira, J. Mayra da Silva, A. L. Fernandes de Oliveira, Z. de Lourdes Cardeal, H. C. Menezes, J. M. Gomes, G. H. Campolina-Silva, C. A. Oliveira, S. Macedi, G. P. Garbi, I. M. Alves Dória, A. M. Leopoldino and T. Aparecida Silva	2021	Effects of high-dose bisphenol A on the mouse oral mucosa: A possible link with oral cancers	Bisphenol A (BPA) is an endocrine-disrupting chemical able to promote hormone-responsive tumors. The major route of BPA contamination being oral, the aim of the present study was to investigate BPA effects on oral mucosa. Swiss mice were treated by gavage with 200 mg/kg/day BPA for 30 days. Tongue and buccal mucosa were collected for histological, immunohistochemical, and ultrastructural analyses. BPA induced a significant increase in total tongue epithelium thickness (p< 0.001 and Feret and Min Feret; Squamous Cell Carcinoma (SCC); HSC3 and UM1) and Feret (p< 0.05 for HSC3 and Feret; UM1). Ki67 was also examined. In vivo, BPA was found to induce tumors and to exacerbate an increase in epithelial proliferation activity. BPA disrupted the function of keratinocytes by altering pro-survival and proliferative pathways and the secretion of cytokines and growth factors. In tumor cells, BPA induced proliferative, invasive, pro-angiogenic, and epigenetic paths. Our data highlight the harmful effects of BPA on oral mucosa and, tumorigenic and non-tumorigenic cells. Additionally, BPA may be a modifier of oral cancer cell behavior by prompting a functional shift to a more aggressive phenotype.	Environ Pollut. 2021 Oct 1;286:117296.	10.1016/j.envpol.2021.117296	33971473	動物、in vitro	-	1	1	1	1	0	200 mg/L	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1451	I. Allegui, I. Sidqefa, K. Athmaoui, N. Zammel, F. Guesmi, M. Saoudi, A. M. Giuffrè, M. S. Allegui, S. Nahdi and A. H. Hanafi	2025	Cleome arabica L. mitigates bisphenol A-induced ovarian dysfunction and inflammation in Wistar rats: biochemical, histopathological, pharmacokinetic, and in silico studies	The present study evaluated the antioxidant and anti-inflammatory properties of Cleome arabica (CA) fruit extract against bisphenol A (BPA)-induced ovarian injury in female Wistar rats. The antioxidant activity was ascertained by the total antioxidant capacity (TAC) and superoxide radical (SRC) content. For the in vivo analyses, 32 animals were divided into the following 4 groups; the control group, the BPA group (50 mg/kg BW/48 h), the BPA + CA group (50 mg/kg BW/48 h + 200 mg/kg BW/day), and the CA group (200 mg/kg BW/day). The treatment lasted 28 days. Phytochemical analysis revealed the presence of phenolic compounds, flavonoids, and tannins. Pharmacokinetic properties were also observed, indicating that the phytoconstituents of the fruit extract could reach the ovaries. Moreover, cosmetic, hymenotoxic, nonmutagenic, and nonsensitizing properties were also evaluated. The in vivo findings revealed a significant increase in body weight associated with a significant increase in plasma/C-reactive protein (CRP), proinflammatory cytokines (IL-1, IL-6, and TNF-α), and testosterone levels ($p \leq 0.05$). In addition, ovarian histological disruption was observed. However, co-administration of CA extract significantly improved ovarian histological integrity and attenuated inflammatory and androgenic disturbances. Moreover, in silico investigations showed that CA compounds, interacted more strongly with the active sites of IL-1β, IL-6, or TNF-α. The best binding energy was observed between catechin (five H bonds) and IL-1β and IL-6, as well as quercetin-3-O-rutinoside, and between neoeriocitrin and (five H bonds) and TNF-α, as H bonds) and. The present study supports the use of Cleome arabica in the treatment of infertility in female polycystic ovary syndrome (PCOS) patients.	3 Biotech. 2025 Jan;15(1):21.	10.1007/s13205-024-04169-2	39720094	動物、in vitro	-	1	不明	1	1	0	50 mg/kg BW	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1452	A. S. Al-Shami, M. Hassun, A. E. Essawy, N. Moussa and H. A. E. Abd Elkader	2025	Early-life bisphenol A exposure causes detrimental age-related changes in anxiety, depression, learning, and memory in juvenile and adult male rats: Involvement of NMDAR/PSD-95-PTEN/AKT signaling pathway	Bisphenol A (BPA) is an endocrine-disruptor monomer that is widely used in the manufacturing of epoxy resins and polycarbonate plastics. Several lines of evidence indicate the function of the pro- or perinatally PI3K/Akt/PTEN signaling pathway in the pathogenesis of neurodevelopmental disorders. Therefore, the present study was designed to investigate the effects of BPA exposure during the early stages of life on the behavioral and molecular alterations of early life BPA exposure and its long-lasting influence on juvenile and adulthood stages of development. We investigated the effects of oral BPA doses of 10 and 25 mg/kg/day on the prefrontal cortex (PFC) and hippocampus of male Sprague-Dawley rats from postnatal day (PND) 18 and PND 28-90, which corresponds to juvenile and adolescent stages, respectively. Subsequently, we performed a series of rat behavioral tests, including the open-field, elevated plus maze, forced swimming, and Y-maze. Notably, neurotransmitter levels such as dopamine, serotonin, and gamma-aminobutyric acid, levels of postsynaptic density protein 95 and cAMP response element-binding protein, as well as mRNA levels of N-methyl-D-aspartate receptor subunits, fluctuated between reduction and elevation in the PFC and hippocampus. Furthermore, phosphatase and tensin homolog deleted on chromosome ten (PTEN) and protein kinase B (AKT) mRNA levels were significantly altered in the PFC and hippocampus. Our findings indicate that BPA exposure promotes long-term anxiety and depressive-like behaviors, as well as cognitive impairment, via modulation of the NMDAR/PSD-95-PTEN/AKT pathway. These findings could help to elucidate the potential developmental and neurobehavioral effects of early-life BPA exposure.	Neurotoxicology Vol.106 Pages 17-36	10.1016/j.neuro.2024.11.006	39617347	動物	-	1	1	1	1	0	50, 125 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原則に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献（716報）	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1453	A. S. Al-Shami, H. A. E. Abd Elkader, N. Moussa, A. E. Essawy and M. Hanun	2025	Early-life bisphenol A exposure causes neuronal pyroptosis in juvenile and adult male rats through the NF-κB/IL-1β /NLRP3/caspase-1 signaling pathway: exploration of age and dose as effective covariates using an in vivo and in silico modeling approach	Bisphenol A (BPA), a common endocrine-disrupting chemical, is found in a wide range of home plastics. Early-life BPA exposure has been linked to neurodevelopmental disorders; however, the link between neuroinflammation, pyroptosis, and the development of psychiatric disorders is rarely studied. The current study attempted to investigate the toxic effect of BPA on inflammatory and neuroglial activation markers, as well as behavioral responses, in the brains of male rats in a dose- and age-dependent manner. Early BPA exposure began on postnatal day (PND) 13 at dosages of 10 and 125 mg/kg/day. We started with a battery of behavioral tests, including the open field test (OFT), elevated plus maze (EPM), and novel object recognition test (NORT), on PND 35 and PND 60 to assess the behavioral responses of juvenile and adult rats. In silico analysis revealed for the first time that BPA is a substantial activator of nuclear factor kappa B (NF-κB) chemokine (C-C motif) ligand 2 (CCL2), cysteinyl aspartate 1, and the NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome, with higher Vina Dock 1 and CLSPR levels in BPA-rats' PFC and hippocampus. Furthermore, BPA increased the co-localization of caspase-1 immunoreactive neurons, as well as unique neurodegenerative histopathological hallmarks. In conclusion, our results support the hypothesis that neuroinflammation and neuroglial activation are involved with changes in the brain after postnatal BPA exposure and that these alterations may be linked to the development of psychiatric conditions later in life. Collectively, our findings indicate that BPA triggers anxiety-like behaviors and pyroptotic death of nerve cells via the NF-κB/IL-1β/NLRP3/caspase-1 pathway.	Mol Cell Biochem Vol.480 Issue 4 Pages 2301-2330	10.1007/s11010-024-05039-4	38941031	動物	-	1	1	1	1	0	50, 125 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1454	M. A. Al-Griw, S. M. Zaed, I. M. Hilal and T. Shabi	2023	Vitamin D ameliorates liver pathology in mice caused by exposure to endocrine disruptor bisphenol A	BACKGROUND: Increasing evidence suggests that bisphenol A (BPA) induces liver pathological changes. Further, an association between BPA and circulating vitamin D (VitD) levels were documented. AIM: The role of VitD in BPA-induced liver pathological changes was explored in this study. METHODS: Healthy 6-7 week-old male (n = 35) and female (n = 35) Swiss albino mice were used in this study. The animals were randomly divided into control and treated groups. The control groups were further divided into sham (no treatment) and vehicle (corn oil), whereas the treated groups were also divided into VitD (1500 i.U/kg), BPA (50 μg/kg), and BPA + VitD (50 μg/kg + 1500 i.U/kg) groups. For 6 weeks, hence a week, the animals were dosed intraperitoneally. One week later (at 10-11 weeks -old), the animals were sacrificed for biochemical and histological analyses. RESULTS: BPA produces a considerable rise in the body and liver weights, in both genders of mice when compared to control mice. BPA also caused significant increases in the liver damage markers, alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) in both genders of mice. Furthermore, BPA increased the liver lipid peroxidation marker, malondialdehyde (MDA), while it significantly reduced liver damage and slightly decreased the apoptotic index rate. The ALP, ALT, and AST levels were also markedly reduced. VitD has been proven to have a protective effect on both genders. CONCLUSIONS: According to our findings, VitD protects mice from BPA-induced liver damage, possibly via suppressing liver damage markers.	Open Vet J Vol.13 Issue 1 Pages 90-98	10.5455/OVJ.2023.v13.i1.9	36777431	動物	-	1	0	1	1	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1455	M. A. Al-Griw, S. M. Shalabi, R. O. Alghtaswi, A. H. Elnfati, S. A. Treesh, A. E. Benjana, G. Shamlan, M. M. Habibullah, A. A. Eskeirani, A. M. Alrajawi, N. A. Bakreen and W. S. Alansari	2023	Nigella sativa Oil Alleviates Mouse Testis and Sperm Abnormalities Induced by BPA Potentially through Redox Homeostasis	BACKGROUND: Significant evidence indicates that endocrine disrupted bisphenol A (BPA) seriously endangers human health. In males, BPA affects testis architecture and sperm quality, and ultimately reduces fertility. This study examined the therapeutic potential of Nigella sativa (NS) and extract on testis and sperm abnormalities in BPA-exposed mice and characterized the underlying mechanisms. METHODS: Forty male Swiss albino mice (5-5 weeks old, N.I. 8 per group) were randomly divided into five groups: Group1, normal control; Group 2, vehicle control (sterile corn oil); Group3, 100 mg/kg/d BPA; Group 4, BPA-exposed (100 mg/kg) Group 5, BPA-exposed (100 μg/kg body weight) mice. Animals were treated for 6 weeks, then sacrificed for biochemical and histological examination. RESULTS: The mice exposed to BPA alone showed significant testis and sperm abnormalities. Specifically, BPA promoted a marked reduction in the body and testis compared with the control group. Histopathological findings showed that BPA caused a widespread degeneration of the seminiferous tubules, germinal epithelium, and Leydig cells, and significantly reduced the sperm count, motility, and viability. Furthermore, BPA exposure increased the levels of the lipid peroxidation marker, malondialdehyde (MDA), and reduced the levels of the antioxidant marker, reducing glutathione (GSH). Treatment with NS at various doses/BPA-exposure significantly alleviated testis and sperm abnormalities, reduced MDA levels, and enhanced GSH levels. CONCLUSION: The results demonstrate that NS oil protects mice against BPA-induced sperm and testis abnormalities, likely by suppressing levels of the oxidative stress marker, MDA, and enhancing the levels of the antioxidant marker, GSH.	Comb Chem High Throughput Screen Vol.26 Issue 2 Pages 301-312	10.2174/1386207325666220514135606	35570547	動物	-	1	不明	1	1	0	400 μg/kg 体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1456	M. A. Al-Griw, Z. M. Marwan, I. M. Hilal and T. Shabi	2021	Vitamin D mitigates adult onset diseases in male and female mice induced by early-life exposure to endocrine disruptor BPA	BACKGROUND: During early development, environmental compounds can induce adult-onset diseases, and disrupt the circulating vitamin D (VitD) levels. AIM: This study aimed to examine the protective role of VitD against the adverse effects of BPA on male and female mice. METHODS: A total of 60 male and female Swiss albino mice (3 weeks, old) were randomly divided into 6 control and treated groups (2 mice in each male and female) and was treated as follows: Group I received no treatment (sham control); Group II, sterile corn oil only (vehicle control); Group III, BPA (300 μg/kg); Group IV, VitD (1,500 IU/kg) and Group V, BPA + VitD. At 10 weeks, the animals were sacrificed and investigated to conduct histological examinations. RESULTS: BPA exposure induced severe histopathological abnormalities, mean kidney, and lung diseases, with increased apoptosis, kidney, in both sexes. On the other hand, the treatment of BPA mice with VitD altered this scenario with modulated tissue activity, enhanced body and organ weights, and prevented the heart, kidney, and lung architecture, alongside a decreased percent apoptotic index. CONCLUSION: Our findings illustrate that VitD protects mice against BPA-induced heart, kidney, and lung abnormalities.	Open Vet J Vol.11 Issue 2 Pages 407-417	10.5455/OVJ.2021.v11.i3.12	34722204	動物	-	1	0	1	1	0	400 μg/kg 体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1457	M. A. Al-Griw, H. N. Balog, T. Shabi, M. F. Elmabaet, I. S. A. AbuGanjia, A. B. AlBadawi, G. Shamlan, A. Ahliga, A. A. Eskeirani, A. M. Alrajawi, N. A. Bakreen, W. S. Alansari and R. Alghazawi	2023	Therapeutic potential of vitamin D against bisphenol A-induced spleen injury in Swiss albino mice	Bisphenol A (BPA), a ubiquitous plasticizer, is capable of producing oxidative splenic injury, and ultimately led to spleen pathology. Further, a link between VitD levels and oxidative stress was reported. Hence the role of VitD in BPA-induced oxidative splenic injury was investigated in this study. Sixty male and female Swiss albino mice (5-5 weeks old) were randomly divided into 6 control and treated groups (2 mice in each male and six females) and was treated as follows: Group I received no treatment (sham control); Group II, sterile corn oil only (vehicle control); Group III, BPA (300 μg/kg); Group IV, VitD (1,500 IU/kg) and Group V, BPA + VitD. At 10 weeks, the animals were sacrificed and investigated to conduct histological examinations. RESULTS: BPA exposure induced severe histopathological abnormalities, mean kidney, and lung diseases, with increased apoptosis, kidney, in both sexes. On the other hand, the treatment of BPA mice with VitD altered this scenario with modulated tissue activity, enhanced body and organ weights, and prevented the heart, kidney, and lung architecture, alongside a decreased percent apoptotic index. CONCLUSION: Our findings illustrate that VitD protects mice against BPA-induced heart, kidney, and lung abnormalities.	PLoS One Vol.18 Issue 3 Pages e0280719	10.1371/journal.pone.0280719	36893148	動物	-	1	0	1	1	0	50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1458	M. A. Al-Griw, Z. O. Alshibani, R. Alghazwi, M. Elharchani, R. M. Tabagh, A. A. Eskeirani, W. S. Alansari, M. M. Habibulla and G. Shamlan	2022	Histone deacetylase 2 inhibitor valproic acid attenuates bisphenol A-induced liver pathology in male mice	Accumulating evidence indicates the role of endocrine disruptor bisphenol A (BPA) in many pathological conditions. Histone deacetylase (HDAC) inhibition has potential for the treatment of many diseases/abnormalities. Using a mouse BPA exposure model, this study investigated the hepatoprotective effects of the FDA-approved Drug Administration exposed HDAC2 inhibitor valproic acid (VPA) against BPA-induced liver pathology. Six randomly divided 30 adult male Swiss albino mice (8 weeks old; N = 6) mice/liver groups; group I, no treatment (sham-control (SC)); group 2, only oral sterile corn oil (vehicle control (VC)) group 3, 5 mg/kg/day of oral BPA (BPA-5); group 4, 10 mg/kg/day of oral BPA (BPA-10); group 5, 300 mg/kg/day of oral VPA (VPA); and group 6, BPA-10 + VPA (BPA-10 + VPA) were treated for 28 days. BPA administration considerably exacerbated a significant decrease in the body weight (BW), and increase in liver weight, and a significant increase in the levels of liver damage markers, aspartate aminotransferase and alanine aminotransferase in the BPA group compared to SC, as well as pathological changes in liver tissue. We also found an increase in the rate of apoptosis among hepatocytes. In addition, BPA significantly increased the levels of oxidative stress indices, malondialdehyde, and protein carbonylation but decreased the levels of reduced glutathione (GSH) in the BPA group compared to SC. In contrast, treatment with the HDAC2 inhibitor VPA significantly attenuated liver pathology, oxidative stress, and apoptosis and also enhanced GSH levels in VPA group and BPA + VPA group. The HDAC2 inhibitor VPA protects mice against BPA-induced liver pathology, likely by inhibiting oxidative stress and enhancing the levels of antioxidant-related GSH.	Saudi J Biol Sci Vol.28 Issue 1 Pages 948-955	10.1016/j.sjbs.2020.11.003	33424387	動物	-	1	1	1	1	0	4 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1459	M. A. Al-Griw, R. O. Alghazwe, N. M. Salama, B. A. Lwaleed, A. A. Eskandrani, W. S. Alansari, A. M. Alrajawi, N. A. Bakreen, G. Shamlan and A. H. Elnfati	2021	Paternal bisphenol A exposure induces testis and sperm pathologies in mice offspring: Possibly due to oxidative stress?	Bisphenol A (BPA), an endocrine and metabolic disruptor, is widely used to manufacture polycarbonate plastics and epoxy resins. Accumulating evidence suggests that paternal BPA exposure adversely affects male germlines and results in atypical reproductive phenotypes that might persist for generations to come. Our study investigated the exposure on testicular architecture and sperm quality in mouse offspring and characterized underlying molecular mechanism(s). A total of 18 immature male Swiss albino mice (10 weeks old) were randomly divided into three groups and treated as follows: Group I, no treatment (sham control); Group II, sterile corn oil only (vehicle control); Group III, BPA (400 μg/kg) in sterile corn oil. At 10 weeks, the animals were sacrificed and investigated to conduct histological examinations. RESULTS: BPA exposure resulted in significant decrease in the body weight (BW), and increase in liver weight, and a significant increase in the levels of liver damage markers, aspartate aminotransferase and alanine aminotransferase in the BPA group compared to SC, as well as pathological changes in liver tissue. We also found an increase in the rate of apoptosis among hepatocytes. In addition, BPA significantly increased the levels of oxidative stress indices, malondialdehyde, and protein carbonylation but decreased the levels of reduced glutathione (GSH) in the BPA group compared to SC. In contrast, treatment with the HDAC2 inhibitor VPA significantly attenuated liver pathology, oxidative stress, and apoptosis and also enhanced GSH levels in VPA group and BPA + VPA group. The HDAC2 inhibitor VPA protects mice against BPA-induced liver pathology, likely by inhibiting oxidative stress and enhancing the levels of antioxidant-related GSH.	Bisphenol A (BPA), an endocrine and metabolic disruptor, is widely used to manufacture polycarbonate plastics and epoxy resins. Accumulating evidence suggests that paternal BPA exposure adversely affects male germlines and results in atypical reproductive phenotypes that might persist for generations to come. Our study investigated the exposure on testicular architecture and sperm quality in mouse offspring and characterized underlying molecular mechanism(s). A total of 18 immature male Swiss albino mice (10 weeks old) were randomly divided into three groups and treated as follows: Group I, no treatment (sham control); Group II, sterile corn oil only (vehicle control); Group III, BPA (400 μg/kg) in sterile corn oil. At 10 weeks, the animals were sacrificed and investigated to conduct histological examinations. RESULTS: BPA exposure resulted in significant decrease in the body weight (BW), and increase in liver weight, and a significant increase in the levels of liver damage markers, aspartate aminotransferase and alanine aminotransferase in the BPA group compared to SC, as well as pathological changes in liver tissue. We also found an increase in the rate of apoptosis among hepatocytes. In addition, BPA significantly increased the levels of oxidative stress indices, malondialdehyde, and protein carbonylation but decreased the levels of reduced glutathione (GSH) in the BPA group compared to SC. In contrast, treatment with the HDAC2 inhibitor VPA significantly attenuated liver pathology, oxidative stress, and apoptosis and also enhanced GSH levels in VPA group and BPA + VPA group. The HDAC2 inhibitor VPA protects mice against BPA-induced liver pathology, likely by inhibiting oxidative stress and enhancing the levels of antioxidant-related GSH.	Saudi J Biol Sci Vol.28 Issue 1 Pages 948-955	10.1016/j.sjbs.2020.11.003	33424387	動物	-	1	0	1	1	0	400 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1460	R. Al-Eisa, F. Alsaleni, R. K. Zaish, H. Hamd, R. Sami, S. Alsuchal, N. A. Alghelaiy, M. Alarasi, F. Tayeb, A. A. Hassani, A. M. Almehmadi, N. Alfehyani and A. A. Abu-Zaid	2024	Protective roles of herbal teas against the toxicity of Bisphenol A on morphometry of uterus and improving murine reproductive health (incomplete title and amended by the EIC)	The purpose of the current study was to investigate the potential ameliorating rector reproductive effects of herbal tea extracts against bisphenol A induced (BPA) cytotoxicity. A comparative study was applied among 40 mature female albino rats divided into four groups (10 rats/group). The first group was the negative control group, the second group received BPA (50 mg/kg/day) dissolved in corn oil, and the third and fourth groups received the same dosage of BPA and the herbal tea extracts (Thymus vulgaris and Matricaria chamomilla), respectively, for 14 consecutive days. The uterine weights of the mice groups with herbal teas ranged from 0.12g to 0.17 g. Thus Pumping weights of litter from dams after exposure to BPA and various herbal teas ranged from 13.56g to 15.21g and from 24.09 to 26.91 g for females and males, respectively. The BPA toxicity exposure increased BUL levels to reach 35.28g/ml in the BPA + BPA group as compared with the negative control group (20.15 mg/ml). The exposure to BPA toxins decreased the leptin level in the negative control group from 32.85ng/ml to 24.93ng/ml in the BPA + BPA group, while the cortisol levels reached 31.0ng/ml in the CTX + BPA group. The appearance of the luminal epithelial cells and endometrium in the BPA + BPA group was close to normal. It was indicated that herbal teas, particularly thyme tea can be able to improve necrin reproductive, while the harmful effects of BPA cannot entirely be mitigated.	Pak J Pharm Sci. 2024 Nov-Dec;37(6):1281-1287.	-	39799443	動物	-	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1461	M. S. Akhter, H. Rashid, H. A. Hamid, S. Alshikani, L. Dobbs, M. Qadri, A. M. Mukthal and A. A. Mobaki	2023	Hematotoxicity of Co-Administration of Bisphenol A and Acetaminophen in Rats and Its Amelioration by Melatonin	BACKGROUND: Hematotoxicity is an extraorganismal endpoint of toxicity in most of the chemical exposures. An adverse effect on the hematological system arising out of xenobiotic exposure causes impaired hemostasis and coagulation leading to disease. BPA and acetaminophen are widely used synthetic chemicals, worldwide and both are known and have numerous toxic effects. Since both are simultaneously exposed to humans over a period of time, we hypothesized that their exposure can cause hematotoxicity, which may be ameliorated by melatonin. OBJECTIVE: In the current study, we aimed to find the effect of single and co-treatment of bisphenol A and acetaminophen in rats. Also, the ameliorative potential of melatonin was investigated against the toxicity induced by co-exposure. METHODS: In a 28-day repeated dose oral toxicity study, male and female rats were divided into seven groups and received vehicle, bisphenol A, acetaminophen, and bisphenol A plus acetaminophen for 28 days. The effect of melatonin as a hemato-protectant agent was assessed in the co-exposure. RESULTS: An increase in RBC oxidative stress, and decrease in bleeding time, blood clotting time, prothrombin time, and partial thromboplastin time along with an increase in fibrinogen levels were observed with bisphenol A and acetaminophen treatment, which were further aggravated with concomitant of the two. Melatonin treatment, however, was seen to decrease the increase in oxidative stress and ameliorate the impairment in coagulation factors. CONCLUSION: Bisphenol A and acetaminophen cause an increase in the oxidative stress in the red blood cells, and cause a shift toward pro-coagulation, which is alleviated by treatment with melatonin.	Endocr Metab Immune Disord Drug Targets. 2023;23(2):222-229.	10.2174/1871530322666220607124757	35674302	動物	血液毒性	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1462	N. C. Akçay, S. Ömeroğlu, A. Dizakar SÖ, M. Kesoğlu, İ. Türkoğlu, M. A. Eşmekaya and T. V. Peker	2020	The effects of melatonin on possible damage that will occur on adipocytokines and liver tissue by coadministration of fructose and bisphenol a (BPA)	BPA, one of the environmental endocrine disruptors, and fructose, reason of liver steatosis which is frequently encountered in the daily diet, contributes to the formation of metabolic syndrome (MetS). This study examines the possible effects of consumer fructose and BPA administration on MetS and determines the effects of melatonin on this process. In the seven identified groups, a total of forty-two adult male Sprague Dawley rats, weighing between 250 and 300 g, were randomly distributed. Control group received 0.5% CMC-Na by oral gavage for 30 days. Fructose group received 10% fructose + 0.5% CMC-Na by oral gavage for 30 days. BPA group received fructose + 25 mg/kg BPA + 25 mg/kg melatonin, group 6 (25 mg/kg BPA + 25 mg/kg melatonin) received 10% fructose + 25 mg/kg BPA + 25 mg/kg melatonin. At the end of 30 days, serum, immunohistochemical, and biochemical procedures were performed on liver tissue. As a result, it was seen that BPA and fructose + BPA induced morphological alteration and inflammation and increased intracellular lipid quantity and amount of collagen and reticulin fibers. The percentage of apoptotic liver cells substantially amounts F H2O2 was lower in group 2 compared to the group 5 (p < 0.001) and also in group 3 compared to the group 5 (p < 0.001). Both BPA and fructose application caused an increase in lipid peroxidation level due to the increase of oxidative stress. Application of melatonin reduced antioxidant enzyme activity and reduced lipid peroxidation level. Our results indicate that fructose and BPA administration triggered the formation of MetS, whereas melatonin treated these variations, although not entirely.	Environ Sci Pollut Res Int Vol.27 Issue 14 Pages 16231-16245	10.1007/s11356-020-08041-7	32124283	動物	-	1	不明	1	1	0	25 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1463	M. S. H. Akash, M. Fatima, K. Rehman, Q. Rehman, Z. Chaudhary, A. Nadeem and T. M. Ijaz	2023	Resveratrol Mitigates Bisphenol A-Induced Metabolic Disruptions: Insights from Experimental Studies	The aim of this study was to investigate the disruptions of metabolic pathways induced by bisphenol A (BPA) and explore the potential therapeutic intervention provided by resveratrol (RSV) in mitigating these disruptions. Male Sprague-Dawley rats were randomly assigned to four groups: control, BPA (50 mg/kg of BW), RSV (20 mg/kg of BW), and BPA + RSV (50 mg/kg of BW + 20 mg/kg of BW). RSV (20 mg/kg of BW) was administered by oral gavage, while BPA (50 mg/kg of BW) was administered via drinking water. After the treatment period, various biomarkers and gene expressions were measured to assess the effects of BPA and the potential protective effects of RSV. The results revealed that BPA exposure significantly increased the serum levels of α-amylase, α-glucosidase, GIPC, insulin, HbA1c, HMG-CoA reductase, FFAs, TGs, DPP-4, MDA, and proinflammatory cytokines such as TNF-α and IL-6. Concurrently, BPA exposure led to a reduction in the levels of antioxidant enzymes such as catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), as well as GLUT-4 and GLP-1. However, the administration of RSV along with BPA significantly ameliorated these alterations in the biomarker levels induced through BPA exposure. RSV treatment effectively reduced the elevated levels of α-amylase, α-glucosidase, GIPC, insulin, HbA1c, HMG-CoA reductase, FFAs, TGs, DPP-4, MDA, and proinflammatory cytokines (TNF-α and IL-6) while enhancing the activities of CAT, GPx, and SOD. BPA exposure suppressed the mRNA expression of glucokinase (GCK). Insulin-like growth factor 1 (IGF-1), and glucose transporter 2 (GLUT2) and up-regulated the mRNA expression of uncoupling protein 2 (UCP2), which are key indicators of critical biomarkers involved in glucose metabolism and insulin regulation. In contrast, RSV treatment effectively restored the altered mRNA expressions of these biomarkers, indicating its potential to modulate glucose metabolism and insulin sensitivity. In conclusion, the findings of this study strongly suggest that RSV holds promise as a therapeutic intervention for BPA-induced metabolic disorders. By mitigating disturbances in various metabolic pathways and modulating gene expressions related to glucose metabolism and insulin regulation, RSV shows potential in reversing normal metabolic function and counteracting the adverse effects induced by BPA exposure. However, further research is necessary to fully understand the underlying mechanisms and optimize the dosage and duration of RSV treatment for maximum therapeutic benefits.	Molecules Vol.28 Issue 15	10.3390/molecules28155865	37570835	動物	-	1	不明	1	1	0	70 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1464	S. Akarca-Dizakar, D. Erdoğan, T. Peker, N. Coş kun Akçay, İ. Türkoğlu, M. A. Eşmekaya and S. Ö meroğlu	2020	Effects of co-administered melatonin, fructose and bisphenol A (BPA) on rat epididymis and sperm characteristics	Consumption of fructose-rich food and exposure to endocrine disrupting chemicals continue to increase. High fructose consumption is associated with increased incidence of dyslipidemia, hypertension, hyperuricemia and insulin resistance. Bisphenol A (BPA) is an environmental contaminant that exhibits estrogen-like activity. It impairs reproductive organs, sperm production, spermatogenesis and fertility. We investigated the possible ameliorative effects of melatonin on rat epididymis and sperm characteristics following exposure to fructose and BPA. We used 32 adult male Sprague Dawley rats divided into seven groups. Group1, control group, was treated with 25 mg/kg ethanol. F 25 mg/kg BPA and 25 mg/kg melatonin. Group 2 was treated with 10% fructose. Group 3 was treated with 25 mg/kg BPA. Group 4 was treated with 10% fructose and 25 mg/kg BPA. Group 5 was treated with 10% fructose and 25 mg/kg melatonin. Group 6 was treated with 25 mg/kg BPA and 25 mg/kg melatonin. Group 7 was treated with 10% fructose, 25 mg/kg BPA and 25 mg/kg melatonin. After 60 days, epididymal tissue was removed and sperm was collected from cauda epididymis. Sperm motility, viability, concentration, morphology were examined, and sperm-motility and viability were investigated. Administration of BPA caused significant damage in both epididymal tissue and sperm quality. melatonin reduced the damage, but did not prevent it completely.	Biotech Histochem Vol.95 Issue 1 Pages 18-26	10.1080/10520295.2019.1627418	31482760	動物	-	1	不明	1	1	0	25 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1465	T. O. Ajibade, O. O. Esan, I. M. Oseweve, M. O. Adetona, G. O. Aina, O. I. Azeez, A. D. Oloruwae, A. A. Oyagbemi, O. E. Ola-Davies, T. O. Omobowale, A. B. Saba, A. A. Adedapo, M. A. Yakubu and O. O. Ogunmiloju	2024	Cardiovascular and renal oxidative stress-mediated toxicities associated with bisphenol-A exposures are mitigated by Curcuma longa in rats	OBJECTIVE: Curcuma longa (Turmeric (CLT)), due to its potent antioxidant phytochemical constituents, was investigated for its effects on bisphenol-A (BPA)-induced cardiovascular and renal damage. MATERIALS AND METHODS: Twenty-four male rats were randomly assigned into four groups (n = 6) and treated orally (by gavage) as follows: Group I (control): 1 mL/kg distilled water; Group II: BPA (50 mg/kg); and Group III (CLT (50 mg/kg) and Group IV: BPA + CLT (50 mg/kg + 50 mg/kg) for 28 days. Cardiac and renal oxidative stress markers, antioxidant status, blood pressure parameters, genotoxicity, and immunohistochemistry were determined. RESULTS: Rats exposed to the toxic effects of BPA had heightened blood pressure, favored frequency of micronucleated polychromatic erythrocytes, and decreased activities of antioxidant enzymes compared with rats treated with CLT. Moreover, administration of CLT significantly (p<0.05) lowered malondialdehyde concentration and restored the serum myeloperoxidase activity. Immunohistochemical evaluation revealed significantly (p<0.05) increased expressions of cardiac troponin I and Caspase-3 in the BPA group compared with the CLT-treated groups. CONCLUSION: C. longa ameliorated cardiotoxic and nephrotoxic actions of bisphenol-A via mitigation of oxidative stress, hypertension, and genotoxicity.	Avicenna J Phytomed Vol.14 Issue 2 Pages 202-214	10.22038/ajp.2023.23367	38966628	動物	-	1	不明	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価へ進め、当該物質評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1466	P. M. Aja, H. A. Ogwuzi, P. C. Agu, E. U. Ekpono, J. N. Awoke, O. U. Ukachi, O. U. Oji, B. A. Aja, C. P. Nweke, I. O. Igwenyi, E. U. Aloke, D. C. Chukwu, C. E. Offor, A. A. Anuk, E. D. Eze, O. E. Yakubu, J. B. Akobi, O. G. Arc and C. G. Awuchi	2023	Cucumeropsis mannii seed oil protects against Bisphenol A-induced testicular mitochondrial damages	There has been increasing search for the ameliorative properties of seed oils against toxicants. Bisphenol A acts as an estrogenic endocrine disrupting chemical capable of causing male infertility. This study aimed to explore Cucumeropsis mannii seed oil effects against mitochondrial damage in rats using bisphenol A. Forty-eight rats were randomly assigned to six groups (n = 8) of eight rats each and fed the same food and water throughout the study. Group 1 served as the control and received 1 ml/kg distilled water. Group 2 received BPA (50 mg/kg). Group 3 received BPA (50 mg/kg) + CSSO (100 mg/kg). Group 4 received BPA + CSSO at a ratio of 1:1. Group 5 received CSSO (100 mg/kg), and group 6 were pre-administered bisphenol A at 50 mL/kg body weight, followed by treatment with C. mannii seed oil at 7.5, 15, and 30 mL/kg body weight, respectively. Antioxidant enzymes, glutathione, reactive oxygen species, testicular volume, malondialdehyde, body weight, and testicular studies were done using standard methods. The results of the bisphenol A administered group showed a significant (p < 0.05) increase in malondialdehyde, reactive oxygen species, and testicular volume and a significant (p < 0.05) decrease in body weight, glutathione, and antioxidant enzymes. There was a significant increase in BPA-exposed rats' MDA compared to BPA-exposed rats' CSSO-treated rats (p < 0.05). Bisphenol A significantly (p < 0.05) increased testicular atrophy in comparison with that of rats exposed to BPA. Remarkably, C. mannii seed oil co-administered with bisphenol A in administration significantly reversed the abnormalities observed in the dysregulated biochemical biomarkers. Our findings suggest that C. mannii seed oil has considerable antioxidant potential which can be explored in therapeutic development against systemic toxicity induced by exposure to bisphenol A. Cucumeropsis mannii seed oil protects against bisphenol A-induced testicular mitochondria damages.	Food Sci Nutr Vol.11 Issue 6 Pages 2631-2641	10.1002/fsn3.3260	37324897	動物	-	1	1	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1467	P. M. Aja, C. O. Chiadikwadi, P. C. Agu, B. A. Aja, O. G. Arc, E. U. Ekpono, H. A. Ogwuzi, J. N. Awoke, P. N. Ogbu, L. Aja, F. E. Nwite, O. U. Ukachi, O. U. Oji, P. C. Nweke, C. O. Egwu, E. U. Ekpono, G. O. Ewa, I. O. Igwenyi, O. Turu Ibia, C. E. Offor, E. K. Mebalaguwa, E. U. Aloke, D. E. Ichi, A. Njoku, V. A. Atoki and C. G. Awuchi	2023	Cucumeropsis mannii seed oil ameliorates Bisphenol-A-induced adipokines dysfunctions and dyslipidemia	This study demonstrated the therapeutic potentials of Cucumeropsis mannii seed oil (CMSO) capable of alleviating BPA-induced dyslipidemia and adipokine dysfunction. In this study, we evaluated the effects of CMSO on adipokine dysfunctions and dyslipidemia in bisphenol-A (BPA)-induced male Wistar rats. Six-week-old 36 albino rats of 100-200g weight were assigned randomly to six groups, which received varied doses of BPA and/or CMSO. The administration of BPA and CMSO was done as the same time. Group 1 (Control) was fed pellet diet. The adipokine levels and dyslipidemia were measured using standard methods. BPA-induced significant (p < .05) increases in triglycerides, cholesterol, leptin, LDL-C, and atherogenic and coronary risk indices. In adipose tissue and plasma, as well as a decrease in adiponectin and HDL-C levels in BPA-exposed rats. Co-administration of CMSO with BPA significantly (p < .05) reversed the BPA-induced changes in the levels of the adipokines and dyslipidemia in the rats. Histological studies of the adipose tissue and liver tissue of BPA-exposed rats revealed severe damage to the tissues while the co-treating adipocytes in hearts and HDL-C in adipose tissue and plasma (p < .05). The results showed that BPA exposure increased adipose tissue as well as serum levels of the atherogenic index, triglycerides, cholesterol, coronary risk index, LDL-C, leptin, and body weight with decreased adiponectin levels and HDL-C. Treatment with CMSO reduced the toxicities caused by BPA in rats by modulating the body weight, adipocytokine/leptin levels, and lipid profiles in serum and adipose tissue. This study has shown that CMSO ameliorates BPA-induced dyslipidemia and adipokine dysfunctions. We suggest for further clinical trial to establish the clinical applications.	Food Sci Nutr Vol.11 Issue 6 Pages 2642-2653	10.1002/fsn3.3271	37324904	動物	-	1	1	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1468	M. S. Ahmed Zaki, M. A. Haidara, A. M. Abdallha, H. Mohammed, A. M. Sirag and R. A. Eid	2021	Role of dietary selenium in alleviating bisphenol A toxicity of liver albino rats: Histological, ultrastructural, and biomarker assessments	Bisphenol A (BPA) is used as a plasticizer in polycarbonate plastics. It has been used in consumer products and epoxy resins for decades as protective coatings and linings for food and beverage bottles. This carcinogen human reactions is BPA which interferes with estrogen receptors. Our study explored the ameliorative effects of selenium (Se) in male rats on liver damage caused by BPA. Rats were divided into four groups at random (n = 10/group). Group 1 (control) received 1 ml/kg olive oil, Group 2 received BPA (50 mg/kg body weight/day), Group 3 received Se (0.5 mg/kg body weight/day), and Group 4 received BPA (50 mg/kg body weight/day) were given orally in the fourth one. Liver specimens were prepared for light, electron microscopic and the serum samples were screened for biochemical markers. In the BPA-received group, histological findings indicated apoptotic hepatic histological changes such as sinusoidal congestion, cytoplasmic vacuolation and leukocyte infiltration. Ultrastructurally, the same group had mitochondrial degeneration, endoplasmic reticulum dilation, and nuclear membrane irregularity. Biochemical markers revealed significant (p < 0.05) increases in aspartate transaminase (AST), alanine transaminase (ALT), serum urea, and creatinine concentrations. Serum AST, ALT, and ALP levels were lowered significantly (p < 0.05) in the Se-supplied treated with BPA and Se. Also, total protein (TP), albumin, and globulin levels were restored. Besides, histological and ultrastructural improvements were seen in the Se-supplied treated with BPA and Se. Also, AST, ALT levels were lowered, and malondialdehyde (MDA), glutathione peroxidase (GPx), Human C-reactive protein (hCRP), and the serum levels of interleukin-6 (IL-6) were significantly mediated. PRACTICAL APPLICATIONS Bisphenol A (BPA) is used in the manufacturing of polycarbonate plastic (e.g., water bottles, baby bottles) and epoxy resins (e.g., liner coating in metallic food cans). It is a rare polymer preservative for other plastics, one of the contaminants of the atmosphere and a common endocrine estrogenic disruptor. Our study explored the ameliorative effects of selenium (Se) in male rats on liver damage caused by BPA. Rats were divided into four groups at random (n = 10/group). Group 1 (control) received 1 ml/kg olive oil, Group 2 received BPA (50 mg/kg body weight/day), Group 3 received Se (0.5 mg/kg body weight/day), and Group 4 received BPA (50 mg/kg body weight/day) were given in the fourth one. Liver specimens were prepared for light, electron microscopes and the serum samples were screened for biochemical markers.	J Food Biochem Vol.45 Issue 5 Pages e13725	10.1111/jfbc.13725	33847390	動物	-	1	1	1	不明	0	10 mg/kg 体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1469	P. C. Agu, P. M. Aja, E. Ekpono Ugbala, H. A. Ogwuzi, E. M. Ezeh, P. C. Oscar-Amobi, A. Asuk Ateogbe, O. G. Arc, J. N. Awoke, K. E. Ndefo, O. U. Ukachi, O. U. Oji, C. P. Nweke, E. Ekpono Ugbala, G. O. Ewa, I. O. Igwenyi, C. O. Egwu, E. U. Aloke, D. C. Chukwu and A. C. Fortunatus	2022	Cucumeropsis mannii seed oil (CMSO) attenuates alterations in testicular biochemistry and histology against Bisphenol a-induced toxicity in male Wister albino rats	BACKGROUND: Male reproductive health has deteriorated in recent years as a result of industrialization, which has led to the use of desirable chemicals, like Bisphenol A (BPA), of underlying toxicity. Cucumeropsis mannii seed is a common soup thickener that produces vegetable oil as well as nourishful nutrients, making it a source of nutraceuticals endowed with a wide range of therapeutic effects. METHODS: A total of 36 adult albino rats (100-200 g b.w.) were randomly assigned to six groups (n = 6) and treated as follows: Group 1 received 1 ml/kg b.w. distilled water, Group 2 received BPA (50 mg/kg b.w.), Group 3 received CSSO (100 mg/kg b.w.), BPA (50 mg/kg b.w.) and CSSO (100 mg/kg b.w.), Group 4 received BPA (50 mg/kg b.w.) and CSSO (50 mg/kg b.w.), Group 5 received BPA (50 mg/kg b.w.) and CSSO (25 mg/kg b.w.), and Group 6 received BPA (50 mg/kg b.w.) for 28 days. At the end of the administration period, the animals were anesthetized and testes were collected for biochemistry and histological analysis. RESULTS: BPA significantly (P < 0.05) decreased adult testicular protein, epididymal sperm parameters, lysosh volume, and ovel(ls). Mitochondrial Membrane Potential (MMP), body weight, testicular volume, and significantly (P < 0.05) increased testicular oxidative stress markers (testicular phosphatase and lactate dehydrogenase), testicular histological damages. Interestingly, co-administration of BPA and CSSO significantly (P < 0.05) reversed the biochemical and histological changes. CONCLUSIONS: CMSO prevented the biochemistry and histological alterations hence reducing the testicular toxicity. Therefore, CMSO has the potential to be a promising novel nutraceutical for the treatment and management of BPA-induced testicular toxicity.	Heliyon Vol.8 Issue 3 Pages e09162	10.1016/j.heliyon.2022.e09162	35846473	動物	-	1	1	1	1	0	10 mg/kg 体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1470	A. A. Adeyanju, E. A. Akinsuyi-mi, M. E. Kanigidi, O. O. Agboola and O. O. Elekofehinti	2025	Cinnamic acid abrogates bisphenol A-induced hepatotoxicity via suppression of pro-inflammatory cytokine and modulation of gene expressions of antioxidant enzymes in rats	Bisphenol A (BPA) is regularly used to produce plastic products. Its hepatotoxicity has been unsettled. The effects of cinnamic acid on BPA exposure have not been comprehensively studied, and the key mechanism of action is yet to be unraveled. Rats were allocated into 5 groups. Group 1 (control) was given corn oil. Group 2 received BPA for 14 consecutive days. Group 3 received cinnamic acid at 50 mg/kg/d in combination with BPA for 14 days. Group 4 received cinnamic acid at 100 mg/kg/d in combination with BPA for 14 days. Group 5 received cinnamic acid at 100 mg/kg/d for 14 days. Liver function, oxidative stress, inflammation, and molecular markers were investigated. Cinnamic acid significantly diminished aspartate transaminase level. It also reduced the gene expression of oxidative stress biomarkers. Our results revealed that cinnamic acid upregulated the mRNA level of tumor necrosis factor-α and elevated malondialdehyde by BPA. The significantly elevated alanine transaminase and aspartate transaminase activities in addition to increased levels of total cholesterol, triglycerides, and very low-density lipoprotein-cholesterol (high-density lipoprotein-cholesterol) were determined after BPA in the liver. Our results revealed that cinnamic acid could ameliorate the increased pro-inflammatory cytokine level and oxidative stress by downregulating tumor necrosis factor-α gene. The histopathological evaluation confirmed the biochemical results. Hepatic alterations were ameliorated when cinnamic acid was co-administered with BPA. These findings suggest that the ameliorating potential of the TNF-α gene induced by cinnamic acid may participate in suppressing the BPA-induced oxidative stress. This offers a new idea to unravel the mechanism underlying cinnamic acid's ameliorative with BPA-induced hepatic damage.	Toxicol Rep Vol.14 Pages 101995	10.1016/j.toxrep.2025.101995	40226809	動物	-	1	不明	1	1	0	100 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1471	E. O. Adegoke, M. S. Rahman, S. Anjad, W. K. Pang, D. Y. Ryu, Y. I. Park and M. G. Pang	2023	Environmentally relevant doses of endocrine disrupting chemicals affect male fertility by interfering with sertoli cell glucose metabolism in mice	The growing global deterioration in several aspects of human health has been partly attributed to hazardous effects of endocrine disrupting chemicals (EDCs) exposure. Therefore, experts and government regulatory agencies have recommended the evaluation of EDCs effects on human health. Bisphenol A (BPA) and diethylhexyl phthalate (DEHP) are well-known EDCs that are widely distributed in the environment. In BPA, and phthalates compounds affect the Sertoli cell glucose uptake/lactate production to the testis and male fertility. An EDC mixture containing a detected amount of each chemical compound in humans, called Daily exposure (DE), and DE increased in magnitude by 20 (DE20), 200 (DE200), and 2000 (DE2000), and corn oil (control) were administered for six weeks to male mice. We found that DE activated estrogen receptor beta (ESR2) and glucose regulated protein 78 (Grp 78) and disrupted the metabolic ECS balance. In addition, DE20, DE200, and DE2000 doses of the EDC mixture do binding with Estradiol cells of estrogen receptors (ERs) inhibited the glucose uptake and lactate production processes by downregulating glucose transporters (GLUTs) and glycolytic enzymes. As a result, endoplasmic reticulum stress (ERS), marked by unfolded protein response (UPR) activation, was induced in the testis, which was confirmed by the upregulation of Grp 78, CCAAT/enhancer-binding protein homologous protein (CHOP), and inositol-requiring enzyme 1 alpha (IRE1α) signaling promoted antioxidant depletion, testicular cell apoptosis, abnormal regulation of the blood-testis barrier, and decreased sperm count. Therefore, these findings suggest that human and wildlife exposure to multiple environmental chemicals can produce a wide range of reproductive health complications in male mammals.	Chemosphere Vol.337 Pages 139277	10.1016/j.chemosphere.2023.139277	37364641	動物	-	1	不明	0	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1472	E. O. Adegoke, M. S. Rahman, S. Anjad, W. K. Pang, D. Y. Ryu, Y. I. Park and M. G. Pang	2022	Bisphenol A damages testicular junctional proteins transgenerationally in mice	Testicular junctions are pivotal to male fertility and regulated by constituent proteins. Increasing evidence suggests that environmental chemicals, including bisphenol A (BPA), may impact these proteins, but whether the impacts persist for generations, is not yet known. Here, we investigated the effect of BPA (a ubiquitous endocrine disrupting chemical) on testis and sperm functions and whether the effects are transferred to subsequent generations. Male mice were administered BPA (0, 5, 50 mg/kg/bw/day) for 5 weeks (F0 generation) and bred with untreated female mice to produce F1 and F2 offspring. Testes and F1 sperm were analyzed using similar procedures. Our results revealed that BPA doses decreased the levels of some junctional proteins partly by inhibiting nitric oxide synthase-nitric oxide (NOS-NO) complexation at ≥ BPA 5 PBS, at ≥BW, and activation of p38 mitogen-activated protein kinase signaling. Consequently, testicular histological abnormalities, disrupted spermiogenesis, decreased sperm count, and inability to fertilize eggs were observed in mice exposed to BPA. These effects were transferred to successive generations (F1), partly through DNA methylation, but mostly unbalanced in F1 males. Our findings suggest that paternal exposure to chemicals promoting alteration of testicular junctional proteins and its transgenerational inheritance is a key component of the origin of male reproductive health problems.	Environ Pollut Vol.302 Pages 119067	10.1016/j.envpol.2022.119067	35231543	動物	-	1	不明	1	不明	0	5、50 mg/kg体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1473	T. C. Acosu, S. A. Akanu, M. Sönmez, A. Yüce, S. Çerikaya, S. O. Cirkara, S. Kaya, G. Türk and S. G. Ur	2024	Ameliorative effects of Ganoderma lucidum (Reishi) on testicular tissue of rats exposed to bisphenol A	Bisphenol A (BPA), an endocrine disrupting chemical, is an environmental toxicant widely used in the production of polycarbonate plastics, epoxy resins and paints. Ganoderma lucidum (GDL) is a plant with biological activities widely used in Chinese medicine. The present study aims to determine the effects of GDL against testicular dysfunction in rats exposed to BPA. For this purpose, a total of 28 Sprague Dawley rats, 4 rats in each group, were used in the study. Rats were administered 25 mg/kg/bw BPA and 100 mg/kg/bw GDL by oral gavage for 8 weeks. After the treatments, the rats were sacrificed, and testicular tissues were removed. One of the testes was used for biochemical analyses, and the other for histopathologic examinations. The caudal part of the epididymis was trimmed, and semen was obtained. As a result, BPA increased MDA level in blood and testicular tissue, while GDL decreased it. BPA also decreased GSH level in testicular tissue, while GDL increased it. BPA caused a significant decrease in sperm motility, sperm density, testicular somatic weight and blood testosterone levels, increased testicular and epididymal tissue weight (p<0.001). Histopathological examination revealed that BPA caused worrying testicular tubules separation, decreased germinal cell thickness and androgen receptor number. It was determined that GDL administration preserved testicular histology. As a result, it was determined that BPA caused toxicity in the testicular tissue of rats, whereas GDL administration was ameliorative.	Pol J Vet Sci Vol.27 Issue 3 Pages 459-467	10.24425/pjvs.2024.151741	39736129	動物	-	1	1	1	1	0	25 mg/kg/bw	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1474	H. Abulehia, N. S. Mohd Nor, S. H. Sheikh Abdul Kadir, M. Abdul Aziz and S. Zulkifli	2023	The effects of trans fat diet intake on metabolic parameters and pancreatic tissue in offspring of prenatal bisphenol A exposed rats	Bisphenol A (BPA) is a plasticiser used in the manufacturing of many products and its effects on human health remain controversial. Up till now, BPA involvement in metabolic syndrome risk and development is still not fully understood. In this study, we aimed to investigate the effect of prenatal BPA exposure with postnatal trans-fat diet intake on metabolic parameters and pancreatic tissue histology. Eighteen pregnant rats were divided into control (CTL), vehicle-treated (VEH), and BPA (5 mg/kg/day) from gestational day (GD) 7 until GD21. One litter/sex/group with a offspring were fed with normal diet or trans-fat diet (TFD) from postnatal week (PND) 1 until PND61 (n). The rats were then sacrificed and the blood (biochemical analysis) and pancreatic tissues (histological analysis) were collected. Glucose, insulin, and lipid profile were measured. The study found that prenatal BPA exposure with postnatal TFD intake significantly (p < 0.05) increased the fasting blood glucose (FBG) level in male offspring compared to offspring that consumed TFD. Furthermore, the pancreatic histomorphometry was also affected whereby the study findings revealed that there was a significant increase in the mean number of pancreatic islets in rats from BPA-TFD group (9.88 ± 0.1599 islets/field, p < 0.0001) compared to those that with ND and BPA-non-exposed. In addition, the results have found that prenatal BPA exposure resulted in a significant decrease in the pancreatic islets diameter of the BPA-ND group (283.3 ± 23.26 μm, p < 0.0001) compared to all other groups. In conclusion, prenatal BPA exposure with postnatal TFD in the offspring may affect glucose homeostasis and pancreatic islets. In adulthood, and the effect may be more aggravated in late adulthood.	Sci Rep Vol.13 Issue 1 Pages 9322	10.1038/s41598-023-36043-1	37291156	動物	-	1	1	1	1	0	5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1475	H. Abulehia, N. S. Mohd Nor and S. H. Sheikh Abdul Kadir	2025	Intake of Trans-Fat Diet With Prenatal Bisphenol A Exposure Induce Global DNA Methylation in Rats Offspring	BACKGROUND: Bisphenol A (BPA) is a ubiquitous industrial compound found in an enormous variety of consumer goods such as plastics, epoxy resins, and thermal paper. Despite its widespread usage, the effects of BPA on the risk and development of metabolic syndrome are not fully understood. Prenatal exposure to BPA has been shown to disrupt the development of offspring's metabolically active tissues and increase later susceptibility to the adverse consequences of a trans-fat diet (TFD). METHODS: In this experiment, pregnant rats (n = 18) were randomly separated into three groups. These groups were treated from pregnancy day (PD) 7 until PD21 with vehicle (VEH), BPA (5 mg/kg/day), or left untreated as control (CTL). Male offspring (n = 1/litter) were fed with ND or TFD from postnatal week (PNW) 1 until PNW9. Rats were euthanized in the adult rat offspring that were exposed to prenatal BPA and subjected to postnatal TFD intake. RESULTS: The study findings have shown that there was an association between prenatal exposure to BPA and a TFD consumption and PPARγ + protein expression within all the study groups in the liver tissue. On the other hand, changes at the molecular level, as reflected by the global DNA hypermethylation induced by prenatal BPA and postnatal TFD intake in adult male SD rat offspring (PNW 32; CON-CL1/BPA). This study underscores the potential impact of prenatal BPA exposure and postnatal TFD intake on epigenetic regulation, as evidenced by global DNA hypermethylation, despite no observable changes in PPARγ + protein expression. These findings suggest that early-life environmental exposures may predispose individuals to metabolic disruptions, including diabetes and obesity, in adulthood or future generations.	Biomedicines Vol.13 Issue 2 Pages e2450	10.1002/bdr2.2450	39953946	動物	-	1	不明	不明	不明	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1476	M. M. H. Abou El-Naga, S. A. El-Hashash, E. M. Yasen, S. Lepoatti and N. A. N. Hersly	2022	Starch-Based Hydrogel Nanoparticles Loaded with Polyphenolic Compounds of Moringa Oleifera Leaf Extract Have Hepatoprotective Activity in Bisphenol A-Induced Animal Models	Bisphenol A (BPA) is an xenoestrogenic chemical used extensively in the fabrication of baby bottles, reusable plastic water bottles and polycarbonate plastic containers. The current study aims to investigate the hepatoprotective activity of Moringa oleifera Lam leaf extract (MOLE) and hydrogel NPs made of starch (MOLE-Biobee Sinoon Kharetta (BSK)) against Bisphenol A induced liver toxicity in male rats. Fabrication and characterization of hydrogel NPs formed of starch (MOLE-BSK) were investigated using FTIR, TEM, and zeta potential. The in vitro antioxidant activity was measured using DPPH and Fluorescence spectrophotometer. The potential efficacy of hydrogel NPs was studied. Compared to the results of control, the level of liver function, oxidative stress markers and lipid profile status were remodulated in the groups treated with MOLE and hydrogel NPs (Group: MOLE). Meanwhile, the group treated with BPA (Group: BPA) showed significant (p < 0.05) changes in the previously mentioned parameters. Histopathological examination of liver tissues of the group treated with BPA (Group: BPA) revealed severe damage that was repaired in the groups treated with MOLE and Group: MOLE compared to the group that received BPA alone. In the present study, MOLE and hydrogel NPs led to remarkable alterations in histological changes during BPA administration. Overall, MOLE has a potential antioxidant activity which can be used in the treatment of liver disorders.	Polymers (Basel) Vol.14 Issue 14	10.3390/polym14142846	35890622	動物	-	1	1	1	1	0	50 mg/kg/daily	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1477	O. A. R. Abo-Zaid, F. S. M. Moawad, H. A. Hassan and E. M. Moustafa	2022	Hydrogen sulfide attenuates lung injury instigated by Bisphenol-A via suppressing inflammation and oxidative stress	The xenoestrogen bisphenol-A (BPA), a commonly used industrial chemical, has been linked to endocrine disruption. The point of the study was to consider the effects of chronic BPA exposure on the respiratory system of adult female rats, and the potential mitigating benefits of Sodium hydrosulfide (NaHS), a donor of hydrogen sulfide (H2S) administration. Dated fluctuations in the bronchial lavage fluid (BALF) including total protein content, Total cell counts, Neutrophils %, IL1Β1 (interleukin adhesion molecule) 1 and TGF-β (Transforming growth factor beta) NaHS significantly reduced pro-inflammatory cytokines (IFN-β and MCAF) also reduced (i.e. 10.68 ± 1.96 ng/L, 10.68 ± 1.96 ng/L) NaHS reduced malondialdehyde and augmented activities of (SOD and GSH-Px), thereby, H2S's industrial method of action in the bronchoalveolar lavage fluid. Histopathological examination of lung tissues revealed that BPA-induced inflammation was ameliorated by NaHS. Immunohistochemical analysis revealed that NaHS regulated inflammation via the suppression of the ERK/ JNK/ p-p38MAPK signaling pathway. Subsequent inhibition of inflammation, epithelial cell injury and apoptosis, may be providing insight into essential avenues for the treatment of lung injury.	BMC Pharmacol Toxicol Vol.23 Issue 1 Pages 98	10.1186/s40360-022-00636-9	36585682	動物	-	1	0	1	1	0	150 mg/kg/ day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1478	O. A. Abo-Zaid, F. S. Moawed, H. A. Hassan and E. M. Moustafa	2022	Bisphenol-A/Radiation mediated inflammatory response activates EGFR/KRAS/ERK1/2 signaling pathway leads to lung carcinogenesis incidence	BACKGROUND: Bisphenol (BPA) and ionizing radiation exposure (IR) are potent oxidants that cause free radical induction, leading to signaling pathways activation that alters cell growth. Due to the insufficient knowledge of the impact of BPA and IR on the lungs, the current study determined the impact of BPA and IR on the lung tissue of adult female Wistar rats. METHODS: Forty Wistar female rats were used in this study and were randomly divided into four groups. The rats received BPA (50 mg/kg body weight/day for 6 weeks) and were exposed to IR at 2 Gy/week up to 12 Gy for 6 weeks. RESULTS: It was found that BPA and IR possess a harmful effect on the lungs via induction of oxidative stress, confirmed by increasing levels of malondialdehyde (MDA), nitric oxide, myeloperoxidase (MPO), and lactate dehydrogenase (LDH). Exposure to BPA and IR similarly inflammatory cytokines TNF-α, IL-6, IL-1β, growth factors such as TGF-β, and gastrin-releasing peptides. BPA/IR exposure induced phosphorylated expression of ERK1/2 and p-MEK1/2 associated with the activation of the EGFR/KRAS/ERK1/2 signaling pathway, leading to lung carcinogenesis. Our findings support the crosstalk role of two deleterious environmental pollutants BPA and IR, on the cytotoxicity in the respiratory system in the form of severe lung damage resulting in cancerous cells.	Int J Immunopathol Pharmacol Vol.36 Pages 3946320221092918	10.1177/03946320221092918	35410520	動物	-	1	0	1	1	0	150 mg/kg/体重/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1479	R. Abo-Elkoud, S. Ahmed Mohamed Abdelaziz, M. Attia Abd Elsalam and S. M. Hazraa	2022	Moringa oleifera alcoholic extract protected stomach from bisphenol A-induced gastric ulcer in rats via its anti-oxidant and anti-inflammatory activities	This study evaluated the protective potentials of Moringa oleifera leaf alcoholic extract (MOLE) against bisphenol A (BPA)-induced stomach distention and inflammation in rats. Control rats received olive oil. Second group received BPA (50 mg/kg b.w.) orally. Third group received BPA + MOLE (50 mg/kg b.w.) orally. Fourth group received MOLE (50 mg/kg b.w.) orally. All treatments were given daily for 30 days. Data revealed that BPA induced gastric ulcer as indicated by increased ulcer index, gastric volume, free acidity, total acidity, and ulcer area. Also, BPA-administered rats showed decreased gastric mucin contents, superoxide dismutase (SOD) activity, and proliferating cell nuclear antigen (PCNA) protein in stomach tissues, while it increased the thiobarbituric acid reactive substances (TBARS) and myeloperoxidase (MPO) activities. Moreover, BPA-administered rats showed increased serum levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and caspase-3 and NF-κ. Alterations in treated tissues were also observed. However, MOLE ameliorated BPA-induced gastric ulceration and significantly increased the volume of gastric juice, PABS, PCNA and IL-10 contents, SOD activity, and PCNA protein while significantly decreased thiobarbituric acid reactive substances (TBARS), MDA, TNF-α and IL-6 contents, and NF-κB and caspase-3 proteins in gastric tissue. This study indicated that MOLE protected stomach against BPA-induced gastric injury via its anti-oxidant, anti-apoptotic, and anti-inflammatory activities.	Environ Sci Pollut Res Int Vol.29 Issue 45 Pages 68830-68841	10.1007/s11356-022-20543-0	35554805	動物	-	1	1	1	1	0	50 mg/kg b.w	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1480	S. M. Abdulkareem	2022	Physiological, biochemical, and hormonal changes in rats exposed to bottled water left in a hot car and the freezer	The aim of this study was to investigate the effects of bottled water left in the car and those left in the refrigerator on the physiological and biochemical parameters of male rats. Eighteen male albino rats were randomly divided into control, car-heated bottled water (WBHC), and cooled bottled water (WBC) groups. This experiment lasted for 30 days. Blood samples were collected for the assessment of the levels of BPA and fibrinogen. Bottled water left in the car and those kept at room temperature (control), relative to the bottled water samples kept in the fridge. Bodyweight, some metabolic indicators, c-TnT and CRP levels, hematological parameters, testosterone level, and sperm quality were significantly affected by storage conditions. These results indicate that storage conditions can substantially affect the quality of bottled water, which in turn can affect the biological parameters of living organisms. Moreover, since the concentrations of BPA and Sb were least in bottled water kept in the refrigerator, we recommend that manufacturers and households should endeavor to keep bottled water under cold storage.	Int J Environ Health Res. 2022 Dec;32(12):2653-2664.	10.1080/09603123.2021.1982876	34933623	動物	代謝	1	1	0	1	0	ボトル水（常温と冷蔵）	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_1481	H. M. Abdou, H. A. E. Abd Elhader, A. H. El-Gendy and S. M. Eweda	2022	Neurotoxicity and neuroinflammatory effects of bisphenol A in male rats: the neuroprotective role of grape seed proanthocyanidins	Exposure to bisphenol A (BPA) contributes to neurological disorders, but the underlying mechanisms are still not completely understood. We studied the neurotoxic effect of BPA and how it promotes inflammation and alterations in the neurotransmitters synthesis, release, and reuptake. This study also designed to investigate the neuroprotective effect of grape seed proanthocyanidins (GSPE) against BPA-induced neurotoxicity in rats. Rats were equally divided into 4 groups: rats in 1st group received 0.5% gum, GSPE + BPA group, and GSPE group. Rats were orally treated with their respective doses (50 mg BPA/kg BW and/or 200 mg GSPE/kg BW) for 6 weeks. BPA exposure induced oxidative stress in the brain tissue as indicated by increased malondialdehyde (MDA) and nitric oxide (NO) and decreased glutathione (GSH) and superoxide dismutase (SOD) and glutathione-S-transferase (GST). BPA exposure induced a significant increase in the activities of acetylcholinesterase (AChE) and reduction in the N-ATPase and total ATPase activities in the brain. Also, BPA induces upregulation in the gene expression of the inflammatory markers, tumor necrosis factor- α (TNF- α) and cyclooxygenase-2 (COX-2), and in the tumor suppressor p53 and caspase-3 protein levels. The pretreatment with GSPE attenuates or ameliorates all the oxidative and neurotoxic parameters induced by BPA. Our results suggest that GSPE has a promising role in modulating BPA-induced neuroinflammation and neurotoxicity and its antioxidant and free radical scavenging activities may in part be responsible for such effects.	Environ Sci Pollut Res Int Vol.29 Issue 6 Pages 9257-9268	10.1007/s11356-021-16311-1	34505250	動物	-	1	1	1	不明	0	50 mg/kg/体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1482	W. Y. Abdelzaher, M. Hassan, N. F. Gamal El-Tahawy, A. Ali, D. Elrody Ali, M. N. N. Rask, Z. H. Saeed and A. Gaddawy	2025	Protective effect of modafinil in bisphenol A-induced lung injury in rats: roles of SIRT1-dependent signaling pathways	BACKGROUND AND AIM OF THE WORK: Bisphenol A (BPA) is a chemical product that is widely used as a plastic precursor. It acts directly on the kidney mitochondria, causing renal dysfunction. Tri-acetylcysteine is effective in protecting the kidneys from chemical-induced damage. Vitamin E is an antioxidant that protects cells from the damaging effects of free radicals. The aim of this study is to further evaluate and compare NAC and vitamin E to assess the methotrexate-induced nephrotoxicity.MATERIALS AND METHODS: Forty male adult albino Wistar rats were divided into 5 groups (8 rats each). Group I: control group. Group II: BPA (50 mg/kg/day) orally for 6 weeks. Group III: BPA plus vitamin E (BPA + 100 mg/kg/day). Group IV: BPA plus NAC (BPA + 150 mg/kg/day). Group V: BPA plus combined NAC and vitamin E (BPA, NAC, vitamin E were given orally at doses of 50 mg/kg, 150 mg/kg, and 100 mg/kg respectively, for 6 weeks. RESULTS: NAC and vitamin E groups showed improved kidney function tests, oxidative stress markers, and histopathological changes. Vitamin E was more effective than NAC in reducing oxidative stress and inflammation. Combining NAC and vitamin E was more effective than NAC in addition to their role in alleviation of renal histopathology. To a lesser extent, vitamin E administration showed significant improvement. However, combined NAC and vitamin E treatment showed more significance than either NAC or vitamin E separate groups. CONCLUSIONS: This study determined the substantial protective effects of NAC and/or vitamin E in BPA-induced nephrotoxicity through modulation of Nrf2 with subsequent improvement of oxidative stress and inflammation. The alleviation was more significant in combined NAC and vitamin E treatment mainly through their synergistic effect on Nrf2.	Immunopharmacol Immunotoxicol Vol.47 Issue 2 Pages 252-262	10.1080/08923973.2025.2469218	40033663	動物	-	1	不明	1	1	0	500 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1483	E. Abdelwalik, H. M. Hassan, Z. Abdallah, A. Magdy and E. A. Farrag	2022	Renoprotective effect of N-acetylcystein and vitamin E in bisphenol A-induced rat nephrotoxicity; Modulators of Nrf2/NF- κ B and ROS signaling pathway	BACKGROUND AND AIM OF THE WORK: Bisphenol A (BPA) is a chemical product that is widely used as a plastic precursor. It acts directly on the kidney mitochondria, causing renal dysfunction. N-acetylcysteine is effective in protecting the kidneys from chemical-induced damage. Vitamin E is an antioxidant that protects cells from the damaging effects of free radicals. The aim of this study is to further evaluate and compare NAC and vitamin E to assess the methotrexate-induced nephrotoxicity.MATERIALS AND METHODS: Forty male adult albino Wistar rats were divided into 5 groups (8 rats each). Group I: control group. Group II: BPA (50 mg/kg/day) orally for 6 weeks. Group III: BPA plus vitamin E (BPA + 100 mg/kg/day). Group IV: BPA plus NAC (BPA + 150 mg/kg/day). Group V: BPA plus combined NAC and vitamin E (BPA, NAC, vitamin E were given orally at doses of 50 mg/kg, 150 mg/kg, and 100 mg/kg respectively, for 6 weeks. RESULTS: NAC and vitamin E groups showed improved kidney function tests, oxidative stress markers, and histopathological changes. Vitamin E was more effective than NAC in reducing oxidative stress and inflammation. Combining NAC and vitamin E was more effective than NAC in addition to their role in alleviation of renal histopathology. To a lesser extent, vitamin E administration showed significant improvement. However, combined NAC and vitamin E treatment showed more significance than either NAC or vitamin E separate groups. CONCLUSIONS: This study determined the substantial protective effects of NAC and/or vitamin E in BPA-induced nephrotoxicity through modulation of Nrf2 with subsequent improvement of oxidative stress and inflammation. The alleviation was more significant in combined NAC and vitamin E treatment mainly through their synergistic effect on Nrf2.	Acta Biomed Vol.93 Issue 6 Pages e2022301	10.23750/abm.v93i6.13732	36533744	動物	-	1	1	1	1	0	50 mg/kg/da	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1484	A. Abdel-Wahab, K. M. A. Hussein, S. S. Ibrahim, D. El-Kassi and A. H. Abdel-Razik	2021	Developmental Programming: Physiological Impacts of Prenatal Melatonin Administration on Reproductive Capacity and Serum Triiodothyronine of Adult Female Offspring Rat Born to Moms Exposed to Bisphenol A During Pregnancy	Gestational bisphenol A (BPA) exposure induced multiple programmed diseases in the adult offsprings. Thus, this study targeted exploring the physiological impacts of melatonin (MEL) as a reprogramming strategy against in utero BPA exposure on reproductive capacity and adult F1 female rat offspring. Forty adult virgin albino Wistar female rats were divided equally into 5 groups (n = 8): group I: Sham; group II: Sham + MEL (4 mg MEL/kg B.w.i.); group III: Bisphenol A (BPA) - 10 mg/ kg/ kg B.w.i.; group IV: High dose BPA (HD) - 50 mg/kg B.w.i.; and group V: High dose BPA + MEL). Treatments were given daily by subcutaneous (s.c) injection from the 1st day of pregnancy (GD1) to the 21st day of lactation (PND21). Maternal exposure to BPA caused significant disturbances in the reproductive performance of F1 female offspring rats and their tissue samples. Findings clarified that in utero BPA exposure (both doses) increased significantly (P < 0.05) the ovarian weights and the ovarian levels of reorganized but decreased that of triiodothyronine (T3) compared to control groups. Significant increasing of serum malondialdehyde (MDA) and decreasing of total antioxidant capacity (TAC) were also detected. Both doses of BPA disturbed remarkably the ovarian cyclin and steroid hormone alterations in ovarian and uterine tissues. Interestingly, prenatal MEL co-treatment with BPA mitigated significantly all of these degenerative changes. Thus, this study first demonstrated that prenatal MEL therapy could be used as a potent reprogramming intervention against BPA-induced reproductive disorders in the adult F1 female rat offspring.	Reprod Sci Vol.28 Issue 7 Pages 1956-1966	10.1007/s43032-020-00452-8	33469879	動物	-	1	0	1	1	0	25, 250 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1485	M. K. Abdel-Rahi and N. M. Thabet	2020	Modulatory effect of methylsulfonylmethane against BPA/ γ-radiation induced neurodegenerative alterations in rats: Influence of TREM-2/DAP-12/ Syk pathway	4680 Methylsulfonylmethane (MSM), is an organosulfur compound, has many health benefits. Bisphenol-A (BPA) and γ- radiation (R) are two risky environmental contaminants that human beings are exposed to in everyday life. This work aims at unveiling the modulatory role of MSM in combating BPA and/or exposure induced neurodegenerative disorder (Alzheimer's (AD) more neuronotoxicity). 4680 METHODS Forty-two rats were randomly divided into five groups. One group was normal control and the other four groups were subjected to subacute BPA intoxication and/or exposure to fractionated weekly doses of R for 4 weeks and either untreated or treated with MSM (500 mg/kg b.w.). 4680 RESULTS Data revealed that BPA and/or R induced significant elevation in brain oxidative stress biomarkers, pro-inflammatory cytokines, tumor necrosis factor- α and interleukin-1 (IL-1), elevated R2 markers, amyloid beta (Aβ 1-42), acetylcholinesterase (AchE) activity and tau-ubiquitination in cortex and hippocampus, as well as up-regulation of microglial pro-inflammatory triggering receptor expressed on myeloid cell 2/TYRO protein (DAP-12)/spleen tyrosine kinase (Syk) pathway and its downstream targets. PLC- γ1/AKt/mTOR/NFK-b hippocampus. Also, neurodegenerative lesions were revealed in histopathological examination of cortex and hippocampus coupled with marked Aβ deposition in hippocampus. Whereas, MSM treatment improved histopathological results and ameliorated level of oxidative stress, neuroinflammation and AD markers, as well as, modulated TREM-2/DAP-12/Syk pathway. 500MPC/BCS Our data suggest that MSM afforded neuroprotection against BPA and R supporting its potential application in the associated neurodegenerative disorders.	Life Sci. 2020 Nov 1:260:118410.	10.1016/j.lfs.2020.118410	32926927	動物	神経毒性	1	0 (腹腔内)	0	1	0	0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1486	F. M. Abdel-Maksoud, F. A. Z. Ali and B. T. Akinghami	2019	Prenatal exposures to bisphenol A and di (2-ethylhexyl) phthalate disrupted seminiferous tubular development in growing male rats	Endocrine-disrupting compounds (EDCs) are found in the environment due to their use in industrial and manufacturing activities. Exposure of the population to bisphenol A (BPA) and di (2-ethylhexyl) phthalate (DEHP) is significant because they are present in many consumer products. EDCs target the reproductive tract because they express high levels of steroid hormone receptors, which act as transcriptional factors to regulate reproductive development. In the present study, timed pregnant Long-Evans female rats (n= 8-10) were administered BPA and DEHP by oral gavage at 2.5 or 25 μg/kg/body weight and 5 or 50 μg/kg body weight, respectively, from gestation day 6 through postnatal day 21. Male offspring were euthanized at 21 and 35 days of age. Testes were collected and processed for histological examination. Sertoli cells are the only somatic cells present in the testis. The FSH receptor is expressed exclusively in Sertoli cells. FSH immunohistochemistry was performed to examine FSH receptor expression as a marker for Sertoli cell differentiation. At day 35 post-partum, testes were obtained from cohorts of control and chemical-exposed male rats and processed to measure 17β -HSD and transcripts expression levels in western blots. Compared to control animals, exposure to BPA and DEHP resulted in a significant (P < 0.05) decrease in testis weight at 21 and 35 days of age and a significant (P < 0.05) decrease in testis weight at 35 days of age compared to control animals (P < 0.05). To assess qualitative cellular changes within the spermatogenic epithelium, testes were obtained from separate cohorts of male rats at 35 days of age and processed for histopathological analysis. Results showed that prenatal exposures of male rats to BPA and DEHP caused disruption of the spermatogenic epithelium evident as disorganization and atrophy of seminiferous tubules as well as desquamation of germ cells into the tubular lumen. Together, results from the present study support the view that developmental exposure to environmentally relevant levels of BPA and DEHP are associated with disruptions of testicular cell development, which have implications, for endocrine and exocrine functions of testis.	Reprod Toxicol Vol.88 Pages 85-90	10.1016/j.reprotox.2019.07.017	31369804	動物	-	1	1	1	1	0	2.5, 25 μg/kg体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1487	H. A. E. Abd Elhader, A. S. Al-Shami and H. S. Darwish	2025	Perinatal bisphenol A exposure has an age- and dose-dependent association with thyroid allostasis adaptive response, as well as anxiogenic-depressive-like and asocial behaviors in juvenile and adult male rats	Thyroid hormones are essential for brain development, and a shortage throughout the fetal and perinatal periods can result in mood disorders. Perinatal exposure to bisphenol A (BPA) affects thyroid activity and dependent processes. Indirectly during pregnancy or early postnatal life. This is particularly important because it may cause changes in brain ontogeny, increasing the risk of developing disorders later in life. The study aimed to investigate the consequences of thyroid hormone deficiency on anxiety, social, and depression behaviors, as well as disruption to thyroidperoxidase (TPO) gene expression, which influences the HPT - α/BAI 1/ND 1/ND 3/ND1 signaling pathway, leading to oxidative stress, inflammation, and DNA fragmentation in perinatal BPA exposure (PBEAD), and whether these effects can be observed in juvenile (PBEAD) and adult (PBEAD) male rats. Pregnant Sprague Dawley rats were divided into four groups. The rats in Group I were considered the control rats, while the rats in Group II were orally administered BPA (125 mg/kg/day) from PBEDI to adult age (PBEAD). Perinatal exposure to BPA causes thyroid insult, by suppressing PCG, increasing FLOX, and HPT - α B-levels these effects, in turn, down-regulate BAI 1/ND 1 signaling, resulting in DNA fragmentation within thyroid tissues. Furthermore, perinatal BPA exposure for 48 and 96 days resulted in a significant fold decrease in TPO-mRNA levels in the thyroid tissues, with an insignificant fold rise in TPO expression levels in BPA-50/60. In conclusion, the present study found that perinatal BPA exposure induced thyroid allostasis adaptive response by inhibiting the HPT - α/BAI 1/ND 1/ND3 signaling pathway and altering the transcriptional expression of TPO, where TSH reinforced a possible association with TPO activity, disrupting thyroid hormone synthesis in juvenile rats and gradual deterioration reaching the adult stage.	Physiol Behav. 2025 Jan 1:288:114732.	10.1016/j.physbeh.2024.114732	39510223	動物	甲状腺ホルモン合成	1	1	1	1	0	0	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_1488	H. A. E. Abd Elhader, H. M. Abdou, O. A. Khamiss and A. E. Essawy	2021	Anti-anxiety and antidepressant-like effects of astragaloside IV and saponins extracted from Astragalus spinosus against the bisphenol A-induced motor and cognitive impairments in a postnatal rat model of schizophrenia	Bisphenol A (BPA) is a chemical endocrine disruptor to which humans are often exposed in daily life. Postnatal administration of BPA results in schizophrenia (SCZ)-like behaviours. In rats. The present study was designed to elucidate whether treatment with astragaloside IV (AS-IV) or saponins extracted from Astragalus spinosus improves the neurobehavioural and neurochemical alterations induced by BPA. Fifty-two juvenile (PND30) male Sprague Dawley rats were divided into four groups. The rats in Group I were considered the control rats, while the rats in Group II were orally administered BPA (125 mg/kg/day) from PND30 to adult age (PND70). Rats in Group III were orally administered BPA (125 mg/kg/day) + AS-IV (20 mg/kg/day) from PND30 to PND70. Rats in Group IV were orally administered BPA (125 mg/kg/day) + saponins (20 mg/kg/day) from PND30 to PND70. Administration of AS-IV and saponins reduced rats' time hanging from the elevated plus maze, increased the entries and the crossed sectors in the open field test, and the crossed sectors in the tank test, which were all increased in rats treated with BPA alone. Additionally, these compounds improved memory impairments, restored dopamine (DA), serotonin (5-HT), and monoamine oxidase (MAO-A) levels and normalized Tph2 mRNA expression towards the control values. Taken together, it can be concluded that orally administered AS-IV and A. spinosus saponins exhibit neuroprotective effects and that these compounds can be used as therapeutic strategies against BPA-induced neuropsychiatric symptoms in a rat model of SCZ.	Environ Sci Pollut Res Int Vol.28 Issue 26 Pages 35171-35187	10.1007/s11356-021-12927-5	33666843	動物	-	1	1	1	1	0	125 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1489	K. Yin, X. Sun, Y. Zhang, W. Zhang and H. Lin	2023	Bisphenol A exacerbates selenium deficiency-induced pyroptosis via the NF- κ B/NLRP3/Caspase-1 pathway in chicken trachea	Selenium deficiency can lead to multiple tissue and organ damages in the body and could control with chronic toxic exposures. Contamination from Bisphenol A (BPA) exposure can induce the occurrence of various injuries, including apoptosis. However, it is not clear whether selenium deficiency and BPA exposure affect tracheal tissue pyroptosis in chickens. To investigate whether selenium deficiency and BPA exposure induce chicken tracheal tissue pyroptosis, the roles of NF-κB/NLRP3/Caspase-1 pathway and the effect of their combined exposure on tissue injury, we developed a model of relevant chicken tracheal injury. Sixty broilers were divided into four groups: the control group (C group), selenium deficiency group (SD group), BPA exposure group (BPA group) and combined exposure group (SeD + BPA group). The study confirmed the toxicity indicators of markers of pyroptosis (NLRP3/GSDMD), NF-κB pathway-related inflammatory factors (NF-κB, NOS, TNF-α, COX-2), pyroptosis-related factors (IGIC, Caspase-1, IL-1β, IL-18), and some heat shock proteins and selenoproteins (HSP70, HSP90, GPX1, SELENOW) in the tracheal tissues of broilers in the SD group, BPA group and SeD + BPA group. The SD + BPA group showed the most severe damage to the tracheal tissue. Furthermore, the expression levels of the above-related indicators were significantly up-regulated in the combined selenium deficiency and BPA exposure groups compared to the groups in which they were individually exposed. It was concluded that selenium deficiency and BPA exposure induced tracheal tissue pyroptosis in chickens through NF-κB/NLRP3/Caspase-1 pathway, and BPA exposure exacerbated selenium deficiency-induced tracheal apoptosis. The present study provides new ideas that studies related to the co-exposure of organisms' micronutrient deficiency and chronic toxicants.	Comp Biochem Physiol C Toxicol Pharmacol Vol.263 Pages 109488	10.1016/j.cbpc.2022.109488	36257570	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1490	T. Xu, T. Chen, X. Shi, J. Ding, S. Chen and H. Lin	2024	Co-exposure of bisphenol A and selenium deficiency induces pyroptosis via ROS/NLRP3 pathway in chicken spleen	Bisphenol A (BPA) is widely applied in plastic products, which will produce immunotoxicity to organisms after spilling in the environment, and become a kind of endocrine disruptor. Selenium (Se) is an essential trace element and plays an important role in maintaining redox homeostasis and immune function. BPA exposure and Se deficiency often occur together in livestock and poultry farming; however, studies on the effects of joint exposure to BPA and Se deficiency on the spleen are still lacking. Therefore, this study aimed to explore the effects of BPA exposure and Se deficiency on the chicken spleen. These chemicals induced low BPA exposure and Se deficiency induced differential enrichment of oxidative stress-regulatory pathways and low BPA inflammatory responses and cellular oxidative stress responses. In the Se+BPA group, pathological damage was significantly increased. Se content decreased, BPA accumulation, oxidative stress and pyroptosis. Meanwhile, the roles and mechanisms of oxidative stress and pyroptosis in BPA exposure in Se-deficiency-induced splenic tissue injury were investigated by using IP and siRT-PCR methods. The results showed that joint BPA exposure with Se deficiency resulted in more significant changes in the above outcomes than 1 of them. The oxidative stress inhibitor NAC effectively reduced Se deficiency and BPA-induced oxidative stress and pyroptosis, further suggesting that oxidative stress mediated Se deficiency co-led BPA-induced pyroptosis. This study revealed that BPA exposure and Se deficiency induced spleen pyroptosis in chickens via the ROS/NLRP3 pathway. These results provide the theoretical basis for the toxicity of BPA in poultry and enrich the toxicological mechanism of combined exposure of Se deficiency and environmental toxins.	Poult Sci Vol.103 Issue 10 Pages 104150	10.1016/j.psj.2024.104150	39146921	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1491	D. Wu, Y. Su, G. Hu and X. Lin	2024	Bisphenol A and selenium deficiency exposure induces pyroptosis and myogenic differentiation disorder in chicken muscle stomach	Bisphenol A (BPA), which is commonly found in the environment due to its release from the use of plastics and food containers, has become a major stressor for environmental sustainability and livestock and poultry production. Selenium (Se) deficiency is widespread in livestock and poultry farming. Co-exposure to BPA and Se deficiency can occur in livestock and poultry farming. However, studies on the effects of joint exposure to BPA and Se deficiency on chicken muscle stomach are still lacking. Therefore, this study aimed to explore the effects of BPA exposure and Se deficiency on chicken muscle stomach. These chemicals induced low BPA exposure and Se deficiency-induced differential enrichment of oxidative stress-regulatory pathways and low BPA inflammatory responses and cellular oxidative stress responses. In the Se+BPA group, pathological damage was significantly increased. Se content decreased, BPA accumulation, oxidative stress and pyroptosis. Meanwhile, the roles and mechanisms of oxidative stress and pyroptosis in BPA exposure in Se-deficiency-induced gastric tissue injury were investigated by using IP and siRT-PCR methods. The results showed that joint BPA exposure with Se deficiency resulted in more significant changes in the above outcomes than 1 of them. The oxidative stress inhibitor NAC effectively reduced Se deficiency and BPA-induced oxidative stress and pyroptosis, further suggesting that oxidative stress mediated Se deficiency co-led BPA-induced pyroptosis. This study revealed that BPA exposure and Se deficiency induced spleen pyroptosis in chickens via the ROS/NLRP3 pathway. These results provide the theoretical basis for the toxicity of BPA in poultry and enrich the toxicological mechanism of combined exposure of Se deficiency and environmental toxins.	Poult Sci Vol.103 Issue 6 Pages 103641	10.1016/j.psj.2024.103641	38626692	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物飼及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1505	O. A. Adeseranye, A. O. Abolaji, T. R. Faboye, H. O. Olaseye and A. O. Adedara	2020	Luteolin-Supplemented diets ameliorates Bisphenol A-Induced toxicity in Drosophila melanogaster	Bisphenol A (BPA) is an industrial chemical used in the production of various plastic materials. It is associated with reproductive, immunological and neurological disorders. Luteolin, a flavonoid found in fruits and vegetables, possesses anti-oxidative, anti-inflammatory and free radical scavenging properties. Here, we carried out studies to ascertain if Luteolin could ameliorate BPA-induced toxicity in Drosophila melanogaster. Adult flies were exposed to BPA (0.05 mM) and co-exposed to BPA (0.05 mM) + Luteolin (0.05 mM, 0.1 mM and 0.2 mM) for 7 days. Flies exposed to BPA (0.05 mM) were exposed to 21 mM paraquat for 7 days for the evaluation of intrinsic oxidative stress. Antioxidant status, oxidative stress, histology of the body, antioxidant (Glutathione-S-transferase, catalase and total thiol), oxidative stress (hydrogen peroxide) and behavioural (negative geotaxis and acetylcholinesterase) markers. The results showed that BPA induced antioxidant oxidative stress, imbalance and behavioural deficit in flies. Luteolin increased survival rate and augmented antioxidant markers in flies. Importantly, Luteolin ameliorated BPA-induced degeneration in the fat body around the neural tissues and abdominal regions, oxidative stress, behavioural deficit, reduction in cell viability and activities of CF, melanogaster (p < 0.05). Overall, this study offered further insights on the antioxidative and chemoprevention properties of Luteolin against BPA-induced toxicity.	Food Chem Toxicol Vol.142 Pages 111478	10.1016/j.fct.2020.111478	32504732	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1506	T. Xu, Y. Zhang, H. Liu, X. Shi and Y. Liu	2024	BPA exposure and Se deficiency caused spleen damage in chickens by nitrification stress-TNF-α	With the increasing production and demand of plastic products in life, inescapable bisphenol A (BPA) exposure results in a threat to the health of organisms. Selenium (Se) is an essential trace element for living organisms. The insufficient Se intake can cause sub-health status. Spleen injury damages limited access of pathogenic microorganisms to the body. However, the mechanism of BPA and Se deficiency on spleen damage is unclear. In this study, the models of chicken with BPA exposure and/or Se deficiency was duplicated, the states of nitrification stress, apoptosis, necroptosis, and changes in TNF-α/RIP3 signaling pathways in chicken spleen were examined. At the same time, nitrification stress inhibitor and TNF-α inhibitor were introduced into BPA + Se deficient chickens to verify the role of nitrification stress in BPA and Se deficiency up-regulated TNF-α/RIP3 signaling pathways. The results showed that BPA induced antioxidant oxidative stress, imbalance and behavioral deficit in flies. Luteolin increased survival rate and augmented antioxidant markers in flies. Importantly, Luteolin ameliorated BPA-induced degeneration in the fat body around the neural tissues and abdominal regions, oxidative stress, behavioural deficit, reduction in cell viability and activities of CF, melanogaster (p < 0.05). Overall, this study offered further insights on the antioxidative and chemoprevention properties of Luteolin against BPA-induced toxicity.	J Environ Manage. 2024 Sep;367:121994.	10.1016/j.jenvman.2024.121994	39083939	動物、in vitro	-	0	不明	不明	不明	不明	不明	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1507	W. Sun, Y. Lei, Z. Jiang, K. Wang, H. Liu and T. Xu	2025	BPA and low-Se exacerbate apoptosis and mitophagy in chicken pancreatic cells by regulating the PTEN/PI3K/AKT/mTOR pathway	METHOD/CTION: Bisphenol A (BPA) is a widespread environmental pollutant which has various toxic effects on organisms. One of the crucial trace elements, is selenium (Se), whose shortage can form biological tissues and enhance the toxicity of contaminants. In which apoptosis and autophagy are crucial events. OBJECTIVES: An in vivo model was established to investigate the effects of BPA and low-Se on chicken pancreatic tissue, and then provide potential molecular mechanism. METHODS: A total of 80 1-day-old broiler chickens (Jinghua Chicken Farm, Harbin, China) were stochastically allotted into 4 groups (n = 20/group): Control group, BPA group, low-Se group, and low-Se + BPA group. Pancreatic tissue was collected at day 42 to detect changes in markers. RESULTS: First, the data showed that BPA and low-Se could induce pancreatic tissue and ultrastructure, in pancreatic tissue, oxidative stress, mitochondrial dysfunction and homeostasis imbalance, apoptosis and mitophagy. In addition, the co-exposure of BPA and low-Se caused the most serious damage to pancreatic tissue. In terms of mechanism, it was found that apoptosis and mitophagy induced by BPA and low-Se were related to the activation of PTEN/PI3K/AKT/mTOR pathway. CONCLUSION: In summary, the study found that BPA and low-Se exacerbated mitochondrial damage, apoptosis and mitophagy by regulating the PTEN/PI3K/AKT/mTOR pathway.	J Adv Res Vol.67 Pages 61-69	10.1016/j.jare.2024.01.029	38311007	動物	-	0	不明	不明	不明	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1508	T. Shaik, K. L. Williams, R. W. Mueller, D. Crump and J. M. O'Brien	2025	Avian-Specific Evidence for an Estrogen Receptor Agonism Adverse Outcome Pathway Based on Chicken Embryos and LMH 3D Spheroids Exposed to Ethinylestradiol and Bisphenol A	Several adverse outcome pathways (AOPs) describe the effects of endocrine disrupting compounds on estrogen signaling. Substantial data support an AOP related to estrogen receptor (ER) antagonism, leading to decreased fecundity in fish. In this study, data were generated for an ER agonism AOP leading to reduced fecundity in avian species (AOP107). Chicken embryos and the chicken leghorn male hepatoma cell line, LMH, were exposed to ethinylestradiol (EE2) and bisphenol A (BPA) to evaluate the potential for these chemicals to induce estrogenic effects in avian species. Gene expression data were collected at multiple timepoints. Exposure to EE2 (1–2 ng/egg in ovo) and BPA (100–200 ng/egg) significantly altered hepatic gene expression responses (

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1518	X. Fan, Y. Wang, J. Zhang, H. Lv, Z. Bai and S. Li	2024	Bisphenol A Regulates the TNFR1 Pathway and Excessive ROS Mediated by miR-26a-5p/ADAM17 Axis to Aggravate Selenium Deficiency-Induced Necroptosis in Broiler Veins	Selenium (Se) deficiency can affect the expression of microRNA (miRNA) and induce necroptosis, apoptosis, etc., resulting in damage to various tissues and organs. Bisphenol A (BPA) exposure can cause adverse consequences such as oxidative stress, endothelial dysfunction, and atherosclerosis. The toxic effects of combined treatment with Se deficiency and BPA exposure may have a synergistic effect. We replicated the BPA exposure and Se deficiency model in broiler to investigate whether the combined treatment of Se deficiency and BPA exposure induced necroptosis and inflammation of chicken vascular tissue via the miR-26a-5p/ADAM17 axis. Our results showed that BPA exposure and Se deficiency induced oxidative stress in the vascular tissue of broiler, leading to an increase in ROS production. Subsequently, we discovered that the tumor necrosis factor receptor (TNFR1) which can be highly expressed, activated the necroptosis pathway through receptor-interacting protein kinase 1 (RIPK1), receptor-interacting protein kinase 3 (RIPK3), and mixed lineage kinase domain-like (MLKL), and regulated the heat shock proteins related genes expressions and inflammation-related genes expressions after exposure to BPA and selenium deficiency in vitro. we found that miR-26a-5p knockdown and increased ADAM17 and reduce necroptosis by activating the TNFR1 pathway. Similarly, both Se-butyl-L-cysteine (SeBC) fluorouracil-1 (5-FU), and miR-26a-5p mimic prevented necroptosis and inflammation caused by BPA exposure and Se deficiency. These results suggest that BPA exposure activates the miR-26a-5p/ADAM17 axis and exacerbates Se deficient-induced necroptosis and inflammation through the TNFR1 pathway and excess ROS. This study lays a solid foundation for future ecological and health risk assessments of nutrient deficiencies and environmental toxic pollution.	Biol Trace Elem Res Vol.202 Issue 4 Pages 1722-1740	10.1007/s12011-023-03756-3	37422542	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1519	F. Elzethouy, H. S. Xu, E. Punch, A. Kerkaura, M. Khaty, S. Elgendy, S. M. Williams, K. Navara and T. L. Guo	2023	Modulation of folliculogenesis in adult laying chickens by bisphenol A and bisphenol S: Perspectives on ovarian morphology and gene expression	Both bisphenol A (BPA) and its analog bisphenol S (BPS) are industrial chemicals that have been used to make certain plastic products applied in chicken farms, including food and water containers. They are endocrine disrupting chemicals (EDCs) that can interfere with the normal functions of hormones and have been associated with reproductive toxicity in mammals. However, the effects and mechanisms of disruption of the ovarian physiology, using either genomic or non-genomic receptors, in hen gynecologic organs remain unclear. This study investigated the deleterious effects of BPA and BPS on the ovaries of pre-adult laying hen chickens. Hens were orally treated with these EDCs at 50 μg/kg body weight, the reference dose for chronic oral exposure of BPA established by the U.S. EPA. The chickens in both BPA and BPS-treated groups showed a decreased number of the preovulatory follicles. BPA-treated chickens showed a significant decrease in the diameter of F1. Additionally, both BPA and BPS treatments increased the infiltrations of lymphocytes and plasma cells in ovaries. Moreover, it was found that the ovaries of BPA-treated chickens weighed the most among the groups. RNA sequencing and subsequent pathway enrichment analysis of differentially expressed genes revealed that both BPA- and BPS-induced ovarian dysfunction was associated with the activation of immune responses and inflammation, and the suppression of steroidogenesis. Taken together, both BPA and BPS are potentially carcinogenic and have deleterious effects on the fertility of laying chickens by inducing inflammation, suggesting that BPS may not be a safe replacement for BPA.	Reprod Toxicol Vol.103 Pages 181-190	10.1016/j.reprotox.2021.06.010	34147626	動物	-	0	不明	不明	不明	不明	不明	50 μg/kg 体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1520	J. T. Dzungwe, K. Tuzo and C. Chyvantome	2022	Growth performance, mortality, and carcass yield evaluation of pure and reciprocal crosses between Sasso and Wassache chickens	The indigenous chicken production has become an integral part of smallholder farming systems in Africa. Their products are preferred due to their taste and flavor, crossbreeding using exotic breeds can improve the productivity of these chickens without sacrificing their genetic merits. This study was aimed at improving the Wassache chicken. F(1) generations of the crosses between the Wassache and Sasso chickens were simultaneously evaluated for growth traits, mortality, and carcass yield in a pure and reciprocal cross design. Data on body weight, performance, and mortality were collected on 811 birds (Sasso = Sasso (SSS) = 120, Wassache = Wassache (WWW) = 120, SSW = 286, WSS = 285). The birds were reared under the deep litter system and fed on a standard broiler starter and finisher diet for 56 days. At the end of the trial, 10 birds selected and analyzed using Minitab 16. The results showed significantly higher (P < 0.05) body weight for the SSS genotype in all assessments studied. Likewise, the SSS genotype had a higher performance in growth and carcass traits next to pure Sasso. However, the feed conversion ratio and dressing percentage of the hybrids did not differ (P > 0.05) from those of the SS and WW genotypes. Within the reciprocal crosses, there was no significant difference (P > 0.05) in all parameters measured except for body weight where the WS chickens had a higher (P < 0.05) body weight compared to the SW ones. The study encourages the crossbreeding of the Wassache and Sasso chickens for improved meat production in this region.	Trop Anim Health Prod Vol.54 Issue 5 Pages 298	10.1007/s11250-022-03272-x	36103006	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1521	H. Chen, Y. Zhang, M. Zou, X. Qi and S. Xu	2022	Bisphenol A aggravates renal apoptosis and necroptosis in selenium-deficient chickens via oxidative stress and PI3K/AKT pathway	Bisphenol A (BPA) in the environment can have deleterious effects on humans and animals. BPA can exert nephrotoxicity by inducing oxidative stress. Selenium (Se) deficiency can specifically impair kidney tissues and additionally shows a synergistic effect on the toxicity of several environmental chemicals. However, the toxic effects of BPA on the chicken kidney and whether Se deficiency produces synergistic effects on the toxicity of BPA remain unclear. Therefore, we established a chicken model to explore the effects of BPA exposure and Se deficiency on the chicken kidney and the underlying mechanisms. Our results showed that BPA exposure induced chicken kidney injuries, including the expansion of oxidative stress, and dysregulated selenoprotein 15 kDa selenoprotein (SEP15)/AKT signaling pathway. We found that BPA exposure increased caspase-dependent and caspase-independent cell deaths, reduced activities of catalase, GPx, and superoxide dismutase, downregulated PI3K and AKT expression, activated Bcl2/Bax-Caspase 9-Caspase 3, and receptor-interacting protein kinase 3-mixed lineage kinase like protein signaling pathways, resulting in apoptosis and necroptosis in the chicken kidney. In addition, Se deficiency significantly promoted the expression of renal apoptosis and necroptosis in BPA-exposed chicken kidneys. Altogether, our results showed that BPA aggravates apoptosis and necroptosis in Se-deficient chicken kidneys via regulation of oxidative stress and PI3K/AKT signaling pathway. Our findings elucidate the mechanisms of BPA nephrotoxicity and Se deficiency exacerbates toxicity in chickens and will provide great significance for the protection of the ecological environment and animal health.	J Cell Physiol Vol.237 Issue 8 Pages 3292-3304	10.1002/jcp.30781	35616291	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1522	H. Chen, Y. Zhang, X. Qi, X. Shi, X. Huang and S. W. Xu	2022	Selenium deficiency aggravates bisphenol A-induced autophagy in chicken kidney through regulation of nitric oxide and adenosine monophosphate activated protein kinase/mammalian target of rapamycin signaling pathway	Bisphenol A (BPA), a phenolic compound, is harmful to humans and animals as its residue in the water threatens multiple organs, especially the kidney. Low selenium (Se) diets are consumed in many regions of the world, and poor Se status has exacerbating effect on toxicity of several environmental chemicals. Here, we described the discovery path of Se deficiency aggravation on autophagy in BPA-treated chicken kidney through regulating nitric oxide (NO) and adenosine monophosphate activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) signaling pathways. The actual dosage for BPA in diets was 0.28 mg/kg in control group and 620 mg/kg in Low Se group, and BPA exposure concentration for chicken was 0.28 g/kg. Chicken embryo kidney (CEK) cells were used in vitro and the BPA exposure concentration for CEK cells was 0.28 mM. Our results showed that BPA exposure induced chicken kidney injuries, including the expansion of oxidative stress, and dysregulated selenoprotein 15 kDa selenoprotein (SEP15)/AKT signaling pathways. We found that BPA exposure increased caspase-dependent and caspase-independent cell deaths, reduced activities of catalase, GPx, and superoxide dismutase, downregulated PI3K and AKT expression, activated Bcl2/Bax-Caspase 9-Caspase 3, and receptor-interacting protein kinase 3-mixed lineage kinase like protein signaling pathways, resulting in apoptosis and necroptosis in the chicken kidney. In addition, Se deficiency significantly promoted the expression of renal apoptosis and necroptosis in BPA-exposed chicken kidneys. Altogether, our results showed that BPA aggravates apoptosis and necroptosis in Se-deficient chicken kidneys via regulation of oxidative stress and PI3K/AKT signaling pathway. Our findings elucidate the mechanisms of BPA nephrotoxicity and Se deficiency exacerbates toxicity in chickens and will provide great significance for the protection of the ecological environment and animal health.	Environ Toxicol Vol.37 Issue 10 Pages 2503-2514	10.1002/tox.23613	35830335	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1523	S. Çetin and T. Özaydın	2021	The effects of bisphenol A given in ovo on bursa of Fabricius development and percentage of acid phosphatase positive lymphocyte in chicken	Bisphenol A (BPA), one of the endocrine-disrupting chemicals, is the object of great concern because of its widespread use throughout the world. In this study, it was aimed to determine the effects of in ovo-administered BPA on the bursa of Fabricius and percentage of acid phosphatase positive lymphocyte in peripheral blood by means of histological and enzyme histochemical methods. For this purpose, 324 hatchlings of Isa Brown laying hens were randomly divided into 3 groups as control, 0.05 mg/kg BPA and 0.5 mg/kg BPA. Each group was divided into 3 subgroups as 18 hatchlings in each subgroup and 6 hatchlings in each of the three replicate groups. Tissue samples were taken from the bursa of Fabricius embryos and processed for enzyme histochemical methods in addition to routine histological techniques. It was observed that, in BPA-treated groups, embryonic development of bursa of Fabricius was retarded. It was also indicated that the percentage of peripheral blood ACP+ve positive lymphocytes was significantly decreased. These results suggested that a limited maternal transfer of BPA into the eggs might be lead to immunosuppression in chicks.	Environ Sci Pollut Res Int Vol.28 Issue 31 Pages 41688-41697	10.1007/s11356-021-13640-z	33791960	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1524	Y. Wang, T. Gai, L. Zhang, L. Chen, S. Wang, T. Ye and W. Zhang	2023	Neurotoxicity of bisphenol A exposure on Caenorhabditis elegans induced by disturbance of neurotransmitter and oxidative damage	Bisphenol A (BPA) is putatively regarded as an environmental neurotoxicant found in everyday plastic products and materials, however, the possible neurobehavioral adverse consequences and molecular mechanisms in animals have not been clearly characterized. The nematode Caenorhabditis elegans has become a promising animal model for neurotoxicological researches. To investigate neurobehavioral effect relationships of BPA-induced neurotoxicity effects, the locomotion behavior and developmental parameters of the nematode were determined after BPA exposure. The present data demonstrated that BPA caused neurobehavioral toxicities, including locomotion behavior, defecation behavior, and egg-laying behavior. Moreover, BPA exposure induced developmental toxicity, as indicated by the significant reductions in body length. The dopaminergic neurons were damaged by BPA. Furthermore, basal levels of mRNA expression related to dopamine, serotonin and GABA were detected in the worms exposed to 50 μM BPA. Increased SOD-3 expression might be adaptive response to BPA exposure. Moreover, oxidative damage triggered by BPA was manifested by changes in GST-4 expression, accompany with abnormity of ATP synthesis, but not nuclear localization of DAF-16/FOXO. Finally, we observed that supplementation 5 μg/ml ascorbic partially rescued BPA-induced reactive oxygen species (ROS) production and neurobehavioral toxicity. Altogether, the neurobehavioral and developmental toxicity of BPA may be induced by neurotransmission abnormity and oxidative damage. The present data imply that oxidative stress is linked to neuronal damage and neurobehavioral harm resulting from developmental BPA exposure.	Ecotoxicol Environ Saf Vol.252 Pages 114617	10.1016/j.ecoenv.2023.114617	36758510	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1525	A. Kaighod, Z. Bárdyová, P. Hockicková, A. Zvolenská, K. Melnikov and S. Kucharková	2025	Caenorhabditis elegans as a Model to Assess the Potential Risk to Human Health Associated with the Use of Bisphenol A and Its Substitutes	Given its simplicity, Caenorhabditis elegans appears to be a promising model for future research on endocrine disruptors, including bisphenol A and its supposedly safer alternatives. The aim of this study was to investigate the impact of embryonic exposure of C. elegans to different concentrations (0.5, 1.0, and 5 μM) of bisphenol A and its analogs, bisphenol S, bisphenol F, and bisphenol AF on selected biological characteristics of the nematode C. elegans and to compare them with an unexposed control group. Embryonal exposure of C. elegans to bisphenol A, as well as bisphenol S, F, and AF at concentrations of 0.5, 1.0, and 5 μM resulted in a significant reduction in the survival of the nematode C. elegans in the fourth larval stage (L4) and in the number of offspring. Exposure to bisphenol A, S, and F at concentrations of 0.5, 1.0, and 5 μM also led to a reduction in the body length of the nematode C. elegans in the fourth larval stage (L4). Exposure to bisphenol A, S, and F in concentrations of 0.5, 1.0, and 5 μM, as well as bisphenol AF in concentrations of 1.0 and 5 μM resulted in a significant reduction in the width of the head of the nematode C. elegans in the fourth larval stage (L4). Our findings confirm prior research that bisphenol S and its supposedly safer analogs exert a detrimental effect on diverse biological processes. Therefore, bisphenol A analogs should be employed with caution, particularly until a comprehensive risk assessment has been conducted.	Int J Mol Sci Vol.26 Issue 5	10.3390/ijms26052013	40076635	動物	-	0	不明	不明	不明	1	0.5、1.0、5 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1526	M. Hyun, L. Rathor, H. J. Kim, T. McElroy, K. H. Hwang, S. Wohlgemuth, S. Curry, R. Kieu, C. Leeuwenburgh, J. D. Heo and S. M. Han	2021	Comparative toxicities of BPA, BPS, BPF, and TMBPF in the nematode Caenorhabditis elegans and mammalian fibroblast cells	Bisphenol A (BPA) is a chemical compound commonly used in the production of plastics for daily lives and industry. As BPA is well known for its adverse health effects, several alternative materials have been developed. This study comprehensively analyzed the toxicity of BPA and its three substitutes including bisphenol S (BPS), bisphenol F (BPF), and tetramethyl bisphenol F (TMBPF) on aging, healthspan, and mitochondria using an in vivo Caenorhabditis elegans (C. elegans) model system and cultured mammalian fibroblast cells. C. elegans exposed to 0.1 mM BPA exhibited abnormalities in the key neural regulation of C. elegans behavior, including delayed development, decreased body growth, reduced reproduction, and abnormal tissue morphology. Exposure to the same concentration of each alternative including TMBPF, which has been proposed as a safer BPA substitute, also showed similar toxicities to BPA. Moreover, BPA and its substitutes induced mitochondrial dysfunction, including mitochondrial fragmentation and depolarization, in C. elegans. Exposure to BPA and BPF resulted in mitochondrial abnormalities, such as reduced oxygen consumption and ultrastructural membrane potential. In contrast, the ATP levels were remarkably higher after treatment with all bisphenols. In mammalian fibroblast cells, exposure to increasing concentrations of all bisphenols ranging from 50 μM to 500 μM caused a severe decrease in cell viability in a dose-dependent manner. BPA increased ATP levels and decreased ROS but did not affect mitochondrial permeability transition pore. Interestingly, TMBPF was the only bisphenol that caused a significant increase in mitochondrial ROS and mPT opening. These results suggest that the potentially harmful physiological effects of BPA alternatives should be considered.	Toxicology Vol.461 Pages 152924	10.1016/j.tox.2021.152924	34474090	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1527	M. F. Honrao Carneiro, N. Shin, R. Karthikraj, F. Barbosa, Jr., K. Kannan and M. P. Colaiácovo	2020	Antioxidant CoQ10 Restores Fertility by Rescuing Bisphenol A-Induced Oxidative DNA Damage in the Caenorhabditis elegans Germline	Endocrine disrupting chemicals are ubiquitously present in our environment, but the mechanisms by which they adversely affect human reproductive health and strategies to circumvent their effects remain largely unknown. Here, we show in Caenorhabditis elegans that supplementation with the antioxidant Coenzyme Q10 (CoQ10) rescues the reproductivity induced by the widely used plasticizer and endocrine disruptor bisphenol A (BPA). We found that BPA exposure causes oxidative DNA damage, leading to double-strand breaks (DSBs) and germline apoptosis. Moreover, BPA exposure induces chromosome segregation defects in oocytes (~2-cell embryos) (~3- cell embryos). Finally, CoQ10 treatment also reduced the levels of aneuploid embryos and BPA-induced defects observed in early embryonic divisions. We propose that CoQ10 may counteract BPA-induced reproductivity through the scavenging of reactive oxygen species and free radicals, and that this natural antioxidant could constitute a low-risk and low-cost strategy to attenuate the impact on fertility by BPA.	Genetics Vol.214 Issue 2 Pages 381-395	10.1534/genetics.119.302939	31852725	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1528	C. M. Higley, K. D. Wallgren, J. R. Clore, S. C. Timmons and A. Kazmarzak	2025	Effects of bisphenol A, bisphenol S, and tetramethyl bisphenol F on male fertility in Caenorhabditis elegans	Research has shown that exposure to bisphenol A (BPA), a widely used plasticizer, can lead to meiotic errors, resulting in poor reproductive cell quality and infertility. Health-related concerns have prompted the search for BPA alternatives, however, evidence suggests that currently used BPA analogs, such as bisphenol S (BPS), may pose similar risks to human health. While the effects of BPA on female fertility are well documented, the impacts of BPA and its analogs on male fertility remain poorly understood. Here, we exposed Caenorhabditis elegans males to BPA, BPS, bisphenol F (BPF), and tetramethyl bisphenol F (TMBPF), and compared the resultant reproductive potential to that of males exposed to BPA and BPS analogs' chemical relatives, bisphenol B (BPB) and bisphenol AF (BPAF). Adult C. elegans males were exposed to 0.1 mM of each bisphenol for 24 h. We then mated individual bisphenol-exposed males to unexposed hermaphrodites and quantified the number of self- and cross-progeny produced. We evaluated the presence of aneuploid cells, embryonic viability, and oocyte fertilization in males treated with 0.1 mM of each bisphenol. Bisphenol analogs for 48 h as well as their cross-progeny number and viability. Our results indicated that all of the evaluated bisphenol analogs (BPA, BPS, and TMBPF) adversely affect male fertility to varying degrees. Whereas all three bisphenol analogs reduced brood size, only BPS exposure resulted in impaired germline proliferation and significantly reduced brood size. In addition, a decrease in embryonic viability, suggestive of an increased incidence of sperm chromosomal aberrations, was observed following exposure to all of the tested bisphenols. Further investigation is necessary to fully elucidate the underlying mechanisms and implications of BPA, BPS, and TMBPF on spermatogenesis.	Toxicol Ind Health Vol.41 Issue 1 Pages 11-19	10.1177/0748233724128796 7	39344986	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1529	S. E. Ha, M. H. Lee, S. M. Han, S. H. Kim, M. Hyun and J. D. Heo	2025	Comparative toxicity of eleven bisphenol analogs in the nematode Caenorhabditis elegans	Bisphenol analogs are widely used as industrial substitutes for Bisphenol A (BPA) and are included in water bottles, food containers, and receipts commonly encountered daily. However, there are currently no specific regulations on these substitute substances, and reports on their harmful effects are also lacking. In this study, we examined the toxicity of eleven bisphenol analogs, including BPAP, BPZ, BPC, BPE, BPG, BPP, BPPH, BPS, and TMBPA at 1 mM concentration using the C. elegans model. Our findings revealed that several bisphenol analogs, most notably BPB, BPC, BPE, and BPZ, significantly increased lethality in embryonic and L1 larval stages. Additionally, developmental delays were observed with BPAP, BPB, BPC, and BPZ, with a reduction in the number of animals reaching adulthood. Regarding reproductive toxicity, we found that BPAP, BPB, BPC, BPZ, and BPE noticeably impacted brood size. Furthermore, exposure to the analogs significantly shortened the lifespan of C. elegans, particularly with BPAP, BPB, BPC, and BPZ, causing concerns about their potential impact on aging. This study suggests their potential harmful effects on development, reproduction, and longevity.	Toxicol Lett Vol.409 Pages 12-20	10.1016/j.toxlet.2025.04.008	40287112	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1530	G. Ficociello, V. Gerardi, D. Uccelletti and A. Setini	2021	Molecular and cellular responses to short exposure to bisphenols A, F, and S and eluates of microplastics in C. elegans	Bisphenol F (BPF) and bisphenol S (BPS) have been developed as an alternative to bisphenol A (BPA), a well-known endocrine disruptor, leading to their detection in the aquatic environment. In this work, we used the animal model Caenorhabditis elegans to improve our understanding of their potential effects on the biota and the environment. Our findings demonstrated that, after 72 h exposure, all the bisphenols examined increased the number of apoptotic corpses and the expression of the detoxifying enzymes SOD-3 and GST-4, without affecting the ROS levels, while BPA and BPS significantly enhanced DNA fragmentation. Furthermore, similarly to BPA, BPF and BPS did not alter the lifespan through the activation of SKN-1 and DAF-16 pathways. Thus, this study raises the attention of the risks associated with exposure to BPA alternatives. We also examined the effects of microplastic (MP) eluates on C. elegans. Aqueous extracts of weathered microplastic samples, both at high and low degradation state and pellets, have been evaluated for their effects on lifespan, DNA fragmentation, and expression of genes involved in the response. Overall, our findings showed that eluates of low degraded plastics exert a genetic toxic effect on the nematode C. elegans compared with the aqueous sample of high degraded plastic fragments and pellets.	Environ Sci Pollut Res Int Vol.28 Issue 1 Pages 805-818	10.1007/s11356-020-10498-5	32820443	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	毒性性評価基準適合論文（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1531	Y. Chen, B. Parrier, A. Hussain, K. Gibbs, D. Ferreira and P. Allard	2019	BPA interferes with StAR-mediated mitochondrial cholesterol transport to induce germline dysfunctions	Bisphenol A is an endocrine disruptor associated with hormone synthesis and reproduction alterations. However, the initiating events underpinning these dysfunctions are still unclear. Here, we address the hypothesis that bisphenol A (BPA) impairs the mitochondrial cholesterol transport mediated by the steroidogenic acute regulatory protein (STAR) in the nematode Caenorhabditis elegans. We show that exposure to environmentally relevant concentrations of BPA compromises fertility and germline apoptosis, hallmarks of BPA reproductive toxicity in C. elegans, one fully rescued by fat oxaregenic cholesterol supplementation. We also observed that increasing BPA concentrations proportionally reduced mitochondrial cholesterol levels. Mutants for scl-1 (ortholog of StAR), but not C14D7.9 (ortholog of TSPO), show reproductive defects similar to BPA while BPA exposure in a scl-1 loss-of-function background did not worsen these effects. Finally, cholesterol supplementation rescued these defects for all scl-1 genotypes/BPA combinations assessed. Together, these results uncover a novel mechanism underlying BPA's germline toxicity through the alteration of cholesterol transport.	Reprod Toxicol Vol.90 Pages 24-32	10.1016/j.reprotox.2019.08.001	31445225	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1532	B. R. Bedford, N. E. Bréard, N. Fasciachi, E. D. Genasis, A. M. Nowakowski, T. C. FitzGibbon, S. Mauvais, A. V. Benjamin, M. Kelly and P. M. Checchi	2020	Counteracting Environmental Chemicals with Coenzyme Q10: An Educational Primer for Use with "Antioxidant CoQ10 Restores Fertility by Rescuing Bisphenol A-Induced Oxidative DNA Damage in the Caenorhabditis elegans Germline"	Environmental toxicants are chemicals that negatively affect human health. Although there are numerous ways to limit exposure, the ubiquitous nature of certain environmental toxicants makes it impossible to avoid them entirely. Consequently, scientists are continuously working toward developing strategies for combating their harmful effects. Using the nematode Caenorhabditis elegans, a model with many genetic and physiological similarities to humans, researchers in the Catalano laboratory have developed a model to study the effects of environmental toxicants on fertility, which has been published in JoVE. The model system described here uses bisphenol A (BPA), a widely available compound, Coenzyme Q10 (CoQ10), can rescue BPA-induced damage. This work is significant in that it paves a low-cost method for improving reproductive success in humans. The goal of this educational primer is to provide additional information to the JoVE publication "CoQ10 Restores Fertility by Rescuing Bisphenol A-Induced Oxidative DNA Damage in the Caenorhabditis elegans Germline" It is ideally suited for interpretive labs as an upper-level undergraduate course such as Genetics, Cell and Molecular Biology, Developmental Biology, or Toxicology. The primer provides background information on the history of BPA, the utility of the C. elegans gem line as a model for studying reproductive toxicity, and research methods including assessment of programmed cell death, fluorescent microscopy applications, and assays to quantify gem line expression. Questions for deeper exploration in class or online are provided.Related article in JOVE:TCS: Invivo Genetic Mf: Ditchi, Kanthiwa N, Barbaux Y. in Kumar A., Caldarone MF. Antioxidant CoQ10 restores fertility by rescuing bisphenol A-induced oxidative DNA damage in the Caenorhabditis elegans. Genetics. 216:361-386.	Genetics Vol.216 Issue 4 Pages 879-890	10.1534/genetics.120.303577	33268390	動物	-	0	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1533	A. Zygmuntowicz, W. Markiewicz, T. Grabowski and J. Jaroszewski	2022	Effects of Bisphenol A and Bisphenol F on Porcine Uterus Contractility	METHODS AND MATERIALS: The effects of BPA and BPF on the contractile activity of the pig uterus. MATERIAL AND METHODS: The investigation utilized smooth muscles from immature pigs (n = 6) cyclic pigs on days 12–14 of the estrous cycle (n = 6) or early-pregnant pigs on days 12–14 of pregnancy (n = 6). Strips of the myometrium were exposed to BPA and BPF at concentrations of 10−10–10−5 M. Strain gauge transducers connected to data-processing equipment for measuring isometric contractions. RESULTS: BPA caused a significant decrease in contraction amplitude, and frequency and in myometrial tension in all groups examined. BPF caused a decrease in the amplitude and frequency of contractions in all groups and in myometrial tension in the early-pregnant group. CONCLUSION: The obtained results indicate that both BPA and BPF relaxed the porcine myometrium, but these changes, especially in the amplitude and frequency of contractions, were more evident after BPF treatment. The extent of relaxation is dependent on the physiological status of the animals.	J Vet Res. 2022 Jul 5;66(2):257-265.	10.2478/jvetres-2022-0031	35892107	in vitro	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1534	Z. Zou, L. K. Harris, K. Forbes and A. E. P. Heazell	2022	Sex-specific effects of bisphenol A on the signaling pathway of ESRRG in the human placenta	Bisphenol A (BPA) exposure during pregnancy is associated with low fetal weight, particularly in male fetuses. The expression of estrogen-related receptor gamma (ESRRG), a receptor for BPA in the human placenta, is reduced in fetal growth restriction. This study sought to explore whether ESRRG signaling mediates BPA-induced placental dysfunction and determine whether changes in the ESRRG signaling pathway are sex-specific. Placental villous explants from 28 normal term pregnancies were cultured with a range of BPA concentrations (1 nM–1 μM). Baseline BPA concentrations in the placental tissue used for explant culture ranged from 0.8 to 5.3 nM (median 2.3 ± 1.5 nM, n = 6). Expression of ESRRG by gestational age-matched male and female placentae (n = 6 per group) was quantified. BPA (1 μM) increased ESRRG mRNA in placental tissue from 23 to term (p = 0.031). ESRRG mRNA in placental explants expressed in male placentae at 23 to 36 weeks' gestation was increased in female placentae treated with 1 μM BPA for 24 h but was decreased in male placentae treated with 1 nM or 1 μM for 48 h. Levels of 17β-hydroxysteroid dehydrogenase type 1 (HSD17B1), which converts estrone to estradiol, were increased in female placentae treated with 1 nM BPA for 24 h (p = 0.031) and 1 μM BPA for 48 h (p = 0.031). Levels of 17β-HSD2 (HSD17B2), which converts estradiol to estrone, were increased in male placentae at 23 to 36 weeks' gestation treated with 1 nM BPA for 24 h (p = 0.031). Expression of 17β-HSD1 and 17β-HSD2 was unaffected by BPA exposure in female placentae at 23 to 36 weeks' gestation. BPA altered the expression of ESRRG and its downstream targets HSD17B1 and HSD17B2 in placental villous explants. This study has demonstrated that BPA affects the ESRRG signaling pathway in a sex-specific manner in human placentae, and a possible biological mechanism to explain the differential effects of BPA exposure on male and female fetuses observed in epidemiological studies.	Biol Reprod. 2022 Jun 13;106(6):1278-1291.	10.1093/biolre/ioac044	35220427	in vitro	-	-	-	-	-	-	-	-	-	1	0	1 nM–1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1535	L. Zimmermann, G. Dierkes, T. A. Ternes, C. Völker and M. Wagner	2019	Benchmarking the in Vitro Toxicity and Chemical Composition of Plastic Consumer Products	Plastics are known sources of chemical exposure and few, prominent plastic-associated chemicals, such as bisphenol A and phthalates, have been thoroughly studied. However, a comprehensive characterization of the complex chemical mixtures present in plastics is missing. In this study, we benchmark plastic consumer products, covering eight major polymer types, according to their toxicological and chemical signatures using in vitro bioassays and nontargeted high-resolution mass spectrometry. Most (70%) of the 36 plastic extracts considerably cytotoxic, and 14 extracts induced oxidative stress response, including baseline toxicity (≥3.5-fold induction of cytotoxicity (50%), oxidative stress response (≥3×), and antiandrogenicity (23%). In total, we detected 302 features, tentatively identified 260, including monomers, additives, and nonintentionally added substances, and prioritized 5 of these for their potential to cause toxicity. Migration experiments revealed that polyethylene terephthalate (PET), polyamide (PA), and polyurethane (PUR) materials can leach toxicants. Baseline toxicity was detected in all "hazardous" leaks of polyacrylic acid (PLA). The toxicities of low-density polyethylene (LDPE), polystyrene (PS), and polypropylene (PP) varied. Our study demonstrates that consumer plastics contain compounds that are toxic in vitro but remain largely unidentified. Given the risk of unknown compounds cannot be assessed, this poses a challenge to manufacturers, public health authorities, and researchers alike. However, we also demonstrate that products not inducing toxicity are already on the market.	Environ Sci Technol. 2019 Oct 1;53(19):11467-11477.	10.1021/acs.est.9b02293	31380625	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1536	X. Zhu, G. Wu, Y. Xing, C. Wang, X. Yuan and B. Li	2020	Evaluation of single and combined toxicity of bisphenol A and its analogues using a highly-sensitive micro-biosensor	Bisphenol analogues have been developed as alternatives to bisphenol A (BPA), a common chemical with potential adverse effects on human health. It is imperative to perform a fast and sensitive evaluation for the toxicity of these bisphenol analogues. This study introduces a label-free electrochemical biosensor based on a screen-printed electrode modified with the carboxylated multi-walled carbon nanotube/Fe3O4@Au@Ag nanoparticle. Clonorchis sinensis tubulin binary (CSB) cells were used as the biological recognition agent to detect changes in electrochemical signals and indicate the cell viability. Only 35 μL of sample was required for detection, which was much lower than that of other conventional electrochemical methods (> 1 mL). This biosensor was examined for the cytotoxicity of BPA, bisphenol AF (BPAF), bisphenol F (BPF), bisphenol S (BPS), and bisphenol B (BPB) in CSB cells. The half inhibition concentration (IC50) values after 30 h of exposure indicated that the rank order of cytotoxicities was BPAF > BPB > BPA > BPF > BPS. The toxicological changes in CSB cells were also investigated by microscopic observation. The combined toxicities of the binary bisphenol mixtures were determined. Potentially synergistic and additive effects were observed. These findings provide new insights into the cytotoxicity of bisphenol analogues.	J Hazard Mater. 2020 Jan 5:381:120908.	10.1016/j.jhazmat.2019.120908	31352154	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1537	R. Zhu, X. Yu and Y. Li	2025	Identification and validation of biomarkers associated with glycolysis in polycystic ovarian syndrome	Polycystic ovary syndrome (PCOS), an endocrine disorder emerging in adolescence and reproductive years, has been linked to glycolysis in prior studies, though the precise mechanistic role of glycolysis in its pathogenesis remains unclear. Transcriptomic data from PCOS patients and healthy controls were obtained from the GEO database, and glycolysis-related genes were systematically evaluated. Using multiple machine learning algorithms, seven candidate biomarkers were identified via differential analysis, various PPI algorithms, and validation of expression patterns. Subsequent analyses included functional enrichment, tissue-wise cell-specific expression profiling, miRNA-modification site prediction, compound screening, molecular network construction, and molecular docking. RT-qPCR was performed on clinical samples for experimental validation. Two biomarkers, TXNIP and TGFB, were identified and jointly contributed to "complement and coagulation cascades." TXNIP showed elevated expression in ovarian endometrium cells, whereas TGFB was more broadly expressed and enhanced in ovarian fibroblasts. TGFB had 3 high-confidence miRNA modification sites and TXNIP had 1 high-confidence miRNA modification sites. The identified regulatory networks included hsa-miR-4761-5p/TXNIP/PKM2 and hsa-miR-4761-5p/TGFB/PKM2. Molecular docking revealed strong binding affinities between these biomarkers and their corresponding compounds, with TXNIP exhibiting the highest affinity for Ethinylestradiol. Finally, RT-qPCR validation in granulosa cells from PCOS patients confirmed significant upregulation of TGFB and TXNIP, aligning with bioinformatics predictions. These findings suggest that TXNIP and TGFB may serve as potential biomarkers associated with glycolytic dysregulation in PCOS, offering insights into the interplay between metabolic dysfunction and disease mechanisms.	Sci Rep. 2025 Jul 26;15(1):27199.	10.1038/s41598-025-11591-w	40715316	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1538	S. M. Zhou, W. B. Yuan, J. Z. Li, H. Q. Chen, Y. Zeng, N. Wang, J. Fan, Z. Zhang, Y. Xu, J. Cao and W. B. Liu	2023	TET1 involved in bisphenol A induced TM3 Leydig cell toxicity by regulating Cav3.3 hydroxymethylation	Bisphenol A (BPA), an important environmental pollutant, is known to damage reproductive endocrinology. However, the underlying epigenetic mechanism in Leydig cells during BPA exposure has not been explored in detail. In this study, TM3 Leydig cells were treated with BPA (0, 25, 50 and 100 μM) for 24 h. The differentially expressed genes (DEGs) were identified by transcriptome sequencing and bioinformatics analysis. Results showed that BPA exposure significantly inhibited cell viability and increased the apoptosis of TM3 Leydig cells. Moreover, the mRNA of TET1, Cav3.3 and Cav3.3 decreased significantly with increase of BPA exposure. Importantly, TET1 significantly promoted proliferation of TM3 Leydig cells and inhibited apoptosis. Differentially expressed TET1 significantly affected BPA induced toxicity to TM3 Leydig cells. Notably, TET1 elevated the mRNA levels of Cav3.2 and Cav3.3 MeDIP and hMeDIP confirmed that TET1 regulated the expression of Cav3.3 through DNA hydroxymethylation. Our study firstly presented that TET1 participated in BPA induced toxicity to TM3 Leydig cells through regulating Cav3.3 hydroxymethylation modification. These findings suggest that TET1 acts as a potential epigenetic marker for reproductive toxicity induced by BPA exposure and may provide a new direction for the research on male reproductive damage.	Chemosphere. 2023 Jan;312(Pt 1):137171.	10.1016/j.chemosphere.2022.137171	36370755	in vitro	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1539	R. Zhou, M. Xia, L. Zhang, W. Cheng, J. Yan, Y. Sun, Y. Wang and H. Jiang	2021	Individual and combined effects of BPA, BPS and BPAF on the cardiomyocytic differentiation of embryonic stem cells	Exposure to many kinds of bisphenols (BPs) is common, and the effects of BP mixtures may differ from those of individual BPs. Therefore, evaluating combined exposure effects is necessary. Our study evaluated the individual and combined exposure effects of bisphenol A (BPA), bisphenol S (BPS) and bisphenol AF (BPAF) on embryonic development using an embryonic stem cell test (EST) and a concentration addition (CA) model at environmentally relevant levels. Exposure to relatively high doses BPA, BPS and BPAF inhibited embryonic stem cell differentiation into cardiomyocytes and exhibited weak embryotoxicity. Individually, BPA, BPS and BPAF inhibited mesoderm, mesoderm and endoderm marker expression but enhanced pluripotency marker expression. Combined exposure to BPs had an additive effect on cardiomyocyte differentiation and embryonic stem cell proliferation based on the CA model. Environmentally relevant individual or combined BP doses (10 ng/ml for individual BPA, BPS and BPAF doses or 1 ng/ml and 10 ng/ml for BP mixture doses) failed to cause oxidative stress, DNA damage or apoptosis, changes in stem cell differentiation. The cardiomyocyte differentiation ratio also did not change significantly. Individual and combined exposure to environmentally relevant BP doses led to a significant decrease in cardiomyocyte beating rates. Moreover, BPA, BPS and BPAF inhibited the expression of cardiac differentiation marker genes (Nkx2.5, Gata4 and Tbx5) and the formation of F-actin and sarcomeric α-actinin, which may be involved in cardiomyocyte dysfunction. The p38 pathway inhibitor SB203580 inhibited the increase in collagen during cardiomyocyte differentiation caused by low-dose BPs. These results suggest that relatively high-dose BPs in combination have an additive effect on cardiomyocyte differentiation. Low-dose BPs individually and in combination may affect cardiomyocyte collagen through the p38 pathway.	Ecotoxicol Environ Saf. 2021 Sep 1:220:112366.	10.1016/j.ecoenv.2021.112366	34058679	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1540	Y. Zheng, H. Li, Y. Wang, L. Huang, L. Chen, S. Lin and S. Lin	2025	Identification and immunoassay of biomarkers associated with T cell exhaustion in systemic lupus erythematosus	BACKGROUND: Systemic lupus erythematosus (SLE) is an autoimmune disease with unclear etiology. T cell exhaustion (TEX) suppresses the immune response and can be a potential therapeutic strategy for autoimmune diseases. Therefore, this study primarily investigated the mechanism by which TEX influences SLE, offering a novel target for its treatment. METHODS: GSE72326 and GSE61635 were utilized in this study. TEX-related genes (TEX-RGs) were obtained from the published literature. Differentially expressed genes (DEGs) were obtained through differential expression analysis. Subsequently, candidate genes were selected by overlapping DEGs and TEX-RGs. These candidate genes underwent protein-protein interactions (PPI) network analysis for further screening. Machine learning was applied to identify candidate key genes from the PPI-identified genes. The candidate key genes exhibiting an area under the receiver operating characteristic (ROC) curve (AUC) greater than 0.7, along with consistent expression trends and significant differences in GSE72326 and GSE61635 datasets, were identified as biomarkers related to TEX in SLE. Finally, the expression of biomarkers was validated in clinical samples from SLE patients and healthy controls (HCs) using flow cytometry and expressed by reverse transcription-quantitative polymerase chain reaction (RT-qPCR). RESULTS: The biomarkers IL6R, LYN, PTGS2, and CD38, were screened by overlapping DEGs and TEX-RGs. Gene set enrichment analysis (GSEA) showed that these was a significant positive correlation between the expression of these biomarkers, and immune-related pathways, such as the NOD-like receptor signaling pathway, Toll-like receptor signaling pathway, and PID-11br-receptor signaling pathway, a significant positive correlation. The immune infiltration of 8 types of immune cells differed significantly in SLE. Natural killer cells, resting memory CD4 T cells and resting NK cells were significantly down-regulated in the SLE group. It therefore showed the highest correlation with resting memory CD4 T cells. Bisphenol A (targeted CD38), and LY96, whereas, Bisphenol S (targeted PTGS2), and Bisphenol AF (targeted IL6R), were predicted to be the drugs for SLE. CONCLUSIONS: The biomarkers IL6R, LYN, PTGS2, and CD38, were identified as biomarkers related to TEX in SLE. These biomarkers could be detected in the blood for early diagnosis of the disease or to monitor the efficacy of the disease treatment, thus providing a new target for the management of SLE.	Front Immunol. 2025 Mar 26:16:1476575.	10.3389/fimmu.2025.1476575	40207215	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1541	J. Zhang, S. Chen, H. Lu, M. Xia, S. Wang, X. Li, H. Li, Y. Wang, R. Ge, Ge and Y. Liu	2024	Enhanced inhibition of human and rat aromatase activity by benzene ring substitutions in bisphenol A: QSAR structure–activity relationship and in silico docking analysis	Bisphenol A (BPA) is a widely used plastic material, but its potential endocrine disrupting effect has restricted its use. The BPA alternatives have raised concerns. This study aimed to compare inhibitory patterns of 22 BPA analogues on human placental aromatase (CYP19A1) and rat ovarian aromatase (CYP19A1) and to explore the structure–activity relationship (SAR) and quantitative SAR (QSAR). The results showed that 4,4′-sulfonyldiphenol (BPS) and 4,4′-(hexafluoroisopropylidene)diphenol (BPAF) with a 50% inhibitory concentration (IC50) value of 0.04 and 0.08 μM, respectively, were the most potent competitive inhibitors and inhibited aromatase production in human BeWo cells. Molecular docking analysis revealed all BPA analogues bind to the steroid androgen site or in between steroid and heme of CYP19A1 and form a hydrogen bond with catalytic residue Met374. Pharmacophore analysis showed that there were 3 hydrophobic regions for BPA analogues, with bisphenol F occupying 2 regions. Biparietal correlation analysis showed that LumP (log(kOA)) and LogD (octanol–water solubility) of BPA analogues were correlated with their IC50 values. Computational drug metabolism and pharmacokinetics analysis showed that bisphenol M, tetramethylbisphenol A, and tetrachlorobisphenol A had low solubility, which might explain their weaker inhibition on estradiol production in BeWo cells. In conclusion, BPA analogues mostly can inhibit CYP19A1, and the liquid/fatty determines their inhibitory strength.	J Hazard Mater. 2024 Mar 5:465:133252.	10.1016/j.jhazmat.2023.133252	38128231	in vitro	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1542	H. Zhao, M. Liu, Y. Lv and M. Fang	2022	Dose-response metabolomics and pathway sensitivity to map molecular cartography of bisphenol A exposure	In the toxicological regime, the toxicological endpoint and its dose–response relationship are two of the most prominent characters in conducting a risk assessment for chemical exposure. Systems biological methods have been used to comprehensively characterize the impact of toxicants on the biochemical pathways. However, the majority of the current studies are only based on single dose, and limited information can be obtained from the dose–response relationship. Here, we applied a dose–response metabolomics and pathway sensitivity analysis to map the molecular cartography of bisphenol A (BPA) exposure on the human biological host. Here, we applied bisphenol A (BPA), a new alternative to bisphenol A (BPA), as the study chemical (ESC1), as the research model. We first employed the global metabolomics method to characterize the metabolome of breast cancer cells (MCF-7) upon exposure to different doses (0, 25, 50, and 100 μM) of BPA. The dysregulated features with a clear dose–response relationship were also effectively picked up with an R-package named BMDExpress. Furthermore, the pathway sensitivity analysis was performed to map the BPA exposure cartography at the pathway level. The results showed that the pathway sensitivity was correlated with the number of metabolites in the pathway. Interestingly, we found that the pathways with a similar dose–response relationship were also effectively picked up with an R-package named BMDExpress. Furthermore, the pathway sensitivity analysis can be further considered and emphasized in future chemical risk assessments. With the established dose–response relationship, we were able to fully map the metabolic cartography of BPA exposure within a wide range of concentrations, and observe some unique patterns. Furthermore, an effective concentration of certain fatty changes (e.g., EC1) (it means the dose at which metabolic (e.g., 10% upregulated) and metabolite sensitivity were defined and introduced to this dose–response metric information. The result showed that the acetoacetate pathway is the most sensitive target of BPA, which can be a potential endogenous biomarker for its exposure. Overall, this study applied the dose–response metabolomics method to fully understand the biochemical pathway disruption of BPA treatment at different doses. Both dose–response metric strategy and metabolite sensitivity analysis can be further considered and emphasized in future chemical risk assessments.	Environ Int. 2022 Jan:158:106893.	10.1016/j.envint.2021.106893	34592654	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1543	F. Zhao, H. Liu, Z. Li, P. Lin, A. Wang, Y. Jin and Y. Yi	2021	Low-dose bisphenol A impairs the function of mouse decidual stromal cells by activating LUMAN-mediated unfolded protein response	The environmental estrogenic compound bisphenol A (BPA) is widely present in several industrial and medical products including plastic food containers and sealants. In dentistry. There are growing concerns on the toxic effects of this compounds since BPA is known to have reproductive toxicity. This study evaluated the effects of low-dose BPA exposure on decidual stromal cells (DSCs) of mice. The results showed that although 10-nM of BPA have no significant effect on the cell viability, it alters the expression of decidualization-related genes including Prl8a2, Prl3c1, Prg2, and Wnt4. Moreover, we found that low-dose BPA exposure induces UPR response in DSC s. However, the expression of the three major UPR receptors (Perk, Ire 1, and Atg6) did not change significantly. Interestingly, the expression of Luman, a novel receptor of UPR, was significantly increased in DSCs exposed to low-dose BPA. Luman knockdown in DSCs exposed to low-dose BPA significantly reversed the BPA-induced inhibition of the expression of decidualization-related genes in decidual cells after BPA treatment. In summary, these results suggest that Luman plays a key role in low-dose BPA-induced decidual toxicity of DSCs in mice.	Food Chem Toxicol. 2021 Jul:153:112242.	10.1016/j.fct.2021.112242	33930482	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1557	D. Zhang, X. Liu, Y. Qi, Y. Lin, K. Zhao, Y. Jin, J. Luo, L. Xu, D. Yu and C. Li	2023	Binding, activity and risk assessment of bisphenols toward farnesoid X receptor pathway: In vitro and in silico study	Bisphenols have been identified as emerging environmental pollutants of high concern with potential adverse effects through interactions with receptor-mediated pathways. However, their potential mechanism of action and health risks through the farnesoid X receptor (FXR) pathway remain poorly understood. In the present study, we aimed to explore the potential disruption mechanism of bisphenols through the FXR signalling pathway. Receptor binding assays showed that bisphenols bound to FXR directly, with tetrachlorobisphenol A (TBBPA, Ki: 5.46), tetrachlorobisphenol A (TCBPA, Ki: 7.64), bisphenol BP (BPBP, Ki: 2.5) and bisphenol B (BPB, Ki: 3.08) showing the strongest binding affinities. Bisphenols also showed antagonistic activity to FXR, with TBBPA (IC50: 0.19 μM), TCBPA (IC50: 0.21 μM), BPBP (IC50: 0.23 μM) and BPB (IC50: 0.25 μM) exhibiting higher activity than BPA. Molecular docking results indicated that the number of hydrogen bonds dictated their binding strength. Intracellular concentrations of bisphenols were quantified using liquid chromatography tandem mass spectrometry (LC-MS/MS) in receptor activity assays, and it was found that the intracellular concentrations of TBBPA and TCBPA were 60 fold lower than those of BPA. Using the bioactivity concentrations in the FXR receptor activity assay, the liver concentrations of bisphenols were estimated using physiologically based pharmacokinetic (PBPK) models through their serum concentrations, and the hazard quotient (HQ) values were calculated. The results suggest a potentially high concern for the risk of activating the FXR pathway for some populations with high exposure. Overall, these results indicate that bisphenols can bind to and activate FXR receptors, and that the activation mechanism is dependent on cellular uptake and binding strength. This study provides important information regarding the exposure risk of bisphenols, which can promote the development of environmentally friendly bisphenols.	Sci Total Environ. 2023 Apr 15:869:161701.	10.1016/j.scitotenv.2023.161701	36709907	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1558	B. A. Zhang, B. Miao, S. Fu, C. Coarfa, R. Kumar, P. K. Kuribara, B. Park, S. L. Grimm, R. Jangid, J. A. Colacino, L. K. Svoboda, W. Shao, X. Xing, D. Li, S. Liu, R. B. Hamanaka, C. Lalancette, M. A. Santer, C. Knapp, G. E. Crawford, H. B. Patisaul, T. Wilhite, D. Aylor, S. Blewett, G. M. Mutlu, S. Rajagopalan, W. Y. Tang, T. Wang, D. C. Dolinoy, M. S. Bartolomei and C. Walker	2025	Comprehensive Transcriptomic and Epigenomic Insights into Environmental Toxicant Exposures: The TaRGET II Resource	Environmental exposures to toxic chemicals can profoundly alter the transcriptome and epigenome in both humans and animals, contributing to disease development across the lifespan. To elucidate how early-life exposures to environmental chemicals can influence long-term health outcomes, the Toxicant Exposure and Response by Genomic and Epigenomic Regulators of Transcription (TaRGET) II Consortium generated 1,568 epigenome and 1,563 transcriptome from longitudinal studies in mice. All data are publicly available through the TaRGET II data portal and the Gene Expression Omnibus. This resource from target (liver, lung, heart) and surrogate (blood) tissues at weaning (3 weeks) and two adult time points (5 and 10 months) characterized the molecular response to arsenic (As), lead (Pb), bisphenol A (BPA), di (2-ethylhexyl) phthalate (DEHP), tributyltin (TBT), tetrachlorodibenzo-p-dioxin (TCDD), and particulate matter with a diameter of <2.5 μm (PM2.5). The findings revealed persistent, toxicant-specific, sex-dependent epigenomic and transcriptomic perturbations, resulting in disrupted expression of 12,888 genes, altered chromatin accessibility at 87,309 regulatory elements, DNA methylation changes at 112,186 genomic regions, and chromatin state shifts at 1,000,000 genomic loci. Integrative analyses revealed that exposure-induced changes in DNA methylation and chromatin accessibility were associated with altered gene expression. The TaRGET database, offering unparalleled opportunities for the scientific community to investigate the molecular underpinnings of environmental toxicant exposures and their contributions to disease pathogenesis.	bioRxiv [Preprint]. 2025 Jul 31:2025.07.28.667191.	10.1101/2025.07.28.667191	40766696	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1559	B. Zhang, S. Wang, Y. Tang, Z. Hu, L. Shi, J. Lu, H. Li, Y. Wang, Y. Zhu, H. Lin and R. S. Ge	2023	Direct inhibition of bisphenols on human and rat 11 β -hydroxysteroid dehydrogenase 2: Structure-activity relationship and docking analysis	Bisphenols (BPs) as endocrine disrupting compounds have drawn attention to their health hazards. Whether a BP interferes with glucocorticoid metabolism remains unclear. 11 β -Hydroxysteroid dehydrogenase 2 (11 β -HSD2) is a key enzyme in glucocorticoid metabolism. In this study, we investigated the inhibitory effects of 13 BPs on human and rat 11 β -HSD2 in vitro. Results showed that only 7 BPs were found to inhibit human placental and rat renal 11 β -HSD2 and were analyzed for inhibitory potency, mode and site, and docking parameters. BPA had inhibitory potency against human 11 β -HSD2. BPC > BPAP > BPZ > BPB > BPC-BPAP > BPS > TCBPA and the IC(50) values were 0.31, 0.36, 1.06, 3.83, 3.93, 7.57, 10.43, and 21.58 μM, respectively. All BPs are mixed inhibitors except BPAP, which is a competitive inhibitor to human 11 β -HSD2. Some BPs also inhibited rat renal 11 β -HSD2, with BPB (0.58), 2179 ± 3.58) > BPZ (10.12 ± 3.69) > BPAP (16.87 ± 1.70) > BPA (17.31 ± 2.82) > BPC (49.49 ± 5.05). Docking analysis showed that all BPs bound to the steroid-binding site, interacting with the catalytic residue Tyr232 at both enzymes and the most potent human 11 β -HSD2 inhibitor BPC1, only possibly due to its large fluorene ring that has hydrophobic interaction with residues Gly272 and Val270 and a π -stacking interaction with catalytic residue Tyr232. The increase in the size of substituted alkanes and halogenated groups in the methane moiety of bridge of BPs increases its inhibitory potency. Regressions of the ionic binding energy with inhibition constant indicated that there was an inverse regression. These results indicated that BPs significantly inhibited human and rat 11 β -HSD2 activity, and that there were species-dependent differences.	Ecotoxicol Environ Saf. 2023 Apr 1:254:114715.	10.1016/j.ecoenv.2023.114715	36871355	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1560	W. Zeng	2020	Bisphenol A triggers the malignancy of nasopharyngeal carcinoma cells via activation of Wnt/ β -catenin pathway	It is critical to understand the risk factors responsible for the tumorigenesis and progression of nasopharyngeal carcinoma (NPC). Bisphenol A (BPA) can regulate the estrogenic signals to modulation cancer progression. However, the role of BPA in nasopharyngeal carcinoma (NPC) remains unclear. In this study, we investigated the effects of BPA on NPC cells and explored the underlying mechanisms. We found that BPA at 10 μM significantly increased the β -catenin (LEF1) and matrix MMP2 induced cell proliferation of NPC cells, which is due to that BPA could increase phosphorylation of AKT at Ser473 and nuclear translocation of β -catenin. Mechanistically, BPA can increase the mRNA stability of β -catenin (encoded by CTNNB1) via suppressing the expression of miR-202-3p, which can direct target the 3'UTR of β -catenin mRNA. Further, BPA can decrease phosphorylation of β -catenin via repressing the expression of CK1α. Collectively, our data showed that BPA can trigger the proliferation and malignancy of NPC cells via activation of Wnt/ β -catenin pathway. It indicated that body accumulation and inhalation exposure of BPA might be a risk factor for NPC development.	Toxicol In Vitro. 2020 Aug:66:104881.	10.1016/j.tiv.2020.104881	32360864	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1561	J. Zeng, J. Li, S. Liu, Z. Yang, Y. Zhong, X. Chan, G. Li and J. Li	2021	Lipidome disturbances in preadipocyte differentiation associated with bisphenol A and replacement bisphenol S exposure	Bisphenol S (BPS) is the major substitute for the production of bisphenol A (BPA) free products and detected in both food and environment. Although the relationship between BPA exposure and increased risk of obesity and diabetes has been noted, the potential influence of BPS is not fully understood. Here, a non-targeted lipidomic study was performed to investigate BPA/BPS exposure-active lipidome in 3T3-L1 preadipocyte differentiation model, and revealed the comprehensive lipidome disturbance induced by either BPA or BPS exposure at different doses of 0.01, 1 and 100 μM. BPS was more potent than BPS in disturbance of lipid homeostasis during preadipocyte differentiation. Specifically, BPS exposure significantly increased the triglycerides (TG) and diglycerides (DG) accumulation in differentiated preadipocytes, providing novel clues of potential mechanisms in which both BPA and BPS exposure could be associated with increased risk of metabolic disturbance. Our study supplies the perspective into the lipidome response to environmental stress induced by BPA/BPS, and shows that BPA-free products are not necessarily safer. Substitution of BPA by its structural analog BPS should be therefore performed with caution.	Sci Total Environ. 2021 Jan 20:753:141949.	10.1016/j.scitotenv.2020.141949	32891999	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1562	Z. Zamora, S. Wang, Y. W. Chen, G. Diamante and X. Yang	2024	Systematic transcriptome-wide meta-analysis across endocrine disrupting chemicals reveals shared and unique liver pathways, gene networks, and disease associations	Cardiometabolic disorders (CMD) are a growing public health problem across the world. Among the known cardiometabolic risk factors are compounds that induce endocrine and metabolic dysfunctions, such as endocrine disrupting chemicals (EDCs). To date, two EDCs influence molecular programs and cardiometabolic risks has yet to be fully elucidated, especially considering the complexity contributed by species-, chemical-, dose-, and sex-specific effects. Transcriptomic studies have been conducted to investigate the molecular effects of EDCs, but they are limited in scope, focusing on a few chemicals or EDCs in a systematic manner, so established a data-driven computational approach to meta-analyze 26 human, mouse, and rat liver transcriptomic datasets for 5 EDCs, namely bisphenol A (BPA), di(2-ethylhexyl) phthalate (DEHP), tributyltin (TBT), and fluorescent tests: and (PFOS). Our computational pipeline uniformly re-analyzed pre-processed quality-controlled microarray data and new RNA-seq data, derived differentially expressed genes (DEGs) and biological pathways, modeled gene regulatory networks and regulators, and determined CMD associations based on gene-overlap analysis. Our approach revealed that DEHP and PFOS shared stable transcriptomic signatures that are enriched for genes associated with CMDs, suggesting similar mechanisms of action such as perturbations of peroxisome proliferator-activated receptor gamma (PPARγ) pathway. Despite these shared effects, BPA uniquely altered the expression of genes associated with CMDs, including those involved in the PPARγ pathway. Sex-specific analysis of BPA effects in mice and rats found that the rat, mouse, and human BPA studies showed highly variable transcriptomic patterns, providing molecular support for the variability in BPA responses. Our work offers insights into the environmentally and differences in the molecular mechanisms of various EDCs and establishes a streamlined data-driven workflow to compare molecular mechanisms of environmental substances to elucidate the underlying connections between chemical exposure and disease risks.	Environ Int. 2024 Jan:183:108339.	10.1016/j.envint.2023.108339	38043319	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1563	A. Zahra, R. Kerstikas, I. Kyrou, H. S. Randeva, C. Sisu and E. Kanteris	2022	Impact of Environmentally Relevant Concentrations of Bisphenol A (BPA) on the Gene Expression Profile in an In Vitro Model of the Normal Human Ovary	Endocrine-disrupting chemicals (EDCs), including the ammonia-type Bisphenol A (BPA), can interfere with hormonal signalling. Despite increasing reports of adverse health effects associated with exposure to EDCs, there are limited data on the effect of BPA in normal human ovaries. In this paper, we present a detailed analysis of the transcriptomic landscape in normal human Epithelial Ovarian Cells (HOSEpiC) treated with BPA for 24 h. Our findings revealed significant changes in the expression of 1,000 genes (FDR < 0.05), including 500 genes that were upregulated and 500 genes that were downregulated in BPA-treated HOSEpiC cells (1 nM and 10 nM BPA-treated HOSEpiCs, respectively), compared to untreated controls. Biological pathways included mRNA surveillance pathway, oocyte meiosis, cellular senescence, and transcriptional misregulation in cancer. BPA exposure has a considerable impact on 10 genes, BMPR2, AURKA, CDK1, CCNA2, CCNB1, PLK1, BUB1, KIF23, PDE3B, and CCNB2, which are also associated with progesterone-mediated oocyte maturation pathways. Future studies should further explore the effects of BPA and its metabolites in the ovaries in health and disease, making use of validated in vitro and in vivo models to generate data that will address existing knowledge gaps in basic biology, hazard characterisation, and risk assessment associated with the use of xenoestrogens such as BPA.	Int J Mol Sci. 2022 May 10;23(10):5334.	10.3390/ijms23105334	35628146	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1564	S. Yue, J. Yu, Y. Kong, H. Chen, M. Mao, C. Ji, S. Shao, J. Zhu, J. Gu and M. Zhao	2019	Metabolomic modulations of HepG2 cells exposed to bisphenol analogues	Bisphenol analogues including bisphenol A (BPA), bisphenol AF (BPAF), bisphenol F (BPF), and bisphenol S (BPS) share similar chemical structures and endocrine disrupting effects. Their effects on metabolisms, however, are so far only marginally understood. In this study, NMR-based metabolomic profiles of HepG2 cell culture media and PCR array were used to assess the metabolomics disturbances and gene expression levels of HepG2 in response to low (BPA, BPAF, BPF, and BPS). The results indicated that BP analogues could induce disturbances in 15 metabolites that were classified as amino acid, lipid, carbon, glutamine, glutamate, ketone, intermediates and end products in the glycolysis (pyruvate) and the tricarboxylic acid cycle (acetate, lactate). Their roles in order according to the number of metabolites and pathways was BPF > BPA > BPAF > BPS. The disturbed metabolites and pathways revealed that BP analogues could induce cytotoxicity, cause oxidative stress, and promote cell proliferation. Moreover, BPF showed the strongest ability to induce the capability of disrupting glucose metabolism, they may act through different mechanisms. BPAF has increased the population lower PKLR expression level, which implied enhanced glycolysis that was agreed with NMR results. The other three BP analogues, however, decreased the expression level of glucokinase (GCK) that indicated glucose sensing impairment. Our results demonstrated the potential for using metabolomic and PCR array to understand the underlying action of mechanisms, and identify the potential targets for future targeted risk assessments.	Environ Int. 2019 Aug:129:59-67.	10.1016/j.envint.2019.05.008	31121516	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1565	X. Yuan, K. Chen, F. Zhang, S. Xu, Y. Li, Y. Wang, H. Ni, F. Wang, Z. Cui, Y. Qin, D. Xia and Y. Wu	2023	Low-dose BPA and its substitute BPS promote ovarian cancer cell stemness via a non-canonical PINK1/p53 mitophagic signaling	The environmental toxicity of bisphenol S (BPS) and its analog like bisphenol S' (BPS') have drawn wide attention, but their roles in cancer progression remain controversial. Here, we investigated the effect of BPA/BPS on the development of ovarian cancer. Human normal BPA/BPS exposure both were analyzed from MIMOSA (2013-2016) data. We treated human ovarian cancer cells with 0-1000 nM BPA and found that 100 nM BPA/BPS treatment significantly increased Cancer Stem Cell (CSC) markers expression including OCT4, NANOG and SOX2. Cancer cell stemness evaluation induced by BPA/BPS was notably attenuated by the mitophagy inhibitor Mdivi-1 and PINK1 knockdown, but not by mitochondrial fission inhibitor Drp1-IN-1 and Drp1 knockdown. Mechanistically, BPA/BPS induced PINK1 accumulation and higher tumor metastasis incidence compared with the control group, while mitophagy inhibition blocked such a promotion effect. In addition, CSC markers such as SOX2 had been found to be overexpressed in the tumor tissues of BPA/BPS-exposure group. Taken together, the findings herein first provide the evidence that environmentally relevant BPA/BPS exposure could enhance ovarian cancer cell stemness through a non-canonical PINK1/p53 mitophagic pathway, raising concerns about the potential population hazards of BPA and other bisphenol analogs.	J Hazard Mater. 2023 Jun 15:452:131288.	10.1016/j.jhazmat.2023.131288	36989771	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1566	W. B. Yuan, H. Q. Chen, J. Z. Li, S. M. Zhu, Y. Zeng, J. Fan, Z. Zhang, L. Y. Liu, J. Cao and W. B. Liu	2022	TET1 mediated male reproductive toxicity induced by Bisphenol A through Catsper-Ca(2+) signaling pathway	Bisphenol A (BPA) exposure has many adverse effects on the reproductive system in animals and humans. Ten eleven translocation-1 (TET1) is closely related to a variety of biological processes through regulating the dynamic balance of DNA demethylation and methylation. However, the role and mechanism of TET1 during BPA-induced reproductive toxicity are largely unknown. In this study, mouse spermatogonia cell line GC-2 was treated with BPA to the final concentration of 0, 30, 60 and 90 μM for 72 h. The cell model of differential TET1 gene expression was established to explore the role and mechanism. We found that the growth rate of GC-2 cells was significantly inhibited by BPA exposure in a dose-dependent manner. Meanwhile, BPA induced the apoptosis of GC-2 cells. Moreover, BPA exposure could cause the spermatozoa abnormality and decrease of GC-2 cells the increase of calcium ion concentration, and the expression level of Catsper1-4, a key transducer of TET1 family in calcium ion channels. Electronically, TET1 expression promoted the hydroxymethylation of Catsper1-4 and reduced their methylation level. In addition, the expression level of Catsper1-4 was positively correlated with TET1 gene expression level in somatic samples of the population. Our study revealed for the first time that TET1 gene regulates the expression of related molecules in the Catsper calcium signal pathway through its hydroxymethylation modification to affect the calcium level, thereby participating in the process of BPA-induced damage. These results indicated that TET1 gene may be a potential biomarker of BPA-induced male reproductive toxicity.	Environ Pollut. 2022 Mar 1:296:118739.	10.1016/j.envpol.2021.118739	34953956	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1567	B. Yuan, J. Li, Q. Shu, X. Wang, G. Luo and R. Ma	2025	Identification of comorbid genes between type 2 diabetes and migraine through peripheral blood single-cell and Mendelian randomization analysis	BACKGROUND: Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by hyperglycemia and insulin resistance. Migraine is a common chronic neurological disease caused by increased excitability of the central nervous system, both exerting substantial health burdens. However, the shared genetic basis and underlying molecular mechanisms remain largely unexplored. This study integrates single-cell data and Mendelian randomization (MR) analysis to identify comorbidity-associated genes and elucidate potential mechanistic links between these two conditions. METHODS: Single-cell datasets from T2DM and migraine were analyzed to identify differentially expressed genes (DEGs). MR analysis was employed to prioritize key causal genes, followed by network-based functional characterization, disease-drug association analysis, cell-annotation, and pseudotime trajectory analysis. Finally, the expression of hub genes was validated in an independent cohort. RESULTS: We identified 1,000 DEGs in T2DM and 1,000 DEGs in migraine. Among them, 14 genes were highlighted. KPNB1 and HSD17B10 are key regulatory molecules in both conditions. Network analysis further revealed their role in both metabolism and oxidative transport pathways. Comprehensive correlations, including metabolic dysregulation and chemical-induced liver injury, as well as potential therapeutic agents such as valproic acid and bisphenol A. Single-cell annotation identified six major immune cell types in T2DM (T cells, NK cells, B cells, CD16 monocytes, CD14 monocytes, and dendritic cells), with T cells emerging as central players. In migraine, five immune cell types were identified (CD8 T cells, CD4 T cells, B cells, NK cells, and monocytes), with monocytes being the predominant cell type. Pseudo-time analysis delineated seven subpopulations of T cells and four subpopulations of monocytes, suggesting distinct differentiation trajectories. Cell-cell communication revealed significant interactions between monocytes and T cells in both T2DM and migraine, mediated by MIF-(CD74+CXCR4) and MIF-(CD74+CD44) signaling. Genes-immune cell correlation analysis further revealed that KPNB1 and HSD17B10 are shared genetic determinants in T2DM-migraine comorbidity, shedding light on their molecular interplay and potential therapeutic relevance.	J Headache Pain. 2025 Jul 1:26(1):151.	10.1186/s10194-025-02090-4	40596821	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1568	Z. Yu, W. Yang, Q. Zhang and M. Zhang	2025	Unveiling the impact of estrogen exposure on ovarian cancer: a comprehensive risk model and immune landscape analysis	This study examines the impact of estrogenic compounds like bisphenol A (BPA), estradiol (E2), and oxandrolone (ZEA) on human ovarian cancer, focusing on constructing a risk model, conducting gene set variation analysis (GSVA), and evaluating immune infiltration. Differential gene expression analysis identified 882 shared differentially expressed genes (DEGs) in human ovarian cells exposed to BPA, E2, and ZEA, indicating significant transcriptional changes. Functional enrichment analysis revealed that these DEGs are involved in critical biological processes, including cell cycle regulation and DNA damage response, and are enriched in pathways such as the p53 signaling pathway and oocyte meiosis. Protein-protein interaction (PPI) analysis highlighted hub genes, including cyclin-dependent kinase 1 (CDK1), Tp53 and tumor suppressor (TP53), and aurora kinase A (AURKA), as key regulators. Survival analysis further revealed that these genes is both medication and oncotic transport pathways. Computational predictions revealed that these genes is both medication and oncotic transport pathways. Computational predictions revealed two distinct risk categories, showing significant differences in overall survival, disease-specific survival, and progression-free survival. GSVA analysis linked HPDL expression to pathways related to the cell cycle, DNA damage, and repair, while TP53 and PTEN were associated with apoptosis, hypoxia, and proliferation pathways. Immune infiltration analysis revealed distinct immune cell profiles in the high- and low-risk groups, with the high-risk group exhibiting higher levels of activated CD4 memory T cells, M0 macrophages, and resting mast cells, but lower levels of resting CD4 memory T cells, M2 macrophages, and resting dendritic cells. These findings suggest that BPA exposure may significantly alter gene expression and oncogenic pathways in ovarian cancer. The risk model integrating HPDL, TAF1, and PLOD1 offers a strong prognostic tool, while GSVA and immune infiltration analyses provided insights into the interplay between these genes and the tumor microenvironment, suggesting potential targets for personalized therapies.	Toxicol Mech Methods. 2025 Mar;35(3):279-291.	10.1080/15376516.2024.2402865	39252197	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1569	H. Yu and Y. Liu	2023	Impact of Extended and Combined Exposure of Bisphenol Compounds on Their Chromosome-Damaging Effect—Increased Potency and Shifted Mode of Action	Bisphenol (BP) compounds are important environmental pollutants and endocrine disruptors. BPs are capable of inducing DNA/chromosome breaks (clastogenesis, treated in vaccinogenesis), which requires verification by human CYP1A1. We hypothesized that combined BPs and extended (from the standard two-cell cycle) exposure may enhance their genotoxicity via modulating CYP enzymes. In this study, individual and combined BPA/BPF/BPS/BPAF and a human hepatoma (HepG2) cell line were used for testing several previously not-tested points. Exposing for a two-cell cycle period (24 h), each BP alone (0.625–25 μM) was negative in the micronucleus (MN) assay, but combinations of BPA + BPF, BPA + BPS, and BPA + BPAF induced MN. Extending the exposure to 1.5 cell cycles (36 h) increased the MN induction by BPA alone and in combination with tested micronuclei. Indicated that BPA exposure produced centromere-negative micronuclei and phosphorylated histone H2 (γ-H2) (indicating chromosome loss, i.e., aneugenesis), moreover, 1-aminobenzotriazole (CYP inhibitor) selectively blocked the formation of centromere-negative micronuclei and γ-H2AX, without affecting that of centromere-positive micronuclei and γ-H2. This study suggests that the genotoxicity of BPs is potentiated by combined and extended exposure, the latter being specific for aneuploidy formation, a CYP activity-independent effect.	Environ Sci Technol. 2023 Jan 10;57(1):498-508.	10.1021/acs.est.2c06064	36571243	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で排除に基づき排除。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1570	H. Yu, L. Gu, H. Ma and L. Yu	2025	Identification and analysis of diagnostic markers related to lactate metabolism in myocardial infarction	Lactate metabolism is implicated in myocardial infarction (MI), yet the underlying mechanisms are not fully understood. Identifying lactate metabolism-related genes (LMRGs) could uncover new diagnostic and therapeutic targets for MI. We conducted a bioinformatics analysis on GeneCards database to identify 1985 LMRGs, and intersected them with differentially expressed genes (DEGs) from MI samples, yielding 17 key genes. Functional enrichment analysis revealed that these genes were primarily involved in pathways such as the citrate cycle (TCA cycle), pyruvate metabolism, and glycolysis/gluconeogenesis. Using the XGBoost, SVM-RFE, and GLMNET algorithms, we identified 6 LMRGs associated with MI. Ultrasound and Lactate metabolism pathways. Enrichment analysis and immune microenvironment assessments were performed, and networks including drug-gene interactions and transcription factor (TF)-mRNA-miRNA axes were constructed to explore the functions and potential therapeutic implications of these genes. The three biomarkers showed significant correlations with immune cell types, with GLS01 having the highest positive correlation with monocytes and the highest negative correlation with eosinophils. The drug-gene network revealed potential interactions such as metoprolol tartrate with LDHB and Vorinostat with HLDPC. The 3-layer TF-mRNA-miRNA network comprised 208 nodes and 376 edges, indicating complex regulatory mechanisms. Our study identified three key biomarkers, GLS01, LDHB, and HLDPC, in lactate metabolism-associated AMI-MI, providing insights into potential diagnostic markers and therapeutic targets. These findings warrant further investigation into the molecular mechanisms of these biomarkers in MI.	Pathol Res Pract. 2025 Jul:271:156010.	10.1016/j.prp.2025.156010	40367892	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1571	M. H. Yoo, S. J. Lee, W. Kim, Y. Kim, Y. B. Kim, K. S. Moon and B. S. Lee	2022	Bisphenol A impairs renal function by reducing Na(+)/K(+)-ATPase and F-actin expression, kidney tubule formation in vitro and in vivo	The kidney proximal tubule is responsible for reabsorbing water and NaCl to maintain the homeostasis of the body fluids, electrolytes, and nutrients. Thus, abnormal functioning of the renal proximal tubule can lead to fluid and electrolyte imbalance. Bisphenol A (BPA) is a well-known endocrine disruptor that induces various adverse effects in humans and animals. However, the effects of BPA on renal tubular immunohistochemical and cytotoxicity tests were performed using two- and three-dimensional culture models. Enrichment analysis and immune response biomarker assessments were performed, and networks including drug-gene interactions and transcription factor (TF)-mRNA-miRNA were constructed to explore the functions and potential therapeutic implications of these genes. The three biomarkers showed significant correlations with immune cell types, with GLS01 having the highest positive correlation with monocytes and the highest negative correlation with eosinophils. The drug-gene network revealed potential interactions such as metoprolol tartrate with LDHB and Vorinostat with HLDPC. The 3-layer TF-mRNA-miRNA network comprised 208 nodes and 376 edges, indicating complex regulatory mechanisms. Our study identified three key biomarkers, GLS01, LDHB, and HLDPC, in lactate metabolism-associated AMI-MI, providing insights into potential diagnostic markers and therapeutic targets. These findings warrant further investigation into the molecular mechanisms of these biomarkers in MI.	Ecotoxicol Environ Saf. 2022 Nov:246:114141.	10.1016/j.ecoenv.2022.114141	36206637	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1572	Z. Yin, L. Hua, L. Chen, D. Hu, J. Li, Z. An, T. Tian, H. Ning and Y. Ge	2020	Bisphenol-A exposure induced neurotoxicity and associated with synapse and cytoskeleton in Neuro-2a cells	Bisphenol-A (BPA) is an environmental chemical that induces neurotoxic effects for human. Synaptophysin (SYP) and Ankrin (Ank) proteins are involved in regulating synaptic morphology. The stability of the cytoskeleton in nerve cells is the basis to regulating by Tau and MAP2. The study aimed to determine the toxicity of BPA to Neuro-2a cells by investigating the synaptic and cytoskeletal damage induced to these cells by 72 h of exposure to 0 (MEM), 50, 100, 150, 200 μg/MPA or DMSO. MTT and LDH assays showed that the death rates of Neuro-2a cells increased, as the BPA concentration increased. Ultrastructural assays revealed that cells underwent nuclear crumbling as well as nuclear membrane and partial mitochondrial dissolve or condensation, following BPA exposure. Morphological analysis further revealed BPA-induced damage compared with the cells in the control group, the cells in the BPA-treated groups shrunk, became rounded, and exhibited a reduced number of synapses. BPA also significantly decreased the relative protein and mRNA expression levels of Glun, MAP2 and Tau (P < .01), but increased the relative protein and mRNA expression levels of SYP (P < .01). These results indicated that BPA-suppressed the development and proliferation of Neuro-2a cells by disrupting cellular and synaptic integrity and inducing cytoskeleton injury.	Toxicol In Vitro. 2020 Sep:67:104911.	10.1016/j.tiv.2020.104911	32512148	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1573	N. Yin, X. Liang, S. Liang, S. Liang, R. Yang, B. Hu, Z. Cheng, S. Liu, H. Dong, S. Liu and F. Faiola	2019	Embryonic stem cell- and transcriptomics-based in vitro analyses reveal that bisphenols A, F and S have similar and very complex potential developmental toxicities	Bisphenol A (BPA) is a very versatile industrial chemical. Many reports have associated BPA with several health effects. Some bisphenol alternatives have been introduced to replace BPA in its many applications. However, comprehensive toxicological evaluations for these replacements are still lacking. In this study, we examined the potential effects of BPA, bisphenol F (BPF) and bisphenol S (BPS), on embryonic development using mouse embryonic stem cells (mESCs) and transcriptomics. Cytotoxicity tests showed that BPA, BPF, and BPS induced similar concentration-dependent decreases in cell viability. Global transcriptional changes, as seen through RNA-sequencing, were also similar for BPA, BPF, BPS, and DMSO control. Genome-scale calculations of the benchmark concentrations (BMCs) for these three assays, in vitro BPA and PBS-exposed mESCs, BPA, BPF and BPS disrupted many processes, during mESC global and neural differentiations, in very similar manners. In fact, at each time point the three chemicals differentially regulated analogous gene categories, particularly the ones involved in cell metabolism and cell adhesion, signal transduction pathways, and nuclear) conditions such as cardiovascular diseases and cancer. Our findings demonstrate that BPF and BPS may cause more than BPA is absolutes, may not be very safe. They potentially have a very complex developmental toxicity, similarly to BPA, and some even toxic than BPA itself. In addition, our results reveal that stem cell-based developmental toxicity assays can be very comprehensive.	Ecotoxicol Environ Saf. 2019 Jul 30:176:330-338.	10.1016/j.ecoenv.2019.03.115	30951980	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1574	L. Yin, C. Hu, and X. i. Yu	2023	High-content analysis of testicular toxicity of BPA and its selected analogs in mouse spermatogonial, Sertoli cells, and Leydig cells revealed BPAF induced unique multinucleation phenotype associated with the increased DNA synthesis	Bisphenol A is an endocrine disruptor that has been shown to have testicular toxicity in animal models. Its structural analog, including bisphenol S (BPS), bisphenol AF (BPAF), and tetrabromobisphenol A (TBBPA) have been introduced to the market as BPA alternatives. Previously, we developed high-content analysis (HCA) assays and applied machine learning to compare the testicular toxicity of BPA and its analogs in spermatogonial cells and testicular cell co-culture models. There are diverse cell populations in the testis to support spermatogenesis, but their cell type-specific toxicities are still not clear. The purpose of this study is to examine the testicular toxicity of BPA and its analogs in mouse spermatogonial, Sertoli cells, and Leydig cells. Cells were treated with BPA, BPS, BPAF, and TBBPA at 0.1-100 μM for 24 h. Then, cells were stained with a multiplexed fluorescent dye solution to measure changes in several hallmarks of testicular toxicity, including cytotoxicity, cell cycle perturbation, nuclear morphology, DNA synthesis, cell type-progression, mitotic defect, DNA damage response, cytoskeleton structure, DNA methylation status, and autophagy. We introduced an HCA index and spectrum to reveal multiple HCA parameters and observed distinct toxicity profiling of BPA and its analogs among three testicular-type cells. The HCA spectrum shows the dynamic, chemical-specific, dose-dependent impact of each HCA parameter. Each chemical displayed a unique dose-dependent profile within each type of cell. Of these types of cells, cells showed the highest response to BPAF at 10 μM across all endpoints measured. BPAF targeted spermatogonial cell (C18) more significantly at 1 μM. BPS more likely targeted Sertoli cell (TM4) and Leydig cell (TM3) and induced cytotoxicity, cell cycle perturbation, and DNA synthesis at 10 μM. BPA and TBBPA showed similar toxicity profiles in all three types of cells. Interestingly, we observed that BPAF induced a dose-dependent increase in spermatogonial cells, not in Sertoli and Leydig cells. In summary, our current HCA assays revealed the cell type-specific toxicities of BPA and its analogs to different testicular cells. Multinucleation induced by BPAF, along with increased DNA damage and synthesis at low doses, could possibly have a profound long-term effect on reproductive systems.	Toxicol In Vitro. 2023 Jun:89:105589.	10.1016/j.tiv.2023.105589	36958674	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1575	X. Ye, Z. Liu, H. W. Han, J. Y. Noh, Z. Shen, D. M. Kim, H. Wang, H. Gao, J. Ballard, A. Golovko, B. Morpurgo and Y. Sun	2023	Nutrient-Sensing Ghrelin Receptor in Macrophages Modulates Bisphenol A-Induced Intestinal Inflammation in Mice	Bisphenols are environmental toxins with endocrine disruptor activity, yet bisphenol S (BPS) and its analogs are still widely used in manufacturing plastic products. There is evidence showing that BPS elicits inflammation in the intestine, but the mechanisms are not fully understood. Ghrelin receptor (GHSR) is a nutrient-sensing receptor that regulates energy homeostasis and inflammation. Here, we found that GHSR is an important nutrient-sensing hormone, acting through its receptor growth hormone secretagogue receptor (GHSR) to regulate metabolism and inflammation. We found that BPS promotes intestinal inflammation, showing increased infiltrating immune cells in colons and enhanced expression of Ghsr and pro-inflammatory cytokines and chemokines, such as Il6 and Ccl2, in colonic mucosa. Moreover, we found that both long- and short-term BPS exposure elevated pro-inflammatory monocytes and macrophages in mouse peripheral blood monocytes (PBMC) and peritoneal macrophages (PM), respectively. To determine the role of GHSR in BPS-mediated inflammation, we generated Ghsr deletion mutation in murine macrophage RAW264.7 using CRISPR gene editing. In wild-type RAW264.7 cells, the BPS exposure promotes macrophage pro-inflammatory polarization, whereas Ghsr deletion in RAW264.7 cells blocks BPS-induced pro-inflammatory polarization. Mechanistically, BPS exposure activates the AMPK-FoxO1 pathway in macrophages, and Ghsr deletion significantly suppresses BPS-induced activation of AMPK-FoxO1 pathway in macrophages. Taken together, our findings suggest that GHSR is required for the BPS-induced pro-inflammatory response. Further understanding how nutrient-sensing GHSR signaling regulates BPS-intestinal immunotoxicity will help design new strategies to mitigate BPS immunotoxicity and provide policy guidance for BPA biosafety.	Genes (Basel). 2023 Jul 16:14(7):1455.	10.3390/genes14071455	37510359	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1576	A. Yaver, E. Sychrová, J. Ralíšk, P. Babica and I. Sovadinová	2022	Endocrine-disrupting chemicals affect Sertoli TM4 cell functionality through dysregulation of gap junctional intercellular communication in vitro	The frequencies of adverse outcomes associated with male reproductive health, including infertility and testicular cancer, are increasing. These adverse trends are partially attributed to increased exposure to environmental agents such as endocrine-disrupting chemicals (EDCs). The most deleterious effects on EDCs on adjacent prepubertal Sertoli TM4 cells, sized healthy or 3 consecutive days purchased intercellular communication (GJIC), one of the hallmarks of non-genotoxic carcinogenicity. 2) GJIC-building blocks connexins (Cx), and 3) nitrogen-activated protein kinases MAPKs. We selected eight representatives of EDCs – organochlorine chemicals such as pesticides dichlorodiphenyltrichloroethane, lindane, methoxychlor, and chlorinated, industrial chemicals bisphenol A and 2,2′,4,4,5,5′-hexachlorobiphenyl and components of personal care products, triclocarban and triclosan. EDCs rapidly dysregulated GJIC in Sertoli TM4 cells, mainly via MAPK p38 and/or ERK1/2 pathways by the intermediate layer – or else phosphorylation of Cx43 (Ser368). Ser262 and Ser279/282 of Cx43 from the plasma membrane, suggesting disturbed intracellular trafficking of Cx43 protein. Accordingly, EDCs did not significantly alter MAPK-Erk1/2 or p38 nor the total Cx43 protein level activity (phosphorylation). Our results indicate that EDCs might disrupt testicular homeostasis and development via testicular GJIC, positioned another positioned functions of Cx43 and MAPK-signaling pathways in Sertoli cells.	Food Chem Toxicol. 2022 Jun:164:113004.	10.1016/j.fct.2022.113004	35413382	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1577	A. Yaver, E. Sychrová, P. Lahchia, J. Ralíka, T. Jambor, P. Babica and I. Sovadinová	2020	Endocrine-disrupting chemicals rapidly affect intercellular signaling in Leydig cells	A decline in male fertility possibly caused by environmental contaminants, namely endocrine-disrupting chemicals (EDCs), is a topic of public concern and scientific interest. This study addresses a specific role of testicular gap junctional intercellular communication (GJIC) between adjacent preputerial Leydig cells in endocrine disruption and male reproductive toxicity. Organochlorine pesticides (lindane, methoxychlor, DDT), polychlorinated biphenyl congener PCB 153, bisphenol A, and personal care products triclocarban and triclosan were selected as EDCs. Leydig TM3 cells were exposed to EDCs for 24 h, and GJIC was assessed by inhibition of dye coupling (GJIC) between neighboring cells. Connexin (Cx) 43 and its phosphorylation at serine residues Ser262, Ser279/282, and Ser368 were analyzed by Western blot. Lindane, triclocarban, triclosan, and PCB 153 rapidly dysregulated GJIC in Sertoli TM3 cells, mainly via MAPK p38 and/or ERK1/2 pathways by the intermediate layer – or else phosphorylation of Cx43 (Ser368). Ser262 and Ser279/282 of Cx43 from the plasma membrane, suggesting disturbed intracellular trafficking of Cx43 protein. Accordingly, EDCs did not significantly alter MAPK-Erk1/2 or p38 nor the total Cx43 protein level activity (phosphorylation). Our results indicate that EDCs might disrupt testicular homeostasis and development via testicular GJIC, positioned another positioned functions of Cx43 and MAPK-signaling pathways in Sertoli cells.	Toxicol Appl Pharmacol. 2020 Oct 1:404:115177.	10.1016/j.taap.2020.115177	32739526	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1578	V. Yarishkill Jayaram, S. Baggavelli, D. Reddy, S. Sista and R. Malampati	2020	Effect of endosulfan and bisphenol A on the expression of SUMO and UBC9	This study was designed to investigate possible interference of Xenobiotics with SUMO/ubiton in eukaryotic cells. To begin with, we docked 71 chemical structures from PubChem with human SUMO1 and UBC9 protein structures using Auto Dock 4.2 and Vina 1.1 and selected five compounds for binding studies in Surface Plasmon Resonance (SPR) with human SUMO1. In SPR studies, only endosulfan showed binding to SUMO1 (Kd(D) 3.23 × 10−6 M). Further, in cultured HePG2 and differentiated 3T3-L1 cells with endosulfan/Bisphenol A/perfluorooctanic acid (PFOA) to test induction of oxidative stress and SUMO isoform/UBC9 expression. Endosulfan induced oxidative stress in HePG2 cells at 0.5 μg/ml and 3T3-L1 cells at 1 μg/ml. Bisphenol A induced oxidative stress in HePG2 cells at 1 μg/ml and 3T3-L1 cells at 2 μg/ml. Endosulfan resulted in elevated mRNA levels of SUMO1, 2 and UBC9, whereas, treatment resulted in elevated mRNA levels of SUMO1, 2 and UBC9, whereas, treatment with bisphenol A resulted in increased mRNA levels of SUMO2. Exposure to endosulfan and bisphenol A on the expression of SUMO and UBC9 proteins. We propose that one reason for the severe health consequences of exposure to endosulfan/bisphenol could be due to induction of oxidative stress, and modulation in SUMO and UBC9 gene expression.	Drug Chem Toxicol. 2020 Nov;43(6):637-644.	10.1080/01480545.2018.1526179	30426790	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1579	W. Yang, F. Pan, T. Zhao, F. Chen, W. Shao, J. Wang, S. Wang, Z. Zhao, K. Liu, S. Zhao and L. Zhao	2025	Bisphenol A induces apoptosis and disrupts testosterone synthesis in TM3 cells via reactive oxygen species-mediated mitochondrial pathway and autophagic flux inhibition	Bisphenol A (BPA) is a common endocrine disruptor chemical that is widely used in the production of food plastic packaging, and it has been shown to potentially harm the reproductive system. However, the specific mechanism by which BPA induces apoptosis of Leydig cells (LCs) and inhibits testosterone synthesis in LCs remains unclear. In the present study, TM3 cells were used as an experimental model in combination with the reactive oxygen species (ROS) scavenger (N-acetylcysteine), Caspase-3 inhibitor (Ac-DEVD-CHO), autophagy activator (Torin1), and autophagy inhibitor (Chloroquine) to investigate the potential mechanisms by which BPA induces apoptosis and interferes with testosterone synthesis in LCs. The results showed that BPA exposure significantly increased the apoptosis rate and ROS production in TM3 cells. Upregulated ROS cause excessive opening of the mitochondrial permeability transition pore and significantly decrease the expression levels of genes related to membrane potential and mitochondrial function in TM3 cells. The release of cytochrome C from damaged mitochondria into the cytoplasm activated a Caspase cascade reaction. In addition, excessive ROS levels impaired autophagic degradation by inhibiting the fusion of autophagosomes with lysosomes. These abnormalities eventually induced apoptosis and inhibited testosterone synthesis in TM3 cells. The collective findings suggest that BPA induces apoptosis and interferes with testosterone synthesis in TM3 cells by upregulating ROS production, thereby activating the mitochondrial apoptotic pathway and inhibiting autophagic flux. These findings provide novel mechanistic insights into male reproductive toxicity caused by BPA exposure.	Ecotoxicol Environ Saf. 2025 Jan 1:289:117691.	10.1016/j.ecoenv.2025.117691	39799918	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1580	R. Yang, Y. Lu, N. Yin and F. Faiola	2023	Transcriptomic Integration Analyses Uncover Common Bisphenol A Effects Across Species and Tissues Primarily Mediated by Disruption of JUN/FOS, EGFR, ER, PPARG, and P53 Pathways	Bisphenol A (BPA) is a common endocrine disruptor widely used in the production of electronics, sports, and medical equipment, as well as consumer products like milk bottles, dental sealants, and thermal paper. Despite its widespread use, current assessments of BPA exposure risks remain limited due to the lack of comprehensive cross-species comparative analyses. To address this gap, we conducted a study aimed at identifying conserved molecular mechanisms underlying BPA toxicity. We integrated transcriptomic data from 41 BPA exposure studies, encompassing 1,926 samples from 10 species and 15 tissues. Our findings revealed that BPA had a significant changes in processes like DNA metabolism, cell proliferation, and apoptosis, in the mammalian species, in the liver tissues of mammals, fish, and invertebrates. These processes were found to be commonly affected in rodents, fish, mammary atrium, testes, and ovary tissues. Additionally, through an in-depth analysis of signaling pathways influenced by BPA in different species and tissues, we observed that the JUN/FOS, EGFR, ER, PPARG, and P53 pathways, along with their downstream key transcription factors and kinases, were all impacted by BPA. Our study provides compelling evidence that BPA-related endocrine-wide toxic effects across different species and tissues. Furthermore, our investigation sheds light on the underlying molecular mechanisms responsible for these toxic effects. By uncovering these mechanisms, we gain valuable insights into the potential health implications associated with BPA exposure, highlighting the importance of comprehensive assessments and awareness of this widespread endocrine disruptor.	Environ Sci Technol. 2023 Dec 5;57(48):19156-19168.	10.1021/acs.est.3c02016	37978927	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1581	L. Yang, Q. Zhang, M. Cui, L. Zhang and Y. Ma	2024	Effects of bisphenol A and taurourodeoxycholic acid on maturation of porcine oocytes and parthenogenetic development of embryos	Prolonged exposure of bisphenol A (BPA) has adverse effects on in vivo maturation (IVM) of oocytes, but treatment with taurourodeoxycholic acid (TUDCA) can improve the IVM and development of embryos. The purpose of this study was to investigate the effects of BPA and TUDCA on IVM of porcine oocytes and parthenogenetic development of embryos. The results showed that BPA exposure during IVM of oocytes could not only delay body size, mitochondrial distribution of the oocytes after parthenogenetic activation, but also decreased the blastocyst rate and blastocyst cell number of embryos after parthenogenetic development. In addition, BPA treatment upregulated expression of genes related to endoplasmic reticulum stress and apoptosis and increased the intracellular reactive oxygen species (ROS) level, which decreased expression of genes related to oocyte maturation. However, the supplementation of TUDCA relieved these adverse effects of BPA to some extent under body size, blastocyst rate, and expression of BCL2 and PTGS2. In conclusion, the supplementation of TUDCA can partly attenuate the negative effects of BPA on IVM and parthenogenetic development of embryos, possibly by modification of the expression of genes related to endoplasmic reticulum stress, apoptosis and oocyte maturation, intracellular ROS level, and mitochondrial distribution.	Anim Sci J. 2024 Jan-Dec:95(1):e13966.	10.1111/asj.13966	38845341	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1582	L. Yang, C. Baumann, R. De La Fuente and M. M. Viveiros	2022	Bisphenol Exposure Disrupts Cytoskeletal Organization and Development of Pre-Implantation Embryos	The endocrine disrupting activity of bisphenol compounds is well documented, but less is known regarding their impact on cell division and early embryo formation. Here, we tested the effects of acute in vitro exposure to bisphenol A (BPA) and its common substitutes, bisphenol F (BPF), during critical stages of mouse pre-implantation embryo development, including the first mitotic division, cell polarization, as well as morula and blastocyst formation. Timing of initial cleavage was determined by live-cell imaging, while subsequent divisions, cytoskeletal organization and lineage marker labeling were assessed by high-resolution fluorescence microscopy. Our analysis reveals that both values with BPA or BPF impeded cell division and disrupted embryo development at all stages tested. Surprisingly, BPF was more detrimental to the early embryo than BPA. Notably, poor embryo development was associated with cytoskeletal disruptions of the actomyosin network, abnormal chromatin during cell polarization, and/or ring-capping for embryo sealing and abnormal cell lineage allocation. These results underscore that bioplastics can disrupt cytoskeletal integrity and remodeling that is vital for early embryo development and raise concerns regarding the use of BPF as a 'safe' BPA substitute.	Cells. 2022 Oct 14;11(20):3233.	10.3390/cells11203233	36291100	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論文（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1583	J. Yang, Y. Zhou, J. Zhang, Y. Zhang and J. He	2024	Identification of genes related to fatty acid metabolism in type 2 diabetes mellitus	Abstract Fatty acid metabolism is pivotal for lipid synthesis, cellular signaling, and maintaining cell membrane integrity. However, its diagnostic significance in type 2 diabetes mellitus (T2DM) remains unclear. METHODS: In this study, we downloaded the GSE164416 dataset from the Gene Expression Omnibus (GEO) database and identified differentially expressed genes (DEGs) between T2DM and healthy samples. We then identified fatty acid metabolism-related genes. Functional analysis, ceRNA network construction, immune microenvironment assessment, and drug prediction were conducted to explore the underlying molecular mechanisms. RESULTS: The human genes were identified with strong diagnostic performance and were involved in processes such as ribosome function and fatty acid metabolism. Immune cells, including dendritic cells, neutrophils, and neutrophil-myeloid cells, were significantly upregulated in T2DM. ceRNA and drug-target network analysis revealed potential interactions, such as miR-1-3p with the LYN/PLCB4 and RPS6KA5/PLCB4 axes. The expression patterns of the hub genes, except for CYP26B1, were consistently upregulated in T2DM, aligning with trends observed in the training set. CONCLUSION: This study investigated the potential molecular mechanisms of rat fatty acid metabolism-related genes in T2DM, offering valuable insights that may guide future research and therapeutic development.	Biochem Biophys Rep. 2024 Oct 22:40:101849.	10.1016/j.bbrep.2024.101849	39498440	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1584	J. Yang, S. Qin, N. Sun, Y. Cai, J. Li, Z. Zhai, J. An, H. Wang, R. Du and J. Qin	2024	Neohesperidin alleviates the inhibitory effect of bisphenol A on the myogenic differentiation of umbilical cord mesenchymal stem cells via the IGF1R/AKT1/RHOA signaling pathway	Bisphenol A (BPA), a typical environmental endocrine disruptor, has raised concerns among researchers due to its toxicological effects. Whether neohesperidin (NEO) can intervene in the toxic effects of BPA remains unknown. This study aims to investigate the effects and mechanisms of NEO on inhibiting myogenic differentiation of umbilical cord-derived mesenchymal stem cells (UC-MSCs) induced by BPA. Sheep UC-MSCs were isolated, characterized, and induced to myogenic differentiation. BPA decreased cell viability, cell migration, and the expressions of myogenic marker genes, leading to myogenic differentiation inhibition, which were alleviated by NEO. Network pharmacology revealed that IGF1R, AKT1, and RHOA were the key targets of NEO against BPA-induced myogenic differentiation inhibition. NEO activated the IGF1R/AKT1/RHOA regulation of the pathway proteins induced by BPA, and counteracted the effects of the IGF1R inhibitor picropodophyllin (PPP) on NEO. CCK8 displayed that 10 nM NEO is the myogenic differentiation of sheep UC-MSCs. Additionally, the expression levels of Ip-1 (IGF1R, AKT1, and RHOA were positively correlated. Taken together, the mechanisms of NEO resistance to BPA involved the IGF1R/AKT1/RHOA signaling pathway. These findings provide a scientific basis for alleviating BPA toxicity, preventing and treating muscular dysplasia, and promoting muscle damage repair.	Ecotoxicol Environ Saf. 2024 Sep 15:283:116804.	10.1016/j.ecoenv.2024.116804	39083871	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1585	W. Xue, X. Yao, Q. Ting, J. Ling, L. Huimin, Q. Yuan, Z. Chun, Z. Ming and Z. Yuanzhen	2021	BPA modulates the WDR5/TET2 complex to regulate ERβ expression in autopic endometrium and drives the development of endometriosis	Osteoprotection of estrogen receptor β (ERβ) in endometrium contributes to endometriosis (EM) pathogenesis. Trimethylation of the K5 lysine (K) 4 (H3K4me3) in promoters is strongly correlated with gene expression. The WDR5/TET2 complex is a key regulator of H3K4me3 and DNA demethylation. However, the role of the WDR5/TET2 complex in the pathogenesis of EM remains unclear. In this study, a mouse EM model was established to investigate the effects of BPA. Immortalized human normal endometrial stromal cells (hESCs) were cultured and treated with BPA to explore the underlying mechanism. Eutopic endometria from patients with or without EM were collected and analyzed. Results showed that BPA elevated ERβ expression in mouse eutopic endometrium and promoted lesion growth. BPA also promoted EM-related disease. E-WDR5 expression and upregulated H3K4me3 levels in the ERβ promoter and Exon 1–2 when research indicated that WDR5 interacted with but not methylcytosine dioxygenase 2 (TET2). vitro BPA exposure enhanced the interaction between these two proteins, promoted the recruitment of the WDR5/TET2 complex to the ERβ promoter and Exon 1, and inhibited DNA methylation of CpG islands. The WDR5/TET2 interaction was essential for BPA-induced ERβ overexpression. Enhanced WDR5/TET2 interaction was also observed in eutopic endometria from EM patients. Further results observed that BPA upregulated WDR5 expression through the G protein-coupled estrogen receptor (GPER)-mediated PI3K/AKT signaling pathway. In conclusion, our study suggests that BPA exposure promotes EM development by upregulating ERβ expression in eutopic endometrium via the WDR5/TET2-mediated epigenetic pathway.	Environ Pollut. 2021 Jan 1:268(Pt B):115748.	10.1016/j.envpol.2020.115748	33022573	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1586	Q. Xue, K. Liu, X. C. Liu, W. X. Pan, J. J. Fu and A. Q. Zhang	2019	The Effect of Structural Diversity on Ligand Specificity and Resulting Signaling Differences of Estrogen Receptor α	Numerous chemicals have been reported to exert estrogen-like endocrine disrupting effects via a receptor binding mechanism that directly interacts with the ligand-binding domain of estrogen receptor α (ERα). However, not only their binding affinities to ERα, but also their interference in specific cell and tissue functions are clearly different. In this regard, significant regulation differences among three representative estrogenic chemicals (diethylstilbestrol (DES), bisphenol A (BPA), and diarylpropionitrile (DPN)), well-known ERα agonists with very similar structures, have been observed. Molecular dynamics simulation is used to explore the underlying mechanisms of different regulation effects induced by the similar estrogenic-like chemicals. The DPN-ERα complex has a 0.2 nm motion of the VM-H10 loop eventually expands the ligand-binding pocket entrance and a motion of the AF-2 domain, which is consistent with the over-regulation effect of the agonist. In comparison, the 3.5 motion induced by BPA and DPN corresponds to the low-regulation effect of the chemicals. Cross correlation analysis further indicates that the VM-H10 loop motion is highly correlated with the AF-2 domain motion in the DPN-ERα complex, but not in the BPA-ERα complex. Binding free energy calculations further show a slight binding affinity of −32.21 kcal/mol binding free energy. Both the hydrophilic group in DPN and the small molecular size of BPA dramatically decrease the agonist binding ability, and their binding free energies are only −22.03 kcal/mol and −12.82 kcal/mol, respectively. Our study demonstrates that similar chemicals interact differently with ERα and induce different allosteric effects, which explains the observed regulation diversity.	Chem Res Toxicol. 2019 Jun 17;32(6):1002-1013.	10.1021/acs.chemrestox.8b00338	30924335	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1587	X. Xu, J. Wang and Y. Yang	2025	Effects of bisphenol-a on vasopressin regulating synaptic plasticity of hippocampus	The neuropeptide arginine vasopressin (AVP) plays an important role in the hippocampus by regulating neuronal excitability, synaptic plasticity, and other processes. Activity of AVP is regulated by ion hormones. The present study investigated the effects of bisphenol A (BPA), a environmental endocrine disruptor, on AVP regulating synaptic plasticity of hippocampus. AVP at 10-100 nM significantly increased the dendritic complexity of CA1 pyramidal neurons in hippocampal slices. BPA at 10 nM significantly reduced the dendritic complexity of CA1 neurons. BPA at 100 nM significantly reduced the dendritic complexity and spine density, which was partially eliminated by estrogen receptor (ER) antagonist (ICI182,780) but not by membrane ER antagonist (G15). Co-treatment of BPA at 10 nM with AVP at 10-100 nM not only blocked the effect of AVP (100 nM) on the dendritic complexity and spine density, but eliminated the promoting effects of DHT + AVP on the dendritic complexity. BPA at 100 nM not only inhibited the dendritic complexity but also eliminated the promoting effects of AVP. ICI at inactivation (2.5 ICI/2) + AVP, and 12-tetradihydroisoquinoline (DHT) + AVP on the dendritic complexity. In addition, BPA at 100 nM decreased the protein levels of Cofilin and CFN protein expressions. Meanwhile, BPA at 10 nM promoted the maintenance of L-TP in CA2 in the hippocampal slices, but co-treatment of BPA eliminated the effect of 17β-E2 + DHT on L-TP. BPA (10 nM) did not affect the promotion of long-term potentiation (L-TP) by AVP, but eliminated the promotion of L-TP by DHT + AVP. These results suggest that BPA at nanomolar levels affected AVP-regulating modification of dendrite morphology and synaptic plasticity of hippocampus mainly by disrupting the effects of 17β-E2 and/or DHT on AVP activity.	Neurotoxicol Teratol. 2025 Jul-Aug:110:107531.	10.1016/j.ntt.2025.107531	40714127	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1588	S. Xu, L. Jiang, Z. Zhang, X. Luo, H. Wu and Z. Tan	2025	Network Toxicology and Molecular Docking Strategy for Analyzing the Toxicity and Mechanisms of Bisphenol A in Alzheimer's Disease	Alzheimer's disease (AD) is a chronic and progressive neurodegenerative disorder marked by memory deterioration and cognitive impairment. Bisphenol A (BPA), a common environmental pollutant, has been linked to neurotoxicity and potentially to AD. However, the specific mechanisms by which BPA contributes to AD remain unclear. This study employed network toxicology and molecular docking to explore these mechanisms. BPA-related targets were identified from PharmMapper and SwissTargetPrediction databases, while AD-related targets were compiled from GeneCards, DisGeNET, and the Therapeutic Target Database (TTD). Protein-protein interaction (PPI) networks were constructed using STRING and visualized in Cytoscape, and gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were performed. Molecular docking was employed to evaluate the binding interactions between BPA and the identified core targets. Through systematic bioinformatics analysis, 137 candidate targets for BPA-related AD were identified. Screening via PPI network analysis highlighted five key targets: CCK1C, AKT1, BAD, IGFR, and PTEN. GO and KEGG pathway enrichment revealed significant involvement in oxidative stress, neuronal apoptosis, and synaptic dysfunction. Molecular docking revealed that BPA exhibited strong binding affinities to these targets, with docking scores ranging from -5.2 to -7.8 kcal/mol, surpassing those of known AD drug ligands. These findings suggest that BPA may contribute to AD pathogenesis by disrupting oxidative stress responses, promoting neuronal apoptosis, and impairing synaptic function. This study sheds light on the molecular mechanisms underlying BPA's neurotoxic effects in the context of AD and provides a foundation for further research into preventive and therapeutic strategies. The integration of network toxicology and molecular docking offers a robust framework for unraveling toxic pathways of environmental environmental and chemical agents.	J Biochem Mol Toxicol. 2025 Apr;39(4):e70247.	10.1002/jbt.70247	40192506	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1589	H. Xu, X. Zhang, Y. Ye and X. Li	2019	Bisphenol A affects estradiol metabolism by targeting CYP1A1 and CYP19A1 in human placental JEG-3 cells	Estradiol, in some way or another, plays a critically important physiologic role in the establishment and maintenance of pregnancy. This study was designed to investigate whether BPA affects the estradiol level of human placental JEG-3 cells, which may contribute to insights into the reproductive toxicity and endocrine disruption of BPA. The JEG-3 cells were treated with increasing concentrations of BPA (0.1 to 50 μM). We discovered that BPA significantly increased the level of JEG-3 cells' own corresponding CYP1A1 gene was notably elevated and the enzyme was also significantly induced. Besides, BPA at 50 μM, as mentioned in the introduction, we determined that estradiol level of JEG-3 cells own corresponding CYP19A1 gene was notably elevated and the enzyme was also significantly increased in the current. Meanwhile, estradiol was shown considerable (+) CYP19A1 knockdown group. On the contrary, the group silk even expression of CYP19A1 gene increased estradiol level by 8.6 fold while the CYP1A1 knockdown group increased by 0.3 fold. In summary, our research clearly showed that BPA affects JEG-3 estradiol synthesis and catabolism due to its action on CYP19A1 and CYP1A1 protein levels and may interfere with the normal process of placenta formation and embryonic development during early pregnancy.	Toxicol In Vitro. 2019 Dec:61:104615.	10.1016/j.tiv.2019.104615	31374317	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1590	G. Xu, M. Huang, J. Hu, S. Liu and M. Yang	2024	Bisphenol A and its structural analogues exhibit differential potential to induce mitochondrial dysfunction and apoptosis in human granulosa cells	Bisphenol A (BPA) is an endocrine disruptor strongly associated with ovarian dysfunction. BPA is being substituted by structurally similar chemicals, such as bisphenol S (BPS), bisphenol AF (BPF), and bisphenol AF (BPAF). However, the toxicity of these substitutes remains unclear. This study investigated the cytotoxicity of BPA and its analogues in human granulosa cells (KGN cells). BPA and its analogues, especially BPA and BPAF, significantly decreased cell viability and cell viability. The potential of bisphenols to induce mitochondrial dysfunction differed in the following order: BPAF > BPA > BPF > BPS. Flow cytometry revealed that exposure to bisphenols significantly increased mitochondrial ROS levels and decreased mitochondrial Ca2+ levels. Thus, bisphenols exposure causes mitochondrial stress in KGN cells. At the same time, bisphenols exposure significantly induced apoptosis. These results thus emphasize the toxicity of these bisphenols to cells. Our study suggests the active mechanism of BPA and its analogues. A deeper causal to ovarian granulosa cells. Additionally, these novel analogues may be regrettable substitutes, and the biological effects and potential risks of BPA alternatives must be evaluated.	Food Chem Toxicol. 2024 Jun:188:114713.	10.1016/j.fct.2024.114713	38702036	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1591	Y. Xiong, X. Wen, H. Liu, M. Zhang and Y. Zhang	2020	Bisphenol a affects endometrial stromal cells decidualization, involvement of epigenetic regulation	Bisphenol A(BPA) is one of the most widespread endocrine disruptors in the environment and is associated with reproductive diseases. In this study, we focused on the correlation between environmentally relevant levels of BPA exposure and histone modification during endometrial stromal cells decidualization. BPA exposure impaired the morphology of decidualized endometrial stromal cells, with inhibition of mixed lineage leukemia (MLL) 1 and induction of enhancer of zeste homolog2 (EZH2) during in vitro decidualization. The expression of HOXA10, PRL and IGFBP-1 was down regulated upon BPA treatment. Furthermore, chromatin immunoprecipitation (ChIP) revealed that BPA exposure increased the enrichment of EZH2 and decreased the enrichment of MLL1 in the promoter region of HOXA10 and PRL promoters. The decreased H3K4me3 and the increased H3K27me3 at HOXA10, PRL and IGFBP-1 promoter region were consistent with the expression of MLL1 and EZH2 respectively. The effect of BPA on MLL1 and EZH2 could be abrogated by E1-3Q.3Q. Our study provides the first indication that environmentally relevant levels of BPA exposure can regulate the expression of decidualization-related genes by affecting histone modification, impairing endometrial decidualization.	J Steroid Biochem Mol Biol. 2020 Jun:200:105640.	10.1016/j.jsbmb.2020.105640	32087250	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1592	J. Xiong, S. Hu, Z. Xu, C. Li, Z. Li, S. Li, Y. Ma, X. Ren, B. Huang and X. Pan	2024	Different paths, same destination: Bisphenol A and its substitute induce the conjugative transfer of antibiotic resistance genes	Antibiotic resistance genes are primarily spread through horizontal gene transfer in aquatic environments. Bisphenols, which are widely used in industry, are pervasive contaminants in such environments. This study investigated how environmentally relevant concentrations of bisphenol A and its substitute (bisphenol S, bisphenol AF and bisphenol AF) affect the spread of antibiotic resistance genes among Escherichia coli. As a result, bisphenol A and its three substitutes were found to promote the RP4 plasmid-mediated conjugative transfer of antibiotic resistance genes with different penetration efficiency. Particularly, bisphenol A and bisphenol AF at 0.1 μg/L significantly increased the conjugative transfer frequency by 1.5-fold and 1.4-fold, respectively. Bisphenol A and bisphenol AF at 0.1 μg/L significantly increased the permeability of bacterial cell membranes, while bisphenol S and bisphenol AF at 0.1 μg/L had no significant increase in cell death. Bisphenols exposure changed the systemic substances secreted by the bacteria, increased the permeability of bacterial cell membranes, promoted the secretion of antioxidant enzymes and generated reactive oxygen species. They also affected the expression of genes related to conjugative transfer by upregulating replicative and DNA transfer genes and downregulating global regulatory genes. It should be noted that gene expression levels were higher in the BPS-exposed group than in the BPS-unexposed group. The synthesis of bacterial metabolites and functional components was also significantly affected by bisphenols exposure. This research has helped to clarify the potential health risks of bisphenol contamination of aquatic environments.	Chemosphere. 2024 Nov:368:143625.	10.1016/j.chemosphere.2024.143625	39510271	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1593	R. Xie, X. Wang, Y. Xu, L. Zhang, M. Ma and Z. Wang	2023	In vitro to in vivo extrapolation for predicting human equivalent dose of phenolic endocrine disrupting chemicals: PBTK model development, biological pathways, outcomes and performance	In vitro to in vivo (IVIVE) leverages in vitro high throughput biological responses to predict the corresponding in vivo exposures and further estimate the human safe dose. However, for phenolic endocrine disrupting chemicals (EDCs) linked with complicated biological pathways and adverse outcomes (AO), such as bisphenol A (BPA) and 3-monylphenol (3-NP), plausible estimation of human equivalent doses (HED) by IVIVE approaches is challenging. Here, we developed a physiologically based pharmacokinetic (PBPK) model for BPA and 3-NP in rats and humans, and then integrated the PBPK model with IVIVE approaches to derive adverse-specific HEDs using BPA and 3-NP as examples. In vitro HEDs of BPA and 3-NP derived from different adverse outcome pathways, pathways, and testing endpoints and ranged from 0.0013 to 1.2986 mg/kg bw/day and 0.0002 to 1.7280 mg/kg bw/day, respectively. In vitro HEDs associated with reproductive AOs initiated by PPARα activation and ERα activation were the most sensitive. Model verification suggested the potential of using effective in vitro data to determine reasonable approximations of in vivo HEDs for the same EC/ED differences of most AOs ranged in 0.3–2.5 and better predictions of most AOs ranged in 0.1–3.2. Nevertheless, system-specific parameters of cardiac output and its fraction, body weight, as well as chemical-specific parameters of partition coefficient and liver metabolic were most sensitive for the PBTK simulations. The results indicated that the application of IVIVE-PBPK-HARM approach could provide credible pathway-specific HEDs and contributes to high-throughput prioritization of chemicals in a more realistic scenario.	Sci Total Environ. 2023 Nov 1:897:165271.	10.1016/j.scitotenv.2023.165271	37422235	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1594	M. Xiao, Y. Zhang, X. Zhang, Q. Zhang, C. Jin, J. Yang, S. Wu and X. Lu	2023	Bisphenol A and Di(2-Ethylhexyl) Phthalate promote pulmonary carcinoma in female rats via estrogen receptor beta: In vivo and in silico analysis	The prevalence of lung cancer in women currently merits our attentions. However, cigarette exposure alone does not tell the whole story that lung cancer is more prevalent among non-smoking women. Since female lung cancer is closely linked to estrogen levels, many of endocrine disrupting chemicals (EDCs), as the substances similar to estrogen, affect hormone levels, and become a potential risk of female lung cancer. Additionally, co-exposure to EDCs is the real-life exposure scenario. Therefore, we investigated the carcinogenic effects of co-exposure to Bisphenol A (BPA) and Di(2-Ethylhexyl) Phthalate (DEHP) after their exposure alone or in combination, using rat pulmonary tumor model established previously, combining bioinformatics analysis based on The Comparative Toxicogenomics Database (CTD) and The Cancer Genome Atlas (TCGA) databases. It demonstrated that BPA and DEHP enhanced the promotion of pulmonary tumor in female rats, either alone or in combination. Histopathological results showed that co-exposure to BPA and DEHP significantly increased the number of pulmonary tumor nodules and the proliferative lesions, which contributed to the formation of pulmonary tumor in female rats. Remarkably, BPA, rather than DEHP, exhibited a much more critical effect in female lung cancer. Additionally, the transcriptional level of ERβ was affected in carcinogenesis, causing genetic disruption. Furthermore, the TCGA database revealed that ESR2 could enhance the promotion and progression of non-small cell lung cancer in females via activating the MAPK signaling pathway. Finally, our findings demonstrated that BPA and DEHP could enhance the promotion of pulmonary carcinoma via ESR2 in female rats and provide a potential and valuable insight into the causes and prevention of lung cancer in non-smoking women due to EDCs exposure.	Ecotoxicol Environ Saf. 2023 Jan 15:250:114496.	10.1016/j.ecoenv.2022.114496	36608567	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1595	T. Xie, J. Guo, B. Zhang, C. Song, Q. Zhao, B. Cui and Y. Liu	2022	Bisphenol A Promotes the Progression of Colon Cancer Through Dual-Targeting of NADPH Oxidase and Mitochondrial Electron-Transport Chain to Produce ROS and Activating HIF-1 a /VEGF/PI3K/AKT Axis	Bisphenol A (BPA) is a high-production-volume industrial chemical. Despite recent research conducted on its xenobiotic, its role in the development of colon cancer (CC) has been rarely studied. This study aims to evaluate the effects of BPA on the migration and invasion of CC cells. First, we clinically verified that patients with CC exhibit higher serum BPA level than healthy donors. Subsequently, different CC cell lines were exposed to a series of BPA concentrations, and the migration and invasion of cells were detected by the wound healing test and transwell assay. Finally, N-acetyl-L-cysteine (NAC) and siHIF-1 a intervention was used to explore the mechanism of BPA in promoting the migration and invasion of CC cells. The results showed that BPA exposure at environmentally relevant concentrations (0.01 and 0.1 μM) significantly promoted the migration and invasion of CC cells. Mechanistically, BPA exposure induced mitochondrial dysfunction and increased the production of reactive oxygen species (ROS), which was most pronounced in SW-620 cells. ROS production was partially blocked by NADPH oxidase (NOX) and mitochondrial electron transport chain (ETC). Furthermore, the intervention of NAC and siHIF-1 a blocked the HIF-1 a /VEGF/PI3K/AKT axis and inhibited cell migration and invasion. In conclusion, our results suggest that BPA exposure promotes the excessive production of ROS induced by NOX and ETC, which in turn activates the HIF-1 a /VEGF/PI3K/AKT axis to promote the migration and invasion of CC cells. This study provides new insights into the carcinogenic effects of BPA on CC and warns people to pay attention to environmental pollution and the harm caused to human health by low-dose BPA.	Front Endocrinol (Lausanne). 2022 Jul 4:13:933051.	10.3389/fendo.2022.933051	35860704	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該性評価段階で除害に基づき除去。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1596	B. T. Xia, Y. He, Y. Gu, J. L. Huang, X. J. Tang, J. R. Wang, Y. Tan and P. Duan	2022	Multi- and transgenerational biochemical effects of low-dose exposure to bisphenol A and 4-nonylphenol on testicular interstitial (Leydig) cells	Bisphenol A (BPA) and 4-nonylphenol (NP) are well-known endocrine-disrupting chemicals (EDCs) that have been proven to affect Leydig cell (LC) functions and testosterone production, but whether BPA and NP have multi- and transgenerational biochemical effects on testicular LCs remains unclear. We investigated the effects of BPA and NP on testicular LCs in male rats from the F0 to F3 generations. Hematoxylin-eosin (HE) staining and transmission electron microscopy (TEM) revealed that exposure to low doses of BPA and NP induced pathological changes in the tissue specimens

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成機関評価へ進め、当機関評価段階で原則として除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論文（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1609	Y. Wang, X. Su, Q. Wang, L. Zhang, Y. Yu, Y. Zhao and Z. Liu	2025	Bisphenol A exposure enhances proliferation and tumorigenesis of papillary thyroid carcinoma through ROS generation and activation of NOX4 signaling pathways	As a prevalent industrial material and component of consumer products, bisphenol A (BPA) is linked to hormone homeostasis disruption and potential carcinogenicity. However, the precise mechanisms through which BPA contributes to thyroid carcinogenesis, especially in papillary thyroid carcinoma (PTC), are not fully understood. This study investigates how BPA leaves the proliferation and tumorigenic characteristics of thyroid cells. BPA exposure significantly increased cell proliferation in a duration-dependent manner at a concentration of 0.1 μM, which is slightly higher than human exposure levels. Therefore, this study utilized BPA treatment concentrations of 0.1 μM, 0.5 μM, and 1 μM in subsequent experiments. Transcriptome sequencing revealed that BPA exposure significantly altered the gene expression profile of TPC-1 cells. Enrichment analysis further confirmed that BPA-upregulated genes related to oxidative stress and inflammation were significantly enriched in cancer. Consistently, in vivo study revealed significant upregulation of NOX4 in human thyroid cancers compared to normal thyroid tissues, with higher expression levels observed in advanced carcinomas by analysis of the TCGA database. BPA induces the upregulation of NOX4 in human thyroid cells, thereby triggering the activation of MAPK and PI3K/AKT pathways. In xenograft models, BPA treatment resulted in increased tumor size and Ki-67 proliferation index, accompanied by upregulated NOX4 expression. Additionally, BPA exposure led to higher levels of 4-Hydroxynonenal (4-HNE), indicating thyroid hormone disruption. Mechanistically, BPA activates the MAPK and PI3K/AKT pathways via NOX4, leading to increased ROS production and cell proliferation. This was further demonstrated through the use of ROS scavenger treatment and si-NOX4, which reversed that BPA stimulates ROS generation by activating NOX4/MAPK and NOX4/PI3K/AKT pathways in thyroid cells. This finding enhances our understanding of the pathogenesis of PTC related to BPA exposure and highlights the necessity for rigorous health risk assessments regarding BPA exposure.	Ecotoxicol Environ Saf. 2025 Mar 1;292:117946.	10.1016/j.ecoenv.2025.117946	40014988	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	0.1 μM、0.5 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1610	Y. Wang, J. Kang, R. Wang, K. Ramezani, M. Bonakdar, N. Moghimi, M. Salimi, Y. Yao and K. Wang	2023	Bisphenol A interacts with DLGAP5 and regulates IL-6/JAK2/STAT3 signaling pathway to promote tumorigenesis and progression of osteosarcoma	OBJECTIVE: It has been suggested that Bisphenol A (BPA), a high-production volume industrial chemical, can accelerate the development of various type of cancers. However, the effect of BPA on osteosarcoma and the underlying mechanisms remain unclear. METHODS: Cell proliferation, migration and invasion were assessed by CCK-8, wound healing and transwell assays, respectively. Osteosarcoma cells were treated with BPA at the doses of 0.1, 1, 10, μM. DEG-BPA interactions and osteosarcoma methods were constructed by using alternative mediated interactions, and the functional analysis of DEG-BPA was investigated to evaluate the carcinogenic effect of BPA on osteosarcoma through DLGAP5. Xenograft and metastatic mouse model were used to evaluate in vivo experiments. RESULTS: In this study, BPA at 10 μM promoted the proliferation, migration and invasion in vitro, and accelerate the progression and metastasis in vivo. Also, exposure to BPA was associated with poor survival of osteosarcoma in vivo. In addition, we observed that BPA at 10 μM significantly increased the expression of DLGAP5 in osteosarcoma. Silencing DLGAP5 could reverse the effect of BPA on proliferation, migration and invasion. Mechanistically, BPA promoted IL-6, JAK2, and STAT3 phosphorylation, and the effect of BPA was significantly inhibited by DLGAP5 knockdown. Moreover, DLGAP5 knockdown suppressed the expression of cyclin D1, MMP2, and MMP9 in osteosarcoma cells. CONCLUSION: BPA promotes osteosarcoma cells proliferation, migration, invasion of osteosarcoma cells and related to poor survival in a mouse model. DLGAP5 is one of the most critical targets of BPA to act as a carcinogen through IL-6/JAK2/STAT3 signaling pathway.	Chemosphere. 2023 Jan;312(Pt 1):136545.	10.1016/j.chemosphere.2022.136545	36155021	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1、1、10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1611	X. Wang, N. Luo, Z. Ke, X. Zheng, B. Huang and X. Pan	2020	The estrogenic proliferative effects of two alkylphenols and a preliminary mechanism exploration in MCF-7 breast cancer cells	Bisphenol A (BPA) and 4-nonylphenol (4-OP), as estrogen like chemicals, are ubiquitous in the environment media and associated with the occurrence and development of hormone dependent tumors. However, the combinatorial effects of these two structurally similar alkylphenols are not well understood. In the present study, the classic breast cancer cell line MCF-7 was used as in vitro model to evaluate the estrogenic proliferative effects of BPA and 4-OP, MTT assay, reactive oxygen species, cell apoptosis, cell cycle, and real-time fluorescent quantitative Step One Plus Real-time PCR System (Applied Biosystems, CA, USA) were applied to investigate the underlying mechanisms. The results showed that BPA, 4-OP, and their mixture (BPA + 4-OP) at the concentrations ranging from 10(-10) to 10(-6) M significantly promoted cell proliferation, cell cycle was progressed from G0/G1 to S and G2/M phase. Meanwhile, the expression levels of ERα, pS2, and Bcl-2 mRNA were also upregulated. In contrast, 4-OP and Bcl-2 mRNA were also upregulated. In contrast, 4-OP and Bcl-2 mRNA were also upregulated. In contrast, 4-OP

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1622	K. Wang, X. Shi, H. Lin, T. Xu and S. Xu	2025	Selenium deficiency exacerbates ROS/ER stress mediated pyroptosis and ferroptosis induced by bisphenol A in chickens thymus	Bisphenol A (BPA) is an industrial pollutant that can cause immune impairment. Selenium acts as an antioxidant, so selenium deficiency often accompanies oxidative stress, resulting in organ damage. This study is the first to demonstrate that BPA and/or selenium deficiency induce apoptosis and ferroptosis-mediated thymic injury in chickens and elicited lymphoma cell (MDCC-MSB1) as oxidative stress-induced endothelium damage model. Selenium deficiency and BPA exposure, both individually and in combination, induced oxidative stress, as evidenced by increased ROS, MDA, and 8-OHdG levels. Selenium deficiency led to a decrease in antioxidant enzyme activities (T-AOC, GST, and GSH-Px), accumulation of peroxides (H2O2) and lipids (MDA), significant upregulation of ER stress-related markers (GRP78, IRE1, PERK, ATF-2α, ATF6, and CHOP), a significant increase in Iron ion levels, significant upregulation of pyroptosis-related genes (NLRP3, ASC, Caspase1, GSDMD-N, IL-18 and IL-1β), significantly increased ferroptosis-related genes (SYNE1, COX2 and decreased genes (FPN1, HO-1, FTH, NADPH. In vitro experiments conducted in MDCC-MSB1 cells confirmed the results, demonstrating that the addition of antioxidant (NAC), ER stress inhibitor (TUDCA) and pyroptosis inhibitor (VX765) alleviated oxidative stress, endoplasmic reticulum stress, apoptosis, and ferroptosis. Overall, this study concludes that the combined effects of oxidative stress and ER stress mediate pyroptosis and ferroptosis in chicken thymus induced by BPA exposure and selenium deficiency.	J Environ Sci (China). 2025 Feb;148:13-26.	10.1016/j.jes.2024.01.002	39095152	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1623	K. Wang, N. Kim, M. Bagherian, K. Li, E. Chou, J. A. Colacino, D. C. Dolinoy and M. A. Sartor	2024	Gene Target Prediction of Environmental Chemicals Using Coupled Matrix-Matrix Completion	Human exposure to toxic chemicals presents a huge health burden. Key to understanding chemical toxicity is knowledge of the molecular target(s) of the chemicals. Because a comprehensive safety assessment for all chemicals is infeasible due to limited resources, a robust computational method for discovering targets of environmental exposures is a promising direction for public health research. In this study, we implemented a matrix completion algorithm named coupled matrix-matrix completion (CMMC) for predicting direct and indirect exposure-target interactions, which exploits the vast amount of accumulated data regarding chemical exposures and their molecular targets. Our approach achieved an AUC of 0.89 on a benchmark dataset generated using data from the Comparative Toxicogenomics Database. Our case studies with bisphenol A and its analogues, PFAS, dioxins, PCBs, and VOCs show that CMMC can be used to accurately predict molecular targets of novel chemicals without any prior bioactivity knowledge. Our results demonstrate the feasibility and promise of computationally predicting environmental chemical–target interactions to efficiently prioritize chemicals in hazard identification and risk assessment.	Environ Sci Technol. 2024 Apr 2;58(13):5889-5898.	10.1021/acs.est.4c00458	38501580	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1624	K. Wang, D. Huang, P. Zhou, X. Su, R. Yang, C. Shao and J. Wu	2021	BPA-induced prostatic hyperplasia in vitro is correlated with the unbalanced gene expression of AR and ER in the epithelium and stroma	As a typical environmental endocrine disruptor (EED), bisphenol A (BPA) can induce pathological hyperplasia of the prostate's epithelium and stroma. This study concentrates mainly on the effect and underlying mechanisms of BPA on prostatic hyperplasia, which is based on the culture of primary human prostate epithelial cells (HPEpiC) and human prostate fibroblasts (HPSC). In an effort to screen the optimal pre-survival BPA levels, HPEpiC and HPSC were, respectively, exposed to concentration gradients of BPA (10−12 M–10−5 M) cultivation diluted with two corresponding mediums and incubated for 72 h at 37 °C, 5% CO2. A assay showed that 10−9 M BPA for HPEpiC and 10−8 M BPA for HPSC were the optimal pre-survival BPA levels. Then, HPEpiC and HPSC were exposed to 10−9 M BPA and 10−8 M BPA, respectively. The qRT-PCR gene expression measured using quantitative real-time polymerase chain reaction (qRT-PCR) also confirmed the BPA-induced cell proliferation. Additionally, our results considered androgen receptor (AR), estrogen receptor (ERα, ERβ), and NFκB1 gene expressions exhibited up-regulation in HPEpiC treated with 10−9 M BPA for 72 h. However, in HPSC (the identical BPA treatment could activate ERα, ERβ, and NFκB1 gene expressions and down-regulated the expression of AR levels. It is further confirmed that low-dose BPA can indeed promote the proliferation of human prostate cells in vitro, and the mechanisms of BPA's in prostatic epithelial and stromal hyperplasia may not be consistent.	Toxicol Ind Health. 2021 Oct;37(10):585-593.	10.1177/07482337211042986	34486460	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1625	J. Wang, C. Shu, Z. Li, N. Tang, L. Xu, Z. Liu and B. Liu	2020	In vitro impact of bisphenol A on maturation and function of monocyte-derived dendritic cells in patients with primary Sjögren's syndrome	Background: Epidemiological studies have shown that environmental factors accelerate the progress of primary Sjögren's syndrome (pSS). Bisphenol A (BPA), a classic endocrine-disrupting chemical, affects the immune system. However, the impact of BPA on pSS has not yet been reported. The present study aimed to evaluate the potential relationship between BPA, estrogen receptor (ER), and pSS.Methods: We studied the impact of BPA on monocyte-derived dendritic cells (moDCs) from pSS patients and age-matched healthy controls (HCs). Morphological effects were observed under inverted microscope. Surface markers were analyzed by flow cytometry. ER and cytokine profiles were assessed using real-time polymerase chain reaction. The ability of moDCs to activate CD4(+) T cells, activation was assessed by detection of proliferation. Results: moDCs from both pSS patients and HCs expressed ERα as well as ERβ. After BPA exposure, expression of ERα increased significantly in pSS patients, while that of ERβ remained unchanged. moDCs from BPA-treated pSS patients showed significantly increased expression of CD80, CD86, CD83, and HLA-DR, and secretion of IL-6, IL-12p70, and TNF-α. Furthermore, BPA-treated pSS moDCs showed a greater ability to induce CD4(+) T cells to proliferate and secrete IFN-γ. IL-4, IL-17, IL-10, and transcription factors T-bet, GATA3, RoR-γ t, Foxp3 of CD4(+) T cells showed imbalance of Th1/Th2/Th17/Treg polarization, with Th1 and Th17 dominating.Conclusions: BPA altered the function of moDCs through ERα, including antigen capture, secretion of inflammatory factors, and ability to stimulate T cells, as well as accelerated the progression and further deterioration of pSS.	Immunopharmacol Immunotoxicol. 2020 Feb;42(1):28-36.	10.1080/08923973.2019.1706554	31876196	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1626	J. Wang, X. Li, J. Geng, R. Wang, G. Ma and P. Liu	2025	Identification of biomarkers and mechanism exploration of ferroptosis related genes regulated by m6A in type 2 diabetes mellitus	PURPOSE: This study is aims to explore the role of ferroptosis genes regulated by N6-methyladenosine (m6A) in Type 2 diabetes mellitus (T2DM). MATERIAL AND METHODS: Firstly, differentially expressed m6A-FRGs (DE-m6A-FRGs) were obtained by intersecting the differentially expressed genes (DEGs) and the m6A-related ferroptosis genes. Next, PPI(Protein-protein interaction) network, WGCNA(Weighted gene co-expression network analysis) and nomogram models were constructed using 3 biosets(Sets). Moreover, the gene-set enrichment analysis of biomarkers was performed. Furthermore, the transcription factors (TF)-mRNA and competing endogenous RNAs (ceRNA) regulatory networks were constructed to reveal the potential regulation of biomarkers at transcriptional and post-transcriptional levels. In addition, the targeted drugs of biomarkers were predicted. Then, molecular docking was used to study the inter-molecular interactions between biomarkers and targeted drugs by "AutoDockVina". RESULTS: Totally, all 13 DE-m6A-FRGs were obtained by intersecting the 601DEGs and 295 m6A-FRGs. Moreover, the 3 biomarkers (ACSL4, GCH1 and HMOX1) were identified by 3 machine learning algorithms and 3 biosets. Besides, the 3 biomarkers had good diagnostic performance in 3 biosets. Then, the GSEA indicated that the 3 biomarkers were mainly involved in antioxidant-related environmental stimuli-related and immune-related pathways. Furthermore, the 3 biomarkers were closely associated with immune cells. Additionally, the TF-mRNA network was established, which revealed that 3 biomarkers could be regulated by 3 TFs (ELF1, HSF1 and TP53). Besides, the ceRNA network revealed that 3 biomarkers could be regulated by 3 lncRNAs (ADAMTS9-AS2, CDKN2B-AS1 and MIR22HG). Finally, 10 potential therapeutic drugs were predicted by 3 biomarkers, and the molecular docking results showed that ACSL4 had a good binding affinity with Troglitazone, Rosiglitazone and Pioglitazone. CONCLUSIONS: The present study revealed that 3 ferroptosis genes (ACSL4, GCH1 and HMOX1) could be regulated by m6A and could be used as biomarkers for T2DM. Moreover, the 3 biomarkers could be regulated by 3 TFs and 3 lncRNAs, which could influence T2DM. In addition, 10 potential therapeutic drugs were predicted by 3 biomarkers, which could provide novel insights for the clinical diagnosis and treatment of T2DM.	Hereditas. 2025 Feb 3;162(1):24.	10.1186/s41065-025-00385-9	39966875	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1627	J. Wang, X. Hong, W. Liu, L. Zhang, S. Yan, Z. Li and J. Zha	2025	Comprehensive assessment of the safety of bisphenol A and its analogs based on multi-toxicity tests in vitro	As substitutes for bisphenol A (BPA), bisphenol analogs (BPs) have raised concerns due to their frequent environmental detection and unclear safety. Here, the cytotoxicity, endocrine disruption, neurotoxicity, aryl hydrocarbon receptor (AHR) activity, and genotoxicity of nine BPs were evaluated in three types of cell lines. Due half of the tested BPs exhibited greater cytotoxicity than BPA, with ED50 values showing a linear correlation in SH-SY5Y cells (R²=0.69). All tested BPs exhibited at least one endocrine disrupting effect, notably estrogenic, which was observable even at 0.01-0.1 μM. Interestingly, BPAF and BPAP exposure had widespread endocrine-supporting effects. Moreover, all BPs (except BPF) and BPA increased ERα-EGFP cells proteins at 1-10 μM, 2-to-3000 μM, and BPF significantly increased 17-estradiol in L02 cells at 1 μM. Additionally, BPAF and BPAP exposure induced AHR nuclear translocation, and BPAF, BPAP, BPB, and BPZ induced CYP1A1 activity in HepG2 cells. Finally, BPAF, BPAP, BPB, and BPZ induced micronucleus formation in L02 cells. Structure-activity relationship analysis revealed that the presence of halogen atoms and hydroxyl groups in the molecular structure of BPs significantly influenced their cytotoxicity, endocrine disruption, and genotoxicity. Overall, BPAF and BPAP exhibited the most pronounced toxicity, highlighting their notable effects on AHR activity. BPAF significantly induced DNA damage at 1.25 μM, whereas BPA, BPF, and BPP induced damage at 20, 25, and 25 μM, respectively. Finally, TOPP, a weighted scoring system integrating multiple toxicity endpoints, was developed for comprehensively ranking BPs' toxicity. TOPP effectively distinguished stronger contaminants like BPAF and BPAP, emphasizing the urgent need for further research to confirm their potential health implications.	J Hazard Mater. 2025 Mar 15;486:136983.	10.1016/j.jhazmat.2024.136983	39742861	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1628	H. Wang, P. Zhao, Q. Huang, Y. Chi, S. Dong and J. Fan	2019	Bisphenol-A induces neurodegeneration through disturbance of intracellular calcium homeostasis in human embryonic stem cells-derived cortical neurons	Bisphenol-A (BPA) is a representative exogenous endocrine disruptor, which is extensively composed in plastic products. Due to the capability of passing through the blood brain barrier, evidence has linked BPA exposure with multiple neurosynaptological dysfunctions, neurobehavioral disorders and neurodegenerative diseases. However, the underlying mechanism by which BPA induces neurodegeneration still remains unclear. Our study used human embryonic stem cells derived human cortical neurons (hESCs) as a cellular model to investigate the adverse neurotoxic effects of BPA. hESCs were treated with 0, 0.1, 1 and 10 μM BPA for 14 days. Impacts of BPA on hESCs were evaluated by cell viability, neurite outgrowth, synaptic function, neuronal network activity and intracellular calcium homeostasis. Our results showed that BPA exposure at 10 μM significantly impaired synaptic function, neuronal network activity and intracellular calcium homeostasis, while no significant cytotoxicity was observed under the same concentration. Results revealed that chronic exposure of BPA damaged the neural morphology, induced neuronal apoptosis and decreased GSH/GSSG ratio level in the cell. Transcription and translation. The intracellular calcium levels were elevated in hESCs after BPA exposure through NADPH/ROS-mSOD-PSD-95 mediating. Meanwhile, BPA led to oxidative stress by raising the ROS generation and attenuating the antioxidant defense in hESCs. Furthermore, BPA triggered ER stress and increased cytochrome c release by impairing the mitochondrial function. Ultimately, BPA triggered the cell apoptosis by regulating Bcl-2 family and caspase-dependent signaling pathway. Taken together, BPA exerted neurotoxic effects on hESCs by eliciting apoptosis, which might due to the intracellular calcium homeostasis perturbation and cell organelles dysfunction.	Chemosphere. 2019 Aug;229:618-630.	10.1016/j.chemosphere.2019.04.099	31102917	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1629	H. Wang, J. Sang, Z. Li, Y. Yu, S. Wang, Y. Zhu, H. Li, Y. Wang, Q. Zhu and R. Ge	2023	Bisphenol A Analogues Inhibit Human and Rat 11β-Hydroxysteroid Dehydrogenase 1 Depending on Its Lipophilicity	Bisphenol A (BPA) analogues substituted on the benzene ring are widely used in a variety of industrial and consumer materials; however, their effects on the glucocorticoid metabolizing enzyme 11β-hydroxysteroid dehydrogenase 1 (11β-HSD1) remain unclear. In the present study, we found that BPA analogues inhibited human and rat 11β-HSD1 activities with different potencies and 11β-HSD1 was more sensitive to BPA analogues than 11β-HSD2. The potencies of inhibition of BPA analogues toward human 11β-HSD1 were in the order of bisphenol G (BPG, IC50, 0.79 μM) > bisphenol Z (BPZ, IC50, 5.86 μM) > diallyl bisphenol A (DABPA, IC50, 11.36 μM) > dimethyl bisphenol A (DMBPA, IC50, 30.65 μM) > isopropylidenebis(2,6-dimethylphenol-3,5-diyl)diacetonitrile (TMBPA, IC50, 41.83 μM) > tetramethyl bisphenol A (TMBPA, IC50, 51.88 μM) > bisphenol A (BPA, IC50, >100 μM). The inhibitory strength of these chemicals on rat 11β-HSD1 was much weaker than that on the human enzyme, ranging from 32.2 to 256.7 μM. All BPA analogues are mixed competitive inhibitors of both human and rat enzymes. Molecular docking studies predict that bisphenol F and bisphenol Z both bind to the active site of human 11β-HSD1, forming a hydrogen bond with catalytic residue Ser170. The Pearson correlation of IC50 values with LogP (lipophilicity), molecular weight, heavy atoms, and molecular volume revealed a significant inverse regression and the correlation of IC50 values with 4,5-line binding energy) revealed a positive regression. In conclusion, the lipophilicity, molecular weight, heavy atoms, molecular volume, and binding affinity of a BPA analogue determine the inhibitory strength of human and rat 11β-HSD1 activities.	Molecules. 2023 Jun 21;28(13):4894.	10.3390/molecules28134894	37446556	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1630	H. Wang, L. Chang, J. S. Aguilar, S. Dong and Y. Hong	2019	Bisphenol-A exposure induced neurotoxicity in glutamatergic neurons derived from human embryonic stem cells	Bisphenol A (BPA) is a lipophilic, organic, synthetic compound that has been used as an additive in polycarbonate plastics manufacturing since 1957. Studies have shown that BPA interferes with the development and function of the nervous system. However, the effects of BPA on human glutamatergic neurons remain unclear. In this study, we investigated the neurotoxicity of BPA on glutamatergic neurons derived from human embryonic stem cells (hESCs). The results showed that chronic exposure of different concentrations of BPA (0.01, 0.1 and 0.5 μM) to hESCs for 12 days induced neurite outgrowth in a concentration-dependent manner. Using presynaptic protein synaptophysin and postsynaptic protein PSD-95 antibodies, immunofluorescence staining and western blotting results indicated that BPA exposure altered the morphology of dendritic spines and increased synaptophysin and PSD-95 expression. Furthermore, BPA exposure at concentrations higher than 1.0 μM resulted in the increase of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) expression and deterioration of dendritic spines. In addition, our results suggested that these BPA-mediated neurotoxicity effects were due to an increased production of reactive nitrogen species (RNS) and reactive oxygen species (ROS) via mitochondrial membrane (MMP) reversed electric state synthesis (MMSE). N-Nitrosyne expression and Ca2+ influx. These results imply that hESC-based neuronal differentiation is an excellent cellular model to examine BPA-induced neurotoxicity on human neurons at the cellular and molecular level.	Environ Int. 2019 Jun;127:324-332.	10.1016/j.envint.2019.01.059	30953815	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1631	C. Wang, L. Wang, C. Huang, Y. Liu, J. Liu, H. Kuang, Q. Pang, H. Hai and R. Fan	2022	Involvement of NLRP3/Caspase-1/GSDMD-Dependent pyroptosis in BPA-Induced apoptosis of human neuroblastoma cells	Bisphenol A (BPA) induces neurotoxicity via enhancing cell apoptosis and inflammation potently (effective at nanomolar concentrations), but its mechanisms remain unidentified. In this study, human neuroblastoma cell lines, SMS-SY and SK-N-SH cells, isolated from a male and a female subject, respectively, were exposed to BPA at various concentrations, with nigericin and/or glycine (GLY) as an activation/non-promotion, 2'-7'-bis(2-carboxyethyl)-5(6)-carboxyfluorescein acetoxymethyl ester (BCECF-AM) for intracellular pH measurements, and Hoechst 33342/propidium iodide (PI) staining for cell death. Results showed that BPA increased the mRNA levels of IL-1β, ASC, GSDMD and protein levels of NLRP3, caspase-1 (p20), and the N-terminal fragment of GSDMD (GSDMD-N) in SMS-SY cells, but not in SK-N-SH cells. Moreover, BPA induced pyroptosis, as indicated by the increased PI-positive SMS-SY cells but suppressed in SK-N-SH cells, while IL-1β was suppressed in SMS-SY cells but enhanced in SK-N-SH cells. The level of GSDMD-N also increased along with the BPA dose in SMS-SY cells. IL-1β, IL-18, caspase-1 and lactate dehydrogenase (LDH) Moreover, all the above effects of BPA were reversed by 2'-7'-bis(2-CBA), GSDMD-NA, and DSCG. Besides, BPA significantly increased reactive oxygen species production, LDH leakage and apoptosis, while reduced cell viability and mitochondrial membrane potential, in both cell lines, whereas 2'-7'-bis(2-CBA) and DSCG BN significantly alleviated the reduction of Bax, Bcl-2 and caspase-3 protein. In summary, BPA may induce pyroptosis in neuroblastoma cells through NLRP3/caspase-1/GSDMD pathway, as mediated by ER-caspase-1-dependent pyroptosis may also contribute to BPA-induced apoptosis, an effect alleviated by DSCG.	Biochem Pharmacol. 2022 Jun;200:115042.	10.1016/j.bcp.2022.115042	35439536	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1632	C. Wang, J. He, T. Xu, H. Han, Z. Zhu, L. Meng, Q. Pang and R. Fan	2021	Bisphenol A(BPA), BPS and BPB-induced oxidative stress and apoptosis mediated by mitochondria in human neuroblastoma cell lines	The analogues of bisphenol A (BPA), including bisphenol S (BPS) and bisphenol B (BPB), are commonly used to replace the application of BPA in containers and wrappers of daily life. However, their safeties are questioned due to their similar chemical structure and possible physiological effects as BPA. To investigate the neurotoxic effects of BPA, BPS, and BPB as well as their underlying mechanisms, SMS-SY cell line from male and SK-N-SH cell line from female were exposed respectively to BPA, BPS and BPB with concentrations of 1 nM, 10 nM, 100 nM, 1 μM, 10 μM, and 100 μM for 24 h. Additionally, 25 h exposure of BPA combining epigallocatechin gallate (EGCG) (1 μM and 5 μM) for both SY and SH 10 nM BPA exposed cells were conducted. Results demonstrated that BPA, BPS, and BPB exposure could promote reactive oxygen species production and decrease mitochondrial membrane potential (MMP) in SMS-SY cells whereas levels of superoxide dismutase (SOD), transcription study revealed that after exposure to BPA mitochondrial membrane potential (MMP) dropped down and the protein expression levels of Bcl-2, Bax and caspase-3 were altered. Besides, BPA exposure could induce cell apoptosis and necrosis in SMS-SY cells, which could be alleviated by the addition of EGCG. Moreover, the cytotoxicity induced by BPA could be alleviated by the adding of EGCG, which cellular viabilities could be restored to 84% ± 3% and 91% ± 3% in SMS-SY cells, but not in SK-N-SH cells. Meanwhile, the apoptosis induced by BPA could be alleviated by the adding of EGCG, which cellular viabilities could be restored to 84% ± 3% and 91% ± 3% in SMS-SY cells, induced by BPA. Furthermore, BPA's neurotoxic effects were compared to BPS and BPB. Interestingly, the neurotoxic effects of BPA on SMS-SY cells were significantly higher than those on SK-N-SH cells. In conclusion, the results suggested that BPA, BPS and BPB could induce oxidative stress and oxidative via mitochondrial pathway in the neuroblastoma cells and male is more susceptible to BPA than female.	Ecotoxicol Environ Saf. 2021 Jan 1;207:111299.	10.1016/j.ecoenv.2020.111299	32927158	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1633	C. Wang, C. Hu, S. Xu, Y. Gao, K. Wang, M. Liang and K. Hu	2024	Bisphenol A triggers apoptosis in mouse pre-antral follicle granulosa cells via oxidative stress	MACROBSTRACT: Bisphenol A (BPA), an endocrine-disrupting chemical with weak estrogenic and anti-androgenic activity, is widely present in various environmental media and organisms. It has certain reproductive toxicity and can cause a variety of female reproductive system diseases. Although BPA stimulated apoptosis of granulosa cells has been widely elaborated, the effect of BPA on mouse pre-antral follicle granulosa cells (mpGCs) remains unclear. In this study, mpGCs were isolated from 12-day-old female mice and cultured in vitro to investigate the effects of BPA exposure on mpGCs. We confirmed that BPA promotes the proliferation of mpGCs. We confirmed that BPA promotes the proliferation of mpGCs. We confirmed that BPA promotes the proliferation of

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別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ送れ、当該性評価段階で排除に基づき排除。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については≦100nM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1648	E. Thuaennon, V. Delfosse, R. Bailly, P. Blanc, A. Boulahtouf, M. Grimaldi, A. Bacducci, W. Bourguet and P. Balaguer	2019	Insights into the activation mechanism of human estrogen-related receptor γ by environmental endocrine disruptors	The estrogen-related receptor γ (ERRγ; NR3B3) is a constitutively active nuclear receptor which has been proposed to act as a mediator of the toxic dose effects of a number of environmental endocrine disrupting chemicals (EDCs) such as the xenoestrogen bisphenol A (BPA). To better characterize the ability of exogenous compounds to bind and activate ERRγ, we used a combination of cell-based, biochemical, structural and computational approaches. Our results demonstrate that BPA binds to ERRγ with a high affinity (IC50 = 430 nM) and behaves as a full agonist in cell-based assays. Similarly, 4-hydroxytamoxifen (4-OHT), one of the most potent compounds measured by isothermal titration calorimetry even in the 50 nM–5 μM range, in agreement with their nuclear receptor activation potencies. Crystallographic analysis of the interaction between the ERRγ ligand-binding domain (LBD) and compounds of the bisphenol, alkylphenol and naphthol families revealed a partially shared binding mode and minimal alterations of the receptor conformation upon ligand binding. Further biophysical characterizations coupled to molecular dynamics simulations suggested a mechanism through which ERRγ ligands could inhibit their agonistic properties by preventing the transcriptionally active form of the receptor while stabilizing some loop regions with associated functions. This unique mechanism contrasts with the classical one involving a ligand-induced repositioning and stabilization of the C-terminal activation helix H12.	Cell Mol Life Sci. 2019 Dec;76(23):4769-4781.	10.1007/s00018-019-03129-x	31127318	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1649	O. Téteau, A. Vitorino Carvalho, P. Papillier, B. Mondon-Pépin, L. Inuwaa, , F. Jamin-Gallard, A. Desmarchais, M. E. Lebacheller de la Riviere, C. Vignault, V. Maillard, A. Binet, S. Uzbekova and S. Elis	2023	Bisphenol A and bisphenol S both disrupt ovine granulosa cell steroidogenesis but through different molecular pathways	BACKGROUND: Ovarian granulosa cells (GC) are essential for the development and maturation of a proper oocyte. GC are sensitized to endocrine disruptors, including bisphenol A (BPA) and its analogue bisphenol S (BPS), plastic-ware present in everyday consumer products. BPA exhibits greater binding affinity for the membrane estrogen receptor (GPER) than for the nuclear estrogen receptors (ERα and ERβ). Here, we analyzed the effects of BPA and BPS on the steroidogenesis of ovine GC in vitro, as well as their early mechanisms of action, the ovine being a relevant model to study human reproduction (experiment). Disruption of GC steroidogenesis may lead to impaired reproductive competence. RESULTS: Ovine GC were cultured in serum-free conditions and treated with BPA or BPS (0.1 µM) for 24 h (short-term) or 6 days (long-term). BPA or BPS (0.1 µM) did not affect viability or proliferation of GC (+/- 1 µM) and to 0.1 µM) and to 0.1 µM) and to 0.

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成根拠評価への進め、当該性評価段階で除害に基づき除害。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物飼及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1661	S. Suresh and C. Vellapandian	2024	Cyanidin Ameliorates Bisphenol A-Induced Alzheimer's Disease Pathology by Restoring Wnt/ β-Catenin Signaling Cascade: an In Vitro Study	Alzheimer's disease (AD) is a progressive neurodegenerative disorder causing memory loss and cognitive decline, linked to amyloid beta (Aβ) plaques and hyperphosphorylated tau protein accumulation in the brain. Environmental pollutant bisphenol A (BPA) has been implicated in AD pathology due to its neurotoxic effects. This study aims to evaluate cyanidin from flower hearts of Musa acuminata Colla (red variety) (AA) group for its neuroprotective potential against BPA-induced neurotoxicity in SH-SY5Y neuroblastoma cells. Cyanidin was isolated from the flower hearts of Musa acuminata Colla (red variety) (AA) group by ethanolic extraction followed by column chromatography. The isolated compound was identified and characterized using spectroscopic techniques. Cytotoxicity was assessed using the MTT assay, and neuroprotective effects were evaluated against BPA-induced toxicity. Intracellular reactive oxygen species (ROS) levels were measured using DCFH-DA staining, and mitochondrial membrane potential was assessed using JC-1 dye. Apoptosis was analyzed via acridine orange/ethidium bromide (AO/EB) staining and DAPI staining. Gene expression studies were conducted to evaluate the Wnt/β-catenin signaling pathway, including Wnt3a, β-catenin, and GSK-3β. Cyanidin significantly enhanced the mRNA expression of Wnt3a (p < 0.0001), β-catenin (p < 0.0001), and Nurr1 (p < 0.0009), and decreased the expression of GSK-3β (p < 0.0068) and DKK1 (p < 0.0001), which are Wnt antagonist when compared to cells stimulated with BPA. Conclusively, our finding suggests that cyanidin could operate neuroprotective growth factor and promote neuronal differentiation, reduce key hyperphosphorylation by restoring the Wnt/β-catenin signaling cascade, and thereby render its neuroprotective potential against BPA-induced AD pathology.	Mol Neurobiol. 2024 Apr;61(4):2064-2080.	10.1007/s12035-023-03672-6	37843801	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1662	W. Sun, T. Xu, H. Lin, Y. Yin and S. Xu	2024	BPA and low-Se exacerbate apoptosis and autophagy in the chicken bursa of Fabricius by regulating the ROS/AKT/FOXO1 pathway	Bisphenol A (BPA) is a ubiquitous environmental pollutant that can have harmful effects on human and animal immune systems by inducing oxidative stress. Selenium (Se) deficiency damages immune organ tissues and exhibits synergistic effects on the toxicity of environmental pollutants. However, oxidative stress, cell apoptosis, and autophagy caused by the combination of BPA and low Se, have not been studied in the bursa of Fabricius of the chicken's early life. Therefore, in this study, BPA and/or low-Se diet were used to establish a chicken model of oxidative stress. The results showed that BPA and/or low-Se significantly reduced the activity of MDC1-SKBR-3 cells and the expression of the mRNA of GSH-Px1 and SOD1 ($P < 0.05$). Moreover, BPA and/or low-Se significantly increased the activity of MDC1-SKBR-3 cells and the expression of the mRNA of CAT and MDA ($P < 0.05$). Low-Se significantly enhanced the effects of BPA on the bursa of Fabricius by increasing the apoptosis rate and the expression of the mRNA of Caspase-3, Caspase-8, and Caspase-9 ($P < 0.05$). Low-Se significantly increased the effects of BPA on the bursa of Fabricius by increasing the autophagy rate and the expression of the mRNA of LC3-II/LC3-I, Beclin-1, and ATG5 ($P < 0.05$). Low-Se significantly increased the effects of BPA on the bursa of Fabricius by increasing the expression of the mRNA of Nrf2, HO-1, NQO1, CAT, and SOD1 ($P < 0.05$). Low-Se significantly increased the effects of BPA on the bursa of Fabricius by increasing the expression of the mRNA of FOXO1, ATM, and ATR ($P < 0.05$). Low-Se significantly increased the effects of BPA on the bursa of Fabricius by increasing the expression of the mRNA of MST1, AMPK, and LKB1 ($P < 0.05$). Furthermore, combined exposure of BPA and low-Se aggravated the above-mentioned changes. Treatment with N-acetylcysteine (NAC) reduced ROS levels and activated the AKT/FOXO1 pathway to further alleviate BPA and low-Se-induced apoptosis and autophagy. Apoptosis induced by low-Se + BPA was exacerbated after 3-Methyladenine (3-MA, autophagy inhibitor) treatment. Together, these results indicated that BPA and low-Se aggravated apoptosis and autophagy of the bursa of Fabricius in chickens by regulating the ROS/AKT/FOXO1 pathway.	Sci Total Environ Vol.908 Pages 168424	10.1016/j.scitotenv.2023.168424	37944606	動物、in vitro	-	0	不明	不明	不明	不明	不明	-	-	-	-	1	0	60 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1663	M. H. Sun, W. J. Jiang, X. H. Li, S. H. Lee, G. Hou, D. Zhou, J. S. Choi, K. S. Kim, W. Li and X. S. Cui	2023	ATF7-dependent epigenetic changes induced by high temperature during early porcine embryonic development	BACKGROUND: Activating transcription factor 7 (ATF7) is a member of the ATF/cAMP response element (CRE)-B superfamily. ATF1, ATF7, and CRE-BPa are present in vertebrates. Drosophila and frog (xenopus) have only one homologue (ATF7 and ATF1, respectively). Under normal conditions, ATF7 promotes heterochromatin formation by recruiting histone H3K9 di- and tri-methyltransferases. Once the situation changes, all members are phosphorylated by the stress-activated kinase P38 in response to various stressors. However, the role of ATF7 in early porcine embryonic development remains unclear. RESULTS: In this study, we found that ATF7 gradually accumulated in the nucleus and then localized on the pericentric heterochromatin after the late 2-cell stage, while being co-localized with heterochromatin protein 1 (HP1). Knockdown of ATF7 resulted in decreases in the blastocyst rate and blastocyst cell number. ATF7 depletion resulted in decompaction of HP1 and histone 3 lysine 9 dimethylation (H3K9me2) expression. These effects were alleviated when P38 activity was inhibited. High temperatures increased the expression level of ATF7, while reducing the quality of porcine embryos, and led to ATF7 phosphorylation. The expression level of H3K9me2 and ATF7 was decreased and regulated by P38 activity. CONCLUSIONS: Stress-induced ATF7-dependent epigenetic changes play important roles in early porcine embryonic development.	Cell Prolif. 2023 Feb;56(2):e13352.	10.1111/cpr.13352	36254813	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1664	I. O. Suchkova, L. K. Sassina, N. I. Dergacheva, G. A. Safronov and E. L. Patkin	2019	The influence of low dose Bisphenol A on whole genome DNA methylation and chromatin compaction in different human cell lines		Toxicol In Vitro. 2019 Aug;58:26-34.	10.1016/j.tiv.2019.03.010	30876887	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	不明	1	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1665	J. Su, X. Yang, H. Xu, Y. Pei, Q. S. Liu, Q. Zhou and G. Jiang	2024	Screening (anti)agonistic activities of xenobiotics on the retinoic acid receptor alpha (RARα) using in vitro and in silico analysis	Retinoic acid receptors (RARs) are known as crucial endocrine receptors that could mediate a broad diversity of biological processes. However, the data on endocrine disrupting effects of emerging chemicals by targeting RARs are still limited. Therefore, it is necessary to develop a rapid and effective method to screen the (anti)agonistic activities of xenobiotics on RARs. In this study, a reporter gene assay was used to examine the RARα activities of the two chemicals, and the (anti)agonistic potentials of RARα agonist and antagonist of RARα were used to assess the (anti)agonistic activities of these chemicals with RARα agonistic activities, i.e. 3-hydroxybenzo [b]-HP) and bisphenol AF (BPAF), significantly increased the mRNA levels of CYP26B1 and CYP26A1, while 3 select chemicals with RARα antagonistic potentials, including bisphenol A (BPA), tetrabromobisphenol A (TBBPA), 2-tert-octylphenol (2-t-OP), and 4-tert-octylphenol (4-t-OP), commonly decreased the transcriptional levels of the two genes. The in silico molecular docking analysis using 3 different approaches further confirmed the substantial binding between the chemicals with RARα activities and this nuclear receptor protein. This work highlights the promising strategy for screening endocrine disrupting effects of emerging chemicals of concern by targeting RARα. Led hypothesis.	Sci Total Environ. 2024 Oct 15:947:174717.	10.1016/j.scitotenv.2024.174717	38997027	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1666	N. Štefanková, H. Grelfová, T. Jambor, K. Tokárová, L. Zuščíková, D. Bažány, P. Maršalový, M. Capcarová and N. Lukáč	2023	Comparison of the Effect of BPA and Related Bisphenols on Membrane Integrity, Mitochondrial Activity, and Steroidogenesis of H295R Cells In Vitro	Bisphenol A (BPA) is an endocrine disruptor chemical that is widely utilized in the production of polycarbonate plastic and epoxy resin, which are used to make a wide range of consumer products, food and drink containers, and medical equipment. When the potential risk of BPA emerged, it was substituted by allegedly less harmful substitutes such as bisphenols S, F, B, and AF. However, evidence suggests that all bisphenols can have endocrine-disruptive effects, while the extent of these effects is unknown. This study aimed to determine effect of BPA, BPAF, BPB, BPF, and BPS on viability and steroidogenesis in human adrenocortical carcinoma cell line in vitro. The cytotoxicity of bisphenols can show to be considerable at higher doses. However, at low concentrations, it remained viability as well as steroidogenic activation, indicating that bisphenols have a biphasic, hormetic effect in biological systems. The results are consistent with the hypothesis that bisphenols, selectively inhibit some steroidogenic enzymes. These findings suggest that bisphenols may have a biphasic, hormetic effect in biological systems. However, but substantially more detailed and systematic research is needed to gain a better understanding of the risks associated with bisphenols and their endocrine-disrupting effect on humans and wildlife.	LIfe (Basel). 2023 Dec 19;14(1):3.	10.3390/life14010003	38276253	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1667	B. Stanic, D. Samardžija Nenadov, S. Fa, K. Pogenic-Majkic and N. Andric	2021	Integration of data from the cell-based ERK1/2 ELISA and the Comparative Toxicogenomics Database deciphers the potential mode of action of bisphenol A and benzo[a]pyrene in lung neoplasm	Chemicals can activate a variety of signaling pathways, initiating changes in gene expression and cellular functions. Here, we combined experimental data on the chemical-induced extracellular signal-regulated kinase 1/2 (ERK1/2) activation with the Comparative Toxicogenomics Database (CTD) to connect signaling, genes, and phenotypes to model the potential chemicals made of outer (MOA) responsible for the disease state. Experimental data on ERK1/2 activation were derived from the cell-based phospho-ERK1/2 ELISA on human alveolar epithelial cells A549. A549 cells were exposed to bisphenol A (BPA), benzo[a]pyrene (BaP), trifenyltin (TBT), and bisphenol-free (BF-free) 0.01 M to 30 M. Results show that BPA, BaP, and TBT can activate ERK1/2 in A549 cells. We selected BPA and BaP to elucidate the molecular pathways connecting chemical exposure, ERK1/2 signaling, phenotypes, and lung neoplasm (LN) using CTD. CTD analytics showed that BPA and BaP share 26 endogen-activated protein kinase 1/3 (MAPK1/3)-signaling genes associated with LN. Phenotype analysis revealed that BPA and BaP activate ERK1/2 to induce cell proliferation and cell migration, leading to LN. Pathway analysis revealed that BPA and BaP activate the ERK1/2 signaling pathway to induce the expression of cell proliferation and migration genes. Activation of ERK1/2 signaling could be the shared key events (KE) for BPA and BaP. This analysis also identified protein kinase B and ERK1/2-targeting FOXM1, PTGES2, and FOXP3 genes, possible regulators of cell proliferation and angiogenesis, as KE in MOA for BPA, whereas ERK1/2 signaling, GJA and DUSP2 genes, negative regulators of cell proliferation and inflammatory response were identified as KE in MOA for BaP.	Chemosphere. 2021 Dec;285:131527.	10.1016/j.chemosphere.2021.131527	34329126	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	10^{-12} — 10^{-5} M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1668	B. Stanic, D. Kokal, J. Markovic Filipovic, D. Samardzija Nenadov, K. Pogenic-Majkic and N. Andric	2023	Global gene expression analysis reveals novel transcription factors associated with long-term low-level exposure of EA.hy926 human endothelial cells to bisphenol A	Bisphenol A (BPA) is an endocrine disruptor that binds to estrogen receptors (ER). However, studies have shown that the ER pathway was not always the primary molecular mechanism of BPA's action in cells and that gene transcription could be altered by different exposure times and doses. Here, our sought to understand the correlation between the BPA-responsive genes that have associated biological functions, and the transcription factors (TFs) involved in their regulation by repeatedly exposing human endothelial cells (EA.hy926) to three environmentally relevant concentrations of BPA (10-10 M, 10-8 M, and 10-5 M) for 3 weeks, after which cells/cultures in global gene expression were determined by RNA sequencing. Cytosecurity in 3-fluorescence was used to infer TFs involved in the control of BPA-deregulated genes. The results show a minimal overlap in deregulated genes between the three BPA concentrations. Pathway analysis revealed that BPA-induced changes in gene expression were associated with the cell cycle, cancer, and the ER signaling pathway. A unique set of TFs (HDAC2) has been identified for each BPA concentration, including the NF-κ B family and CEBPB for 10-10 M BPA, NRF2 family, AHR/ARNT, and ZBTB33 for 10-8 M BPA, and MEF2 family (MEF2A, MEF2C, and ZBTB33) for 10-5 M BPA, whereas ESR1/2 signaling, GJA and DUSP2 genes, negative regulators of cell proliferation and inflammatory response were identified as KE in MOA for BaP. Overall, our data suggest that long-term low-level exposure of EA.hy926 cells to BPA leads to concentration-specific changes in gene expression that are not controlled by the ER-mediated signaling but rather by other mechanisms.	Chem Biol Interact. 2023 Aug 25:381:110571.	10.1016/j.cbi.2023.110571	37244401	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	10^{-10}, 10^{-8}, 10^{-7}) M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1669	M. Stampar, T. Ravnjak, A. M. Domijan and B. Ž egura	2023	Combined Toxic Effects of BPA and Its Two Analogues BPAP and BPC in a 3D HepG2 Cell Model	Bisphenol A (BPA) is one of the most commonly used substances in the manufacture of various everyday products. Growing concerns about its hazardous properties, including endocrine disruption and genotoxicity, have led to its gradual replacement by presumably safer analogues in manufacturing plastics. The subsequent use of BPA and, more recently, its analogues has increased their residues in the environment. However, our knowledge of their toxicological profile is limited and their combined effects are unknown in the present study, we investigated the toxic effects caused by single bisphenols and by the combined exposure of BPA and its two analogues, BPAP and BPC, after short (24 h) and prolonged (96 h) exposure in HepG2 spheroids. The results showed that BPA did not reduce cell viability in HepG2 spheroids after 24 h exposure. In contrast, BPAP and BPC significantly reduced cell viability in HepG2 spheroids after 24 h exposure. Prolonged exposure to BPA, BPAP, and BPC significantly reduced cell viability in HepG2 spheroids. The combination of BPA/BPC/BPAP, both at 30 μM, After 96 h exposure, none of the BPA models affected cell viability in HepG2 spheroids. Only the combination of BPA/BPAP decreased cell viability in a dose-dependent manner that was significant for the combination of 3 μM BPA and 3 μM BPAP. None of the BPA and their binary mixtures studied affected the surface area and growth of spheroids as measured by planimetry. In addition, all BPA and their binary mixtures studied triggered oxidative stress, as measured by the production of reactive oxygen species and malondialdehyde, at both exposure times. Overall, the results suggest that it is important to study the effects of BPA as single compounds. It is even more important to study the effects of combined exposures, as the combined effects may differ from those induced by single compounds.	Molecules. 2023 Mar 30;28(7):3085.	10.3390/molecules28073085	37049848	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1670	P. Siedlnicka, M. Rozsko, P. Emanowicz, M. Wójcicki, O. Popowski, J. Karabasz and E. Juszczuk-Kubiak	2024	Influence of bisphenol A and its analogues on human gut microbiota composition and metabolic activity: Insights from an in vitro model	Food contamination is a primary route of human exposure to bisphenols (BPs), which are known to affect gut microbiota (GM) and intestinal health. This study comprehensively assessed the impact of bisphenol A (BPA) and three of its substitutes: bisphenol S (BPS), bisphenol F (BPF), and ecosynthetic bisphenol F (TSARBPF), the monomer of saffron (TSI) - on the taxonomic and functional profile of human GM using an in vitro model. Human GM was acutely exposed to 1 mM concentrations of these BPs during a 48-h anaerobic cultivation. We first examined the effects of BPA, BPS, BPF, and TSARBPF on GM taxonomic and metabolic profiles, mainly focusing on short-chain fatty acids (SCFAs) and branched-chain fatty acids (BCFAs). Then, we compared the effects of BPA and TSARBPF on GM composition and metabolic activity. Finally, we assessed cultures' cytotoxicity on intestinal epithelial cells (Caco-2). BPA, BPS, BPF, and TSARBPF similarly disrupted GM taxonomic composition and metabolic activities, significantly reducing SCFAs production. In contrast, TSARBPF exhibited the least disruptive effects, suggesting it may be a safer alternative. Although the GM did not biotransform the BPs, bioadsorption occurred, with affinity correlating to hydrophobicity in the order of TSARBPF < BPS < BPF < BPA. GM reduced the estrogenic activity of BPs primarily through bioadsorption. However, exposure of pre-epithelial cells to Post-Culture Supernatants of BPA, BPF, and TSARBPF significantly reduced Caco-2 cell viability, indicating the potential formation of harmful GM-derived metabolites and/or a depletion of beneficial GM metabolites.	Sci Total Environ Vol.956 Pages 177323	10.1016/j.scitotenv.2024.177323	39489444	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	1 mM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1671	V. Sneby, L. Hennebergen, M. König, J. Huchthausen, J. Braasch and B. I. Escher	2025	Beyond Estrogenicity: A Comparative Assessment of Bisphenol A and Its Alternatives in In Vitro Assays Questions Safety of Replacements	Bisphenol A (BPA) is a well-known endocrine disruptor linked to numerous adverse health outcomes and uses, therefore, banned in food contact materials in the European Union. Numerous alternatives are now in commerce, but their health hazards are often inadequately addressed. This study compared BPA and 24 alternatives in six in vitro bioassays for cytotoxicity, endocrine disruption, xenobiotic metabolism adaptive stress response, and reactivity toward DNA and proteins. Effect concentrations were converted to relative potencies (REPs) to BPA and used to calculate margins of exposure (MOEs) for a comparison of BPA with its alternatives. Several alternatives had lower maximum responses toward endocrine receptors than BPA, for example antagonistic activation of the estrogen receptor α (ERα) by 2,2-bis(4-hydroxyphenyl)-1,1,1,3,3,3-hexafluoropropane (BPAF) to 40%, and 4,4′-(1-phenylethane-1,1-diyl)bis(2-methylphenol) (BPE-MPE) to 60%, even accompanied by a shift toward pseudo-partial antifunctional receptor γ (PPARγ) activation, a receptor that is not relevant for BPA itself. Some alternatives additionally inhibited mitochondrial function and caused more DNA damage than BPA. Cytotoxicity and metabolism induced the cytotoxicity of all alternatives more for methyl-tris(4-hydroxyphenyl)methane (TA) and 4-[2-(4-hydroxyphenyl)ethoxyphenol (BPE-MAE), while estrogenic activity remained unchanged or decreased. This study demonstrates the utility of bioassays for rapid hazard assessment and comparative evaluation, suggesting that many BPA alternatives are regrettable substitutions, although 2,2-bis(4-hydroxyphenyl)-4,7-propanedioxane (TMDO) is a potentially more benign alternative.	Environ Sci Technol. 2025 Aug 26;59(33):17457-17470.	10.1021/acs.est.5c07018	40817891	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1672	J. Špačková, D. Oliveira, M. Pulkkil, I. Ďurovcová, K. Gaplovská-Kyselá, R. Oliveira and A. Ševčovič ová	2020	Endocrine-Independent Cytotoxicity of Bisphenol A Is Mediated by Increased Levels of Reactive Oxygen Species and Affects Cell Cycle Progression	Bisphenol A (BPA) is used for the production of plastics and epoxy resins, which are part of packaging materials for food and beverages, and can migrate into food and the environment, thus exposing human beings to its effects. Exposure to BPA has been associated with oxidative stress, cell cycle changes, and genotoxicity, and is mediated by its known endocrine-disrupting activity. Possible BPA sensitivity to chromatin mediators by estrogen receptors, has been reported in the literature. Here, we show the toxic effects of BPA by live cell imaging on the fission yeast Schizosaccharomyces pombe, an experimental model lacking estrogen receptors, which seems to be sensitive to BPA. We have found that treatment of cells with 150 μ M BPA for 24 h or 36 h affected the cell cycle. Measurements cells for BPA treatment and control, respectively, p < 0.05) as well as delay in cell cycle progression after 48 mM treatments, 48 h - 3.28 and 96 h - 5.69) in vitro cells at 0.1% DMSO content (in BPA treatments and control, respectively, p < 0.05) upon exposure to BPA. These results strongly support the possibilities that BPA-induced cell cycle changes can be independent of estrogen receptors and that live cell imaging is a powerful tool for genotoxic analysis.	J Agric Food Chem. 2020 Jan 22;68(3):869-875.	10.1021/acs.jafc.9b06853	31880940	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1673	J. H. Song, D. Lee, B. Hwang, S. Kim, J. Kim, S. Park, S. Choo, S. K. Hwang, H. Kim, S. J. Yun, Y. H. Choi, W. J. Kim and S. K. Moon	2025	Bisphenol A suppresses colon epithelial cell responses via G(0)/G(1)-phase arrest, MAPK and PI3K/AKT pathway modulation, and MMP-2/9 Inhibition by upregulating p21WAF1	Bisphenol A (BPA) is a non-steroidal endocrine-disrupting chemical compound with applications in the production of epoxy resins and polycarbonates. An escalating evidence suggests that BPA damages various organs and tissues, including those of the reproductive, immune, and neuroendocrine systems. However, the mechanisms by which BPA affects the intestinal tract have not been fully elucidated. We explored the adverse effects of BPA on human colonic epithelial cells in vitro by performing comprehensive viability, proliferation, invasion, and migration assays on HCT 116 and HCT-8 cells. BPA suppressed the proliferation of both cell types by regulating cell cycle progression and modulating the mitogen-activated protein kinase and phosphatidylinositol-3-kinase/protein kinase B pathways. Furthermore, BPA treatment significantly reduced the induction of matrix metalloproteinase-2 and -9 by inhibiting the binding activity of specificity protein 1, nuclear factor kappa B, and activator protein 1, thereby interfering with cell migration and invasion. This BPA-induced regulation of cell cycle progression was associated with the upregulation of p21WAF1 expression. Knockdown of p21WAF1 using small interfering RNA significantly restored the proliferation and viability of human colonic epithelial cells via p21WAF1 induction. This study provides valuable information into the precise mechanisms underlying the adverse effects of BPA on colonic epithelial cells.	Sci Rep. 2025 Jul 23;15(1):26698.	10.1038/s41598-025-11700-9	40695970	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	適応毒性試験	適応毒性試験以外については≦100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1674	J. H. Song, B. Hwang, S. Park, S. Kim, D. H. Kim, Y. H. Choi, W. J. Kim and S. K. Moon	2024	Bisphenol A regulates bladder cells responses via control of G2/M-phase cell cycle, apoptotic signaling, MAPK pathway, and transcription factor-associated MMP modulation	Bisphenol A (BPA), an exogenous endocrine-disrupting chemical, is widely used to produce polycarbonate plastics. The widely used BPA has been detected in human urine samples, raising public anxiety about the detrimental effects of BPA on the bladder. In this study, we examined regulatory mechanisms for the adverse effects of BPA in human bladder (5637) and T24 cells. BPA induced extrinsic and intrinsic apoptosis and G2/M cell cycle arrest caused by the ATM-CHK1/CHK2-CDC25c-CDC2 signaling, which ultimately inhibited the growth of human bladder cells. We also found that BPA decreased the binding activity of AP-1 and NF-κB transcription factors in human bladder cells, which inhibited migration and invasion through matrix metalloproteinase-2 and -9 inactivation. Phosphorylation of MAPKs was implicated with BPA-mediated detrimental effects in human bladder cells. Collectively, our results provide a novel explanation for the underlying molecular mechanisms that BPA induces cytotoxicity in human bladder cells.	J Biochem Mol Toxicol. 2024 Mar;38(3):e23662	10.1002/jbt.23662	38372072	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1675	J. H. Song, B. Hwang, S. B. Kim, Y. H. Choi, W. J. Kim and S. K. Moon	2023	Bisphenol A modulates proliferation, apoptosis, and wound healing process of normal prostate cells: Involvement of G2/M-phase cell cycle arrest, MAPK signaling, and transcription factor-mediated MMP regulation	Bisphenol A (BPA) is a commonly used to produce epoxy resins and polycarbonate plastics. BPA is an endocrine-disrupting chemical that is leaked from the polymer and absorbed into the body to disrupt the endocrine system. Although BPA may cause carcinogenesis in the prostate, a hormone-dependent reproductive organ, its underlying mechanism has not yet been investigated. Here, we investigated the effects of BPA on cell proliferation, apoptosis, and the wound healing process using prostate epithelial cells (RWPE-1) and stromal cells (WPMY-1). Observations revealed that BPA induced G2/M cell cycle arrest in both cell types through the ATM-CHK1/CHK2-CDC25c-CDC2 signaling pathway, which ultimately inhibited the growth of normal prostate cells. BPA also induced extrinsic and intrinsic apoptosis by activating caspase-3, -8, and -9 and transcription factors (c-Jun and c-Fos). Furthermore, BPA interfered with the wound healing process through inhibition of MMP-2 and -9 expression, accompanied by reductions in the binding activities of AP-1 as well as NF-κB. Phosphorylation of MAPKs was associated with the BPA-mediated toxicity of prostate cells. These results suggest that BPA exhibits prostate toxicity by inhibiting cell proliferation, inducing apoptosis, and interfering with the wound healing process. Our study provided new insights into the precise molecular mechanisms of BPA-induced toxicity in human prostate cells.	Ecotoxicol Environ Saf. 2023 Jan 1;249:114358.	10.1016/j.ecoenv.2022.114358	36508820	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1676	M. Song, Y. Y. Lee, J. Park and Y. Lee	2021	Korean Red Ginseng suppresses bisphenol A-induced expression of cyclooxygenase-2 and cellular migration of A549 human lung cancer cell through inhibition of reactive oxygen species	BACKGROUND: Korean Red Ginseng (KRG) is a natural product with anti-inflammatory and anticarcinogenic effects. We have previously reported that the endocrine-disrupting compound bisphenol A (BPA)-induced cyclooxygenase-2 (COX-2) via nuclear translocation of nuclear factor kappa B (NF-κB) and activation of mitogen-activated protein kinase and promoted the migration of A549. Here, in this study, we assessed the protective effect of KRG on the BPA-induced reactive oxygen species (ROS) and expression of COX-2 and matrix metalloproteinase-9 (MMP-9) in A549 cells. METHODS: The effects of KRG on the upregulation of ROS production, COX-2 expression, and MMP-9 activity induced by BPA were examined by 2',7'-dichlorofluorescein diacetate (DCF-DA) staining, western blotting, and gelatin zymography, respectively. The migration ability by KRG was evaluated by migration assay in A549 cells. RESULTS: The KRG significantly suppressed the BPA-induced ROS, COX-2, the activity of NF-κB, the production of PGE2, and the migration of A549 cells. These effects led to the downregulation of the expression of MMP-9. CONCLUSIONS: Overall, our results suggest that KRG exerts an anti-inflammatory effect on BPA-treated A549 cells via the suppression of ROS and downregulation of NF-κB activation and COX-2 expression which leads to a decrease in cellular migration and MMP-9 expression. These results provide a new possible therapeutic application of KRG to protect BPA-induced possible inflammatory disorders.	J Ginseng Res. 2021 Jan;45(1):119-125.	10.1016/j.jgr.2020.01.002	33437163	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1677	D. Song, G. Wu, Q. Wei and F. Shi	2019	Bisphenol A attenuates thyroxine-induced apoptosis in ovarian granulosa cells of pigs	Bisphenol A (BPA) is a chemical of high production volume that is used widely in many industries and is known as a xenoestrogen and anti-thyroid hormone endocrine disruptor. There is little information regarding the effects of BPA in the presence of thyroid hormone on porcine granulosa cell development. Thus, the primary granulosa cells were treated with thyroxine (T4, 10 nM), BPA (50 μM) or T4 plus BPA, we subsequently evaluated the effects of T4 or BPA on T4‐induced cell apoptosis, cellular proliferation and apoptosis. Our data indicated that BPA significantly increased the accumulation of T4‐induced porcine granulosa cell proliferation, whereas T4 significantly decreased T4‐induced cell and had no effects on cellular proliferation. In addition, it was noteworthy that T4 treatment induced apoptosis in porcine granulosa cells and BPA co-treatment significantly increased the accumulation of T4‐induced porcine granulosa cell apoptosis. Moreover, BPA co-treatment significantly increased the accumulation of T4‐induced cell apoptosis mediated signalling pathways. In conclusion, our results demonstrated that T3 affected T4‐induced accumulation and reduced cellular apoptosis, but did not affect granulosa cell proliferation. Exposure to BPA increased T4‐induced accumulation, promoted granulosa cell proliferation and attenuated T4 induced apoptosis in porcine granulosa cells in vitro.	Reprod Domest Anim Vol.54 Issue 6 Pages 864-872	10.1111/rda.13436	30972826	in vitro	-	-	-	-	-	-	-	-	1	0	10 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1678	D. Song, Y. Liu, Y. Yao, F. Liu, W. Tao, X. Zhou, R. Li, X. Zhang and X. Li	2022	Melatonin improves bisphenol A-induced cell apoptosis, oxidative stress and autophagy impairment via inhibition of the p38 MAPK signaling pathway in FLK-BLV cells	The aim of this study was to assess the protective effect and potential mechanism of melatonin against bisphenol A (BPA)-induced apoptosis and oxidative damage in FLK-BLV cells. The results showed that BPA induced cell viability in a dose- and time-dependent manner, caused cell shrinkage and induced oxidative stress and apoptosis in FLK-BLV cells, which were effectively reversed by melatonin. In addition, BPA caused autophagy flux impairment, which was confirmed by the increased LC3-II and p62 levels, whereas melatonin treatment significantly reduced p62 levels under BPA treatment, and western blot analysis related protein expression patterns caused by BPA. However, inhibition of autophagy by CQ partially abolished the protective effect of melatonin on apoptosis, suggesting that melatonin against BPA-induced oxidative injury and apoptosis was partially dependent on the activation of autophagy. Moreover, melatonin inhibited the BPA-induced p38 MAPK signaling pathway, and the p38 MAPK activator anisomycin (ANI, 25 nM) reversed the inhibitory effect of melatonin on BPA-induced apoptosis, which further confirmed the involvement of p38 MAPK signaling pathway in melatonin-mediated autophagy. In conclusion, these results suggest that melatonin may prevent BPA-induced FLK-BLV cell damage by inhibiting p38/MAPK signaling pathway and activating autophagy, and it could be a potential therapeutic compound in preventing BPA-induced cell damage.	Environ Toxicol. 2022 Jul;37(7):1551-1562.	10.1002/tox.23505	35238458	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1679	A. Soltani, S. Alirezaei, F. Abbasnejadsharsi and M. A. Ghiyamipour	2022	Effects of bone marrow-derived mesenchymal stem cells exposed to endocrine-disrupting chemicals on the differentiation of umbilical cord blood hematopoietic stem cells	Endocrine-disrupting chemicals (EDCs), a class of peripheral toxic substances, can cause many environmental and clinical side effects, particularly on the human body's endocrine system. Bisphenol A (BPA) and diethylhexyl phthalate (DEHP) are two well-known EDCs. In the medical industry, however, there are no comprehensive studies on their effects on hematopoiesis. Hence, this study aimed to investigate the effects of these environmental substances on the clonogenic capacity of umbilical cord blood hematopoietic stem cells (CB-HSCs). The HSCs, which express CD34 + stem isolated from umbilical cord blood by the magnetic activated cell sorting (MACS) method. The bone marrow-derived mesenchymal stem cells (BM-MSCs) were cultured with BPA and DEHP, and the number and types of colonies formed by the CB-CD34 + HSCs were co-cultured with bone marrow-derived mesenchymal stem cells (BM-MSCs) in the presence of BPA and DEHP. Finally, the number and types of colonies formed were evaluated after 14 days. Statistical analysis was performed by GraphPad Prism through ANOVA. CB-HSC treated by BPA and DEHP showed a lower absolute colony count than the control group ($P < 0.05$). Decrease in clonogenic potential of HSCs was more significant in co-culture conditions by MSCs. In particular, there was a significant decrease in the BFU-E colonies. In consideration derived fractions ($P < 0.001$). In the presence of EDCs, such as BPA and DEHP, the patterns of differentiation in CD34 + CB-HSCs changed from suppressed erythroid differentiation toward stimulated myelopoietic pathways.	Environ Toxicol. 2022 Jul;37(7):1551-1562.	10.1007/s11356-021-17787-7	35112247	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1680	M. Z. Sakeimari, L. Khamandi, Y. Asadi-Fard, F. Rezaei-Tazangi and A. Ashtari	2025	Protective Effects of Adipose Mesenchymal Stem Cell Secretome On Oxidative Stress-Induced Bisphenol-A in Isolated Rat Testes Mitochondria and Sperm Quality	OBJECTIVE: This study aimed to explore the potential protective effects of adipose-derived mesenchymal stem cell secretome (SOD) on oxidative stress triggered by Bisphenol A (BuA) exposure in testicular mitochondria and sperm quality. MATERIALS AND METHODS: Mitochondria were isolated from rat testes and exposed to BuA (50 μM) with or without SOD. Mitochondrial membrane potential, reactive oxygen species (ROS), antioxidant biomarkers, and sperm parameters were measured. RESULTS: BuA-induced biomarkers of oxidative stress, in mitochondria, while the levels of antioxidant activity and ATP decreased significantly. BuA harmed the morphology, survival rate, and motility of the spermatozoids. SOD lowered malondialdehyde contents and ROS generation in the mitochondria, increased ATP, and reversed sperm quality. CONCLUSIONS: BuA-induced oxidative damage to mitochondria and sperm quality by exerting oxidative stress.	JBRA Assist Reprod Vol.29 Issue 1 Pages 53-60	10.5935/1518-0557.20240089	39688440	in vitro	-	-	-	-	-	-	-	-	1	0	8 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1681	D. G. Sikdar and L. P. Maliić	2020	In vitro estrogenic activity of binary and multicomponent mixtures with bisphenol A	Bisphenol A and its analogs are environmental contaminants with well-known estrogenic and anti-androgenic activities. In studies of human biomonitoring, simultaneous exposure to multiple bisphenols was shown in different biological samples, at concentrations in low nanomolar concentrations. Evaluation of their combined effects is therefore of high importance for the risk assessment of health risks than evaluation of only the single chemicals. In the present study, estrogenic activities of individual bisphenols were evaluated, along with their binary and multi-component mixtures including three- and four-component mixtures, using the E-screen assay. Experimental data on binary mixtures were compared with predictions of the concentration addition model. Although exposure to individual bisphenols remains below their effective doses, their co-exposure to micromolar range. Estrogenic activities of binary and multicomponent mixtures followed a concentration-additive model. Although exposure to individual bisphenols remains below their effective doses, we demonstrate that as a mixture, they can contribute additively to toxicity. This study thus emphasizes the importance of mixture toxicity evaluation for risk assessment of compounds that act like the bisphenols.	Sci Total Environ. 2020 Mar 10;707:135211.	10.1016/j.scitotenv.2019.135211	31869609	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1682	A. Sixto, B. El-Murabit, M. J. Trujillo-Rodríguez, E. J. Carrasco-Correa and M. Miró	2021	An automatic flow-through system for exploration of the human bioaccessibility of endocrine disrupting compounds from microplastics	This article reports on the first attempt towards investigating the leaching rates in the human gastrointestinal (GI) tract of plastic-borne contaminants that can be ingested accidentally using physiologically relevant body fluids. Oral bioaccessibility under fasted and fed states was determined in dynamic mode exploiting an automatic flow setup. The flow system is able to mimic the fast uptake of the released species from the polymeric matrix in the stomach and the subsequent dilution in the small intestine, while ensuring sink conditions. Bisphenol A (BPA) and bisphenol A diglycidyl ether (BADGE) were selected as model analytes. The extent even through in-vitro-ingestible loaded metal was evaluated for semi-continuous leaching of plastic/plastic additives, and water-assignment and movement formulated species. Bisphenol A (BPA) followed by in-line solid-phase extraction and clean-up of 30 minutes prior to liquid chromatography analysis. The temporal extraction profiles were fitted to a first-order kinetic model for the estimation of maximum bioaccessibility pools and apparent leaching rates. Among all studied contaminants, only BPA, dimethylphthalate and diethylphthalate were appreciably released under dynamic GI conditions from high-density polyethylene pellets. Average size of 130 μ m), with average bioaccessibility values spanning from 10 to 80% and 30 to 97% for UBM and Viewtainment methods, respectively. As statistically significant differences in oral bioaccessibility pools were found between fed- and fasted-state digestion models. The apparent kinetic constants under the fed state were properly fit. 20% or a consequence of the effects of the larger amounts of BPA and digestive enzymes in the Viewtainment test on the leaching rates. The estimated average daily intake, in which bioaccessibility rates are contemplated, indicated that plastic materials exceeding 0.3% (w/w) BPA might pose oral risks to human health.	Analyst. 2021 Jun 14;146(12):3858-3870.	10.1039/d1an00446h	34047317	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1683	R. D. Singh, J. L. Wager, T. B. Schmidt, L. T. Conrow, S. Easton, M. A. Callaghan, S. Kintzios-Hinojosa, L. H. Swift, P. Colarusso, A. Jadd, T. E. Shutt, V. Patel and J. A. Thompson	2024	Potentiation of Adipogenesis by Reactive Oxygen Species Is a Unifying Mechanism in the Preadipogenic Properties of Bisphenol A and Its New Structural Analogues	Aims: Structural analogues of bisphenol A (BPA), including bisphenol S (BPS) and bisphenol F (BPF), are emerging environmental toxicants as their presence in the environment is rising since new regulatory restrictions were placed on BPA-containing their products. The adipogenesis-inducing effects of bisphenols may explain the link between human exposure and metabolic disease; however, underlying molecular pathways remain unresolved. Results: Exposure to BPS, BPF, BPA, or reactive oxygen species (ROS) generators enhanced lipid droplet formation and expression of adipogenic markers after induction of differentiation in adipose-derived stromal cells (ADSCs) and 3T3-L1 preadipocytes. Bisphenol-induced adipogenesis was blocked by the antioxidant N-acetyl-L-cysteine (NAC). Bisphenols also induced ROS production in ADSCs consistent with antioxidant-attenuated adipogenesis and abolished the effects of BPS. There was a loss of mitochondrial membrane potential in BPS-exposed cells, and mitochondrial ROS were involved in potentiation of adipogenesis by BPS and its analogues. Main mice exposed to BPS during gestation had higher whole body adiposity, as measured by time domain nuclear magnetic resonance, while postnatal exposure led to insect-on-adiposity in mother rats. Innovation: These findings support existing evidence showing a role for ROS in regulating adipocyte differentiation and are the first to highlight ROS as a unifying mechanism that explains the preadipogenic properties of BPA and its structural analogues. Conclusion: ROS act as signaling molecules in the regulation of adipocyte differentiation and mediate bisphenol-induced potentiation of adipogenesis. Antioxid. Redox Signal. 40, 1–16.	Antioxid Redox Signal. 2024 Jan;40(1-3):1-15.	10.1089/ars.2022.0150	37154733	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1684	M. J. Sim, Y. W. Seo, M. R. Kim, M. S. Song and S. Y. Lee	2025	Bisphenol A enhanced cell migration through Kv3.4 in MCF7 cells	Bisphenol A (BPA) is a well-known endocrine-disrupting chemical (EDC) that has been implicated in cancer development. However, the specific mechanisms of EDCs, including BPA, remain unclear. Voltage-gated potassium (Kv) channels are transmembrane proteins that regulate cell migration in various cancers. This study investigated the role of Kv3.4 in BPA-induced migration of MCF7 cells and explored the mechanism of BPA in relation to Kv3.4 expression in human breast cancer MCF7 cells. BPA treatment significantly increased Kv3.4 expression at both the mRNA and protein levels, and cell migration. Functional analysis demonstrated that Kv3.4 is closely related to integrin-β1 and integrin-regulated FAK signaling. However, BPA-induced cell migration and integrin-regulated FAK signaling were significantly abolished by Kv3.4 silencing. Therefore, our results indicated that BPA is closely associated with cancer cell migration mediated by Kv3.4 via integrin-regulated FAK signaling. These findings provide novel insights into the role of BPA in cancer progression and suggest Kv3.4 as a potential therapeutic target for BPA-associated cell migration.	Biochem Biophys Res Commun. 2025 May 26:760:151678.	10.1016/j.bbrc.2025.151678	40157292	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1685	C. Sillapachaiyaporn, S. Chuchawankul, S. Nilkhet, N. Moungkote, T. Saechara, A. T. Ung, S. J. Baek and T. Tencomnao	2022	Ergosterol isolated from cloud ear mushroom (Auricularia polytricha) attenuates bisphenol A-induced BV2 microglial cell inflammation	Bisphenol A (BPA) has been reported to have neurotoxic properties that may increase the risk of neurodegenerative diseases by inducing neuroinflammation. Auricularia polytricha (AP) is an edible mushroom with several medicinal properties. Herein, the anti-neuroinflammatory effects of AP extract on BPA-induced neuroinflammation in BV2 microglial cells were investigated. Kuwanol E (KE) and ergosterol (ERG) were isolated from AP and identified. AP and KE significantly reduced BPA-induced neuroinflammation in BV2 microglia by reducing microglial activation and the expression of pro-inflammatory cytokines. These anti-inflammatory effects were regulated by the NF-κ B signaling pathway. In addition, AP and AP-exhibited antioxidative effects by increasing the activity of the Nrf2/HO-1 pathway and restoring the mitochondrial function of impaired cells. Moreover, the conditioned medium prepared using BPA-induced BV2 cells demonstrated that the treatment of AP or KE could attenuate HT22 cytotoxicity in HT-22 cells. Further, ergosterol was isolated from AP, and also showed anti-inflammatory and antioxidative activities. In conclusion, AP extracts and ergosterol alleviated neuroinflammation against BPA-induction in BV2 microglial cells through the NF-κ B signaling pathway.	Food Res Int. 2022 Jul;157:111433.	10.1016/j.foodres.2022.111433	35761673	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1686	L. Shiyao, K. Yao, L. Jun, L. Yichao, Z. Tingxiao, Y. Longbao, Z. Hong and Z. Kai	2024	Unraveling the role of bisphenol A in osteosarcoma biology: insights into prognosis and immune microenvironment modulation	BACKGROUND: Bisphenol A (BPA) is a common environmental pollutant, and its specific mechanisms in cancer development and its impact on the tumor immune microenvironment are not yet fully understood. METHODS: Tumor/adjacent data from osteosarcoma (OS) patients were downloaded from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) database. BPA-related genes were identified through the Comparative Toxicogenomics Database (CTD). Univariate Cox regression and LASSO analysis were performed to develop a prognostic model. The model's predictive accuracy was assessed using ROC curves, and a prognostic model using univariate Cox regression and LASSO analysis. The model was validated using the GSE16091 dataset. GO, KEGG, and GSEA analyses were performed to investigate the mechanisms of BPA-related genes. RESULTS: A total of 16 BPA related genes were identified as differentially expressed in OS. Univariate Cox regression and LASSO analysis identified four key prognostic genes (FOLR1, MYC, ESRRA, VEGFA). The prognostic model exhibited strong predictive performance with area under the curve (AUC) values of 0.89, 0.9, and 0.79 for predicting 1-, 2-, and 3-year survival, respectively. External validation using the GSE16091 dataset confirmed the model's high accuracy with AUC values exceeding 0.88. Our results indicated that the prognosis of the high-risk population is generally poorer, which may be associated with an immunosuppressive microenvironment. Moreover, the high-risk group exhibited increased sensitivity to chemotherapeutic agents such as cisplatin, doxorubicin, and methotrexate, suggesting potential implications for tumor cells. These findings revealed a correlation between upregulation of BPA-related genes and formation of an immunosuppressive microenvironment, leading to unfavorable patient outcomes. CONCLUSION: Our study highlighted the significant association of BPA with OS biology, particularly in its potential role in modulating the tumor immune microenvironment. We offered a fresh insight into the influence of BPA on cancer development, thus providing valuable insights for future clinical interventions and treatment strategies.	Discov Oncol. 2024 Sep 4;15(1):404.	10.1007/s12672-024-01280-x	39230832	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1687	X. Shi, T. Xu, X. Li, X. Sun, W. Zhang, X. Liu, Y. Wang, Y. Zhang and S. Xu	2023	ROS mediated pyroptosis-M1 polarization crosstalk participates in inflammation of chicken liver induced by bisphenol A and selenium deficiency	The world's natural environmental factors and man-made industrial pollution often lead to the co-occurrence of environmental pathogenic factors and malnutrition. Bisphenol A (BPA) is a serious environmental endocrine disruptor, and its exposure can cause liver tissue damage. Selenium (Se) deficiency is a worldwide problem that affects thousands of people, and Se deficiency can cause NO/ROS imbalance. In addition, the crosstalk between pyroptosis and M1 polarization can aggravate liver damage. However, the role of pyroptosis in BPA and Se deficiency-induced liver damage and its relationship with M1 polarization through ROS, and the crosstalk between pyroptosis and M1 polarization aggravated liver inflammation in chickens. In this study, the BPA model (50 mg/kg) and Se deficiency chicken model (0.04 and 0.11 mg/kg) were established. The results displayed that BPA or Se deficiency induced liver inflammation accompanied by pyroptosis and M1 polarization through oxidative stress, and increased expressions of chemokines (CCL-4, CCL-C1, CCL-C5, and CXCL-i1) and NRT and inflammatory factors (IL-1β and TNF-α). The vivo experiments further verified the above changes and showed that LNA pyroptosis promoted M1 polarization of HD11 cells, and vice versa. NAC counteracted pyroptosis and M1 polarization caused by BPA and low Se, reducing the release of inflammatory factors. In brief, BPA and Se deficiency treatment can exacerbate liver inflammation by increasing oxidative stress to induce pyroptosis and M1 polarization.	Environ Pollut. 2023 May 1:324:121392.	10.1016/j.envpol.2023.121392	36906056	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1688	J. Shi, C. Liu, M. Chen, J. Yan, C. Wang, Z. Zuo and C. He		The interference effects of bisphenol A on the synthesis of steroid hormones in human ovarian granulosa cells	Numerous studies have shown that endocrine-disrupting chemicals are one of the important pathogenic factors in women with polycystic ovary syndrome. Our previous study has revealed that bisphenol A (BPA) can cause ovarian dysfunction and abnormal follicular development. However, the effects of BPA on steroidogenesis in human granulosa cells remain unclear. In this study, we investigated the effects of BPA on steroidogenesis in primary cultured granulosa cells. Exposure of KGN cells to BPA (0.5, 5, 50, and 500 μg/L) resulted in the decrease in progesterone (P), estradiol (E2), and the ratio of estradiol to testosterone (E2/T). BPA affected the expression of genes related to steroid hormone synthesis in KGN cells, including the decreased expression of the steroidogenic acute regulatory protein, hereditary, and hereditary reductase genes during progesterone synthesis, upregulating the expression of cytochrome p450 aromatase genes associated with E2 and T synthesis, and the upregulated cytochrome P450 family 1 subfamily A member 1 and cytochrome P450 family 1 subfamily B member 1 in E2 degradation. BPA also reduced the expression of stimulatory G proteins (Gs) in follicle-stimulating hormone receptor (FSHR)/Gs/adenylate cyclase (AC)-signaling pathway. In summary, our research has revealed that BPA exposure can disrupt the steroid hormone synthesis and metabolism leads to steroid hormone synthesis disorder in human ovarian granulosa cells, which might cause the reduction of gene expression in hormone synthesis and the suppression of the FSHR/Gs/AC signaling pathway.	Environ Toxicol. 2021 Apr;36(4):665-674.	10.1002/tox.23070	33258555	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.5、5、50、500 μg/L	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1689	Y. Shen, X. Li, H. Wang, Y. Wang, L. Tao, P. Wang and H. Zhang	2023	Bisphenol A induced neuronal apoptosis and enhanced autophagy in vitro through Nrf2/HO-1 and Akt/mTOR pathways	Bisphenol A (BPA) was traditionally used in epoxy resins and polycarbonate plastics, but it was found to be harmful to human health due to its endocrine disrupting effects. It can affect various biological functions of human beings and interfere with brain development. However, the neurotoxic mechanisms of BPA on brain development and associated neurodegeneration remain poorly understood. Here, we reported that BPA (50, 100, 200 μM) induced neuronal apoptosis in HT22 cells. BPA increased the production of reactive oxygen species (ROS), malondialdehyde (MDA), and lactate dehydrogenase (LDH) and decreased the activity of superoxide dismutase (SOD). Besides, decreased mitochondrial membrane potential, reduced the expression of cytochrome c subunit 4 (COX4), downregulated Bcl-2, and initiated caspase-3, -8, and -9 activation. Moreover, BPA induced the accumulation of intracellular acidic vesicles and increased the autophagy marker LC3 II to LC3 I ratio. Furthermore, BPA exposure inhibited Nrf2/HO-1 and Akt/mTOR pathways and mediated cellular oxidative stress, apoptosis, and excessive autophagy, leading to neuronal degeneration. The interactions between oxidative stress, autophagy, and apoptosis during BPA-induced neurotoxicity remain unclear and require further in vivo confirmation.	Toxicology Vol.500 Pages 153678	10.1016/j.tox.2023.153678	38006930	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	100、250、500 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1690	T. Shaikh, K. L. Williams, S. Chiu, D. Crump and J. M. O'Brien	2021	Toxicity Screening of Bisphenol A Replacement Compounds: Cytotoxicity and mRNA Expression in Primary Hepatocytes of Chicken and Double-Crested Cormorant	A market for bisphenol A (BPA) replacement compounds has emerged as a result of restrictions on the use of BPA. Some of these compounds have been detected in the environment; however, little is known about their toxicological properties. In the present study, an easy-to-store, less-expensive approach was used to compare the effects of 6 BPA alternatives. Cell viability and mRNA expression were compared in primary embryonic hepatocytes of chicken (CHH) and double-crested cormorant (DCCH) exposed to 6,7-(propane-2,2-diyl) diphenol (BPG), bis (4-hydroxyphenyl) methane (BPF), bis (3-allyl-4-hydroxyphenyl) sulfone (TGSH), 2-bis (4-hydroxyphenyl)-4-(1-(4-(oxiran-2-ylmethoxy) phenyl)-1-phenylethyl) phenyl) propane (BPXBP), 4,4′-(propane-2,2-diyl) bis (2,6-dibromophenol) (TBBPA), and 4,4′-(propane-2,2-diyl) bis (2,6-dimethylphenol) (TMBPA) for 24 h. Cytotoxicity was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Quantitative real-time polymerase chain reaction (PCR) assays (2 species-specific ToxiChips that contain genes representing toxicologically relevant pathways, and 2 chicken-specific AvianChips that measure receptor responsive genes in the aryl hydrocarbon receptor (AHR), estrogen receptor (ER), androgen receptor (AR), and peroxisome proliferator-activated receptor (PPAR) pathways) were used to measure mRNA expression in exposed cells. The rank-order based on the number of genes altered on the chicken ToxiChip array was TGSH > DCI-BP > BPF > CLF activator (CLF) > BPXBP > BPA. On the commercial ToxiChip array, BPXBP altered the greatest number of genes. Based on the chicken AvianChip data, BPXBP and BPF were slightly estrogenic. These results suggest that the replacement compounds have comparable or even greater toxicity than BPA and act via different mechanisms. Environ Toxicol Chem 2021;00:1368–1378. © 2021 Her Majesty the Queen in Right of Canada. Reproduced with the permission of the Minister of Environment and Climate Change Canada.	Environ Toxicol Chem. 2021 May;40(5):1368-1378.	10.1002/etc.4985	33465250	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1691	T. Shaik , D. Crump and J. M. O'Brien	2022	Toxicity screening of bisphenol A replacement compounds: cytotoxicity and mRNA expression in LMH 3D spheroids	Previously, we showed that the chicken LMH cell line cultured as 3D spheroids may be a suitable animal free alternative to primary chicken embryonic hepatocytes. CCK-8 to assess in vitro chemical screening. In this study, cytotoxicity and mRNA expression were determined in LMH 3D spheroids following exposure to bisphenol S (BPS), five BPA replacement compounds (BPF, TGSH, DCI-TG, BPXBP, BPGDP), and 17β -estradiol (E2). Results were compared to an earlier study that evaluated the same compounds in two-dimensional (2D) LMH cultures. Cytotoxicity was restricted to use to predict human health and the environment. As a result, the industry has begun developing BPA analogues, but there are not yet sufficient toxicity data to state that they are safe. We investigated the adverse toxic effects of BPA and its analogues (BPS, BPAF, BPAP, BPF), and BPC2 cells emphasis, and BPC2 cells were exposed to BPA and its analogues (BPS, BPAF, BPAP, BPF, and BPC) at concentrations ranging from 0.1 μM to 100 μM for 24 h. Cytotoxicity was assessed by an additional mtg current over the most cytotoxic analogues that affected cell viability, spheroid surface area and morphology, cell proliferation, and apoptotic cell death. BPAF, BPAP, and BPAF induced DNA double-stranded breaks formation (γ-H2AX assay), whereas BPAF and BPC increased the percentage of γ-H3 positive cells, indicating their genotoxic activity. All BPs induced DNA single-strand break formation (comet assay), with BPAP>AF>AF>F, μM being the most effective and BPF and BPC the least effective (≥1 μM) under conditions applied. The results indicate that we all of the analogues studied are safe alternatives to BPA and thus more in-depth research is urgently needed to adequately evaluate the risks of BPA analogues and assess their safety for humans.	Environ Sci Pollut Res Int. 2022 Jun;29(29):44769-44778.	10.1007/s11356-022-18812-z	35138540	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1692	M. Serdra, M. Stampar, K. Frac, B. Nowa, A. Figueras and B. Zagura	2023	Adverse (geno)toxic effects of bisphenol A and its analogues in hepatic 3D cell model	Bisphenol A (BPA) is one of the most widely used and versatile chemical compounds in polymer additives and epoxy resins for manufacturing a range of products for human applications. It is known as endocrine disruptor, however, there is growing evidence that it is genotoxic. Because of its adverse effects, the European Union has restricted its use to protect human health and the environment. As a result, the industry has begun developing BPA analogues, but there are not yet sufficient toxicity data to state that they are safe. We investigated the adverse toxic effects of BPA and its analogues (BPS, BPAF, BPAP, BPF), and BPC2 cells emphasis, and BPC2 cells were exposed to BPA and its analogues (BPS, BPAF, BPAP, BPF, and BPC) at concentrations ranging from 0.1 μM to 100 μM for 24 h. Cytotoxicity was assessed by an additional mtg current over the most cytotoxic analogues that affected cell viability, spheroid surface area and morphology, cell proliferation, and apoptotic cell death. BPAF, BPAP, and BPAF induced DNA double-stranded breaks formation (γ-H2AX assay), whereas BPAF and BPC increased the percentage of γ-H3 positive cells, indicating their genotoxic activity. All BPs induced DNA single-strand break formation (comet assay), with BPAP>AF>AF>F, μM being the most effective and BPF and BPC the least effective (≥1 μM) under conditions applied. The results indicate that we all of the analogues studied are safe alternatives to BPA and thus more in-depth research is urgently needed to adequately evaluate the risks of BPA analogues and assess their safety for humans.	Environ Int. 2023 Jan:171:107721.	10.1016/j.envint.2022.107721	36580735	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	≥1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1693	M. Serdra, M. Casia-Salz and P. Muñiz	2024	Are the BPA analogues an alternative to classical BPA? Comparison between 2D and alternative 3D in vitro neuron model to assess cytotoxic and genotoxic effects	BPA is used in a wide range of consumer products with very severe toxicological properties. The European Union has restricted its use to protect human health. Industry has substituted BPA by BPA analogues. However, there is a lack of toxicologic about their impacts. In this work, BPA and 5 BPA analogues (BPS, BPAP, BPAF, BPF, and BPC) have been studied in classical 2D (CTZ) and the alternative 3D in vitro models after 24 and 96 h of exposure. Cell viability, percentage of ROS, cell cycle phases, as well as the morphology of the spheroids were measured. The 3D model was more sensitive than the 2D model, with differences in cell viability higher than 60% after 24 h of exposure, and different mechanisms of ROS production. After chronic exposure, both models were more affected in comparison to the 24 h exposure. After a recovery time (96 h), the spheroids were able to 3 h 48 μM BPA. The 3D model is an suitable candidate to perform more reliable in vitro neurotoxicity tests.	Toxicology. 2024 Feb;502:153715.	10.1016/j.tox.2023.153715	38211720	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1694	M. Segovia-Mendoza, C. T. Gómez de León, R. García-Becerra, L. Ambrosio, K. E. Nava-Castro and J. I. Morales-Montor	2020	The chemical environmental pollutants BPA and BPS induce alterations of the proteomic profile of different phenotypes of human breast cancer cells: A proposed interactome	Breast cancer is one of the most common malignancies and the second leading cause of death in women. Despite efforts for its early detection, its worldwide incidence continues to increase. Thus, identification of risk factors for its development and new targets for its therapy are of vital importance. Environmental pollutants derived from human activity have been associated with predisposition to the development of cancer. Bisphenol A (BPA) is an endocrine disruptor compound (EDC) widely used in the manufacture of polycarbonates, and it has affinity for the estrogen receptor (ER). Scientific evidence has proposed an association between increased incidence of breast cancer and BPA exposure at low doses. Among worldwide concerns with BPA exposure, different industries proceeded to replace BPA with analogs, such as bisphenol S (BPS), which is non-estrogenic. However, BPS has been detected in human samples, and its harmful effects have been demonstrated in different experimental models. In this work, we compared the effect of BPA and BPS on two cell lines of breast cancer, MCF-7 and MDA-MB-231, which represent ER+ and ER- phenotypes, respectively. Most of the effects of both BPA and BPS have been performed in estrogen-dependent breast cancer models, such as MCF-7. However, gaps in knowledge still exist on the roles and mechanisms of both compounds, specifically BPS, may play in cancer initiation and development in hormone-dependent and other types of breast cancer. Thus, the aim of the present study was to deepen the understanding of biological targets modulated by these compounds in breast cancer cells. Cell viability, proliferation, and migration were evaluated in MCF-7 and MDA-MB-231 cells exposed to BPA and BPS. Results showed that BPA and BPS induced cell proliferation in ER positive cells, not showing this effect in the ER negative breast cancer cells. Different targets modified at the proteomic level in both breast cancer cell lines were identified. Stem cell markers, e.g., CD44) and invasion proteins, e.g., MMP-10) were importantly increased by BPA and BPS in ER positive breast cancer cells. In contrast, growth factors and associated receptors such as TGFβ and TGF-β were reduced by BPS in the ER negative breast cancer cells; both pollutants induced an increase of vascular endothelial growth factor (VEGF) protein secretion. This finding suggests that the use of BPS must be considered with more caution than BPA, since it is not independently of the presence of the hormonal receptor. These findings show new evidence that BPA and BPS exposure can contribute to breast cancer development and progression. Our results suggest that both BPA and BPS must be considered equally as outstanding risk factors for this pathology.	Environ Res. 2020 Dec:191:109960.	10.1016/j.envres.2020.109960	33181973	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1695	J. Schroeder, K. M. Polenti, A. Tapparel, L. K. Sodeda, J. Z. Saxton and J. A. Colacino	2024	Investigating phenotypic plasticity due to toxicants with exposure disparities in primary human breast cells in vitro	INTRODUCTION: Breast cancer is the second most diagnosed cancer, as well as the primary cause of cancer death in women worldwide. Of the different breast cancer subtypes, triple-negative breast cancer (TNBC) is particularly aggressive and is associated with poor prognosis. Black women are two to three times more likely to be diagnosed with TNBC than white women. Recent experimental evidence suggests that breast like TNBC, may derive from luminal cells which acquire basal characteristics through phenotypic plasticity, a newly recognized hallmark of cancer. Whether chemical exposures can promote phenotypic plasticity in breast cells is poorly understood. METHODS: To investigate further, we developed a high-content immunofluorescence assay using normal human breast cells to screen chemical exposures can impact luminal/basal plasticity by unbiased quantification of keratin 14 (KRT14), a basal myoepithelial marker, keratin 8 (KRT8), a luminal epithelial marker, and Hoechst 33342, a DNA marker. We cell lines established from healthy tissue donors of different self-reported racial backgrounds, including Black (HBCS-2) and White (HBCS-1) women, and the TNBC cell line HCC1806. Cells were exposed to 0.1% DMSO, 10 μM BPA, and PFOS, with documented exposure disparities in US Black women, in triplicate. Automated fluorescence image quantification was performed using CellProfiler software, and a random forest classifier was trained to classify individual cells as KRT8 positive, KRT14 positive, or hybrid (both KRT8 and KRT14 positive) using CellProfiler Analyst. RESULTS: 70 AND CONCLUSIONS: Results demonstrated significant concentration-dependent increases in hybrid populations in response to BPA, BPS, DEE, and PFOA. The increase in hybrid populations representing both KRT14 and KRT8 is indicative of a phenotypically plastic progenitor-like population in line with known theories of carcinogenesis. Furthermore, BPA, BPS, DEE, and copper produced significant increases in cell proliferation, which could be indicative of a more malignant phenotype. These results further elucidate the relationship between chemical exposure and breast phenotypic plasticity and highlight potential environmental factors that may impact TNBC risk.	Front Oncol. 2024 Jun 10:14:1411295.	10.3389/fonc.2024.1411295	38915368	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1696	P. Šauer, H. Šanczuk, K. Grabicová, F. Gilardi Ayala, T. Machuka, V. Kubek, L. D. Blyth, L. B. Hennings, R. Grabic and H. Kocour Kroupová	2021	Bisphenols emerging in Norwegian and Czech aquatic environments show transthyretin binding potency and other less-studied endocrine-disrupting activities	Bisphenols are increasingly recognized as environmental pollutants with endocrine-disrupting potential. Nonetheless, the study of environmental occurrence and some endocrine-disrupting activities of some bisphenols were widely into focus of research only recently. The aims of the present study were to: 1) determine the predominant bisphenols in Norwegian sewage sludge and sediment and in Czech surface waters, and 2) characterize the binding of bisphenols to a transport protein transthyretin (TTR) and their (anti-)thyroid, (anti-)progestagenic, and (anti-)androgenic activities. High-performance liquid chromatography with atmospheric pressure chemical ionization or photoionization coupled to tandem mass spectrometry (HPLC-APCI/APPI-MS/MS) and Chemically Activated Luciferase gene eXpression (CALUX) in vitro reporter gene bioassays were used for the analyses of target bisphenols and their activities, respectively. Bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF) were the most frequently detected bisphenols in the Norwegian sewage sludge and sediment samples. Bisphenol compounds, in most last sewage sludge. Furthermore, bisphenol TBC (BPTBC) and bisphenol AF (BPAF) frequently occurred in sediment and surface waters, and were the most significant contributors to E of bisphenols in Norwegian sewage sludge with exception of one sample where BPF predominated. Ella also monitored a few bisphenols in sediment but only BPTBC was found. BPA, BPAF and BPF were the dominant bisphenols in Czech surface waters, and BPA was detected in all samples. Bisphenol TTR-binding potency (BPA > BPF > BPS) was somewhat displayed the following endocrine-disrupting activities: anti-thyroid (BPAF), anti-progestagenic (BPTBC > BPA > BPAF), and anti-androgenic (BPAF > BPF > BPA > BPTBC > BPF > BPS) in a noteworthy that BPAF exhibited strongest or similarly potent endocrine-disrupting activities compared to BPA. Our results provide new insights into these less- studied endocrine-disrupting activities of environmentally relevant bisphenols and may be useful in prioritizing these compounds that deserve further attention in environmental monitoring actions toxicological research.	Sci Total Environ. 2021 Jan 10:751:141801.	10.1016/j.scitotenv.2020.141801	32861950	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1697	A. Santovito, M. Lamberini and A. Nota	2024	In Vitro and In Vivo Genotoxicity of Polystyrene Microplastics: Evaluation of a Possible Synergistic Action with Bisphenol A	The ubiquitous presence of plastics represents a global threat for all ecosystems and human health. In this study, we evaluated, in vitro and in vivo, the genotoxic potential of different concentrations of polystyrene microplastics (PS-MPs) and bisphenol A (BPA), administered alone and in combination. The micronucleus assay was performed on human lymphocytes and on Vicia faba root tips. Results showed that PS-MPs induced genomic damage as revealed by the micronucleus assay, and the effect was dose-dependent. Moreover, BPA, at a low concentration (0.1 μg/mL), was not genotoxic when administered alone but showed a synergistic association with BPA (0.100 μg/mL) significantly increased the frequencies of micronuclei and nuclear buds, indicating a possible in vivo genotoxic additive action of these two compounds. Vice versa, PS-MPs, did not result in genotoxicity in hemocytes. Our results indicated that PS-MPs have genotoxic properties only in vitro and at a concentration of 100 μg/mL; moreover, this compound could intensify the genomic damage when mixed with BPA, indicating possible cumulative effects. Finally, PS significantly reduced the growth and the number of tail eggs in L. vaginalis.	J Xenobiot. 2024 Oct 8;14(4):1415-1431.	10.3390/jox14040079	39449420	in vitro	-	-	-	-	-	-	-	-	-	-	不明	1	0.100 μg/mL	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1698	C. Sang, Y. Song, T. W. Jin, S. Zhang, L. Fu, Y. Zhao, X. Zou, Z. Wang, H. Gao and S. Liu	2021	Bisphenol A induces ovarian cancer cell proliferation and metastasis through estrogen receptor-α pathways	Bisphenol A (BPA) is a widely used raw material that can be detected both in the environment and in the human body. Due to its estrogen-like effects, wide concerns have been raised about the potential risks of BPA to human health. However, the effects of BPA on ovarian cancer remain unclear. Here, we investigated the effects of BPA on ovarian cancer cell proliferation and metastasis and explored the underlying mechanisms. BPA, at concentrations as low as 10 nM, promoted cell proliferation and migration in ovarian cancer cells. We discovered that BPA can stimulate proliferation of OVCAR-3 ovarian cancer cells after exposure for up to 5 days. Strikingly, BPA enhanced ovarian cancer cell migration, invasion, and adhesion by vascular endothelial cells through upregulation of matrix metalloproteinase-2 (MMP-2). MMP-9, and vascular cell adhesion molecule-1 (VCAM-1). The stimulatory effects of BPA on cancer cell proliferation and metastasis were reversed by treatment with an ERα inhibitor, but not by treatment with an ERβ inhibitor. Together, these results suggest that BPA induces proliferation and metastasis of ovarian cancer cells through an ERα signaling pathway. This study provides new insights into the carcinogenic effects of BPA with regard to ovarian cancer.	Environ Sci Pollut Res Int. 2021 Jul;28(27):36060-36068.	10.1007/s11356-021-13267-0	33683587	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1699	D. Samardžija Nenadov, B. Tesic, S. Fa, K. Pogrmic-Majkic, D. Kokai, B. Stanic and N. Andric	2022	Long-term in vitro exposure of human granulosa cells to the mixture of endocrine disrupting chemicals found in human follicular fluid disrupts steroidogenesis	Most in vitro studies examine the effects of a single EDC or a mixture of EDCs on granulosa cells using short-term exposure; however, this approach is unlikely to reflect long-term, real-life exposures that are common to humans. We established an in vitro model that mimics long-term exposure of granulosa cells to real-life EDC mixture. Human granulosa cells, HGrC1, were exposed to the mixture consisting of bisphenol A, polychlorinated biphenyl 153, dichlorodiphenyltrichloroethane, and dichlorodiphenyldichloroethylene (BPA, PCB153, DDT, and DDE, respectively) at concentrations found in human follicular fluid for 7 days (short-term) and 30 days (long-term). Cell viability, steroid hormone levels, and CYP19A1 protein after 3 weeks of exposure. By week 4, the cells restored estradiol production and CYP19A1 protein level. BPA increased basal progesterone production after 3 and 4 weeks of exposure but not after STAR and CYP11A1 mRNA. Cells that had been exposed to MIX for 3 weeks showed augmentation of forskolin-stimulated progesterone production. These results demonstrate that only long-term exposure to MIX alters steroidogenesis in HGrC1. This study also revealed that adverse effects of MIX on steroidogenesis in HGrC1 occurred a few weeks into MIX exposure and that this effect can be transient.	Toxicol In Vitro. 2022 Mar:79:105302.	10.1016/j.tiv.2021.105302	34929288	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1700	A. Sarkhoush, F. Shidfar, M. Hedayati, A. Reeskatibni Tahvari, A. A. Farshad and S. Mohammadi	2020	Bisphenol A enhances adipogenic signaling pathways in human mesenchymal stem cells	BACKGROUND: The endocrine disruptor Bisphenol A (BPA), has been involved in dysregulating adipose tissue development and increasing the risk of obesity. The objective of this experiment was to investigate whether treatment of human mesenchymal stem cells with BPA could modulate adipogenesis and adipocyte differentiation. METHODS: In this experimental study, the human adipose derived mesenchymal stem cells (hADSCs) were treated with BPA (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM, 10 μM, 100 μM) and differentiated into adipocytes. Oil Red O staining was used to measure the lipid droplets. Levels of key adipogenic transcription factors and proteins, we used Quantitative real-time polymerase chain reaction (qRT-PCR) and ELISA. RESULTS: The results presented a dose dependent triglyceride accumulation in treated cells with BPA. Additionally, we observed that BPA induced transcription of the Peroxisome proliferator-activated receptor gamma (PPARγ), CCAAT/ enhancer-binding protein alpha (C/EBPα), CCAAT/ enhancer-binding protein beta (C/EBPβ), sterol regulatory element-binding protein 1c (SREBP1c), Fatty acid synthase (FASN), and Lipoprotein lipase (LPL). BPA augmented the expression of Fatty acid binding protein 4 (FABP4) and Estrogen receptor beta (ERβ). CONCLUSIONS: Our findings, supported the hypothesis that BPA enhances adipogenic differentiation thereby may play a role in development of obesity and disregulation of metabolic homeostasis.	Genes Environ. 2020 Mar 11;42:13.	10.1186/s41021-020-00150-6	32175033	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	0(-10)、10(-8) M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1701	A. Sarkhoush, F. Shidfar, M. Hedayati, A. A. Farshad, A. N. Tahvari and S. Mohammadi	2021	Molecular mechanisms of vitamin D plus Bisphenol A effects on adipogenesis in human adipose-derived mesenchymal stem cells	BACKGROUNDS: Obesity is considered a major health concern and mounting evidence suggests that the exposure to environmental endocrine disruptors, including Bisphenol A (BPA), may enhance the risk to develop the disease. Moreover, growing documents propose that the vitamin D may contribute to adipogenic signaling and lipid accumulation during adipocyte differentiation. We focused on the molecular mechanism of vitamin D and BPA in human adipose-derived mesenchymal stem cells (hADSCs) which vitamin D and BPA may influence adipose tissue development and function. METHODS: Human adipose-derived mesenchymal stem cells were treated with BPA (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM, 10 μM, 100 μM) and differentiated into adipocytes. Oil Red O staining was used to measure the lipid droplets. Levels of key adipogenic transcription factors and proteins, we used Quantitative real-time polymerase chain reaction (qRT-PCR) and ELISA. RESULTS: The results presented a dose dependent triglyceride accumulation in treated cells with BPA. Additionally, we observed that BPA induced transcription of the Peroxisome proliferator-activated receptor gamma (PPARγ), CCAAT/ enhancer-binding protein alpha (C/EBPα), CCAAT/ enhancer-binding protein beta (C/EBPβ), sterol regulatory element-binding protein 1c (SREBP1c), Fatty acid synthase (FASN), and Lipoprotein lipase (LPL). BPA augmented the expression of Fatty acid binding protein 4 (FABP4) and Estrogen receptor beta (ERβ). CONCLUSIONS: Our findings, supported the hypothesis that BPA enhances adipogenic differentiation thereby may play a role in development of obesity and disregulation of metabolic homeostasis.	Diabetol Metab Syndr. 2021 Apr 9;13(1):41.	10.1186/s13098-021-00661-4	33836827	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	不明	0	0.1、10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1702	A. C. Saleh, R. Sabry, G. F. Mastromonaco and L. A. Favetta	2021	BPA and BPS affect the expression of anti-Mullerian hormone (AMH) and its receptor during bovine oocyte maturation and early embryo development	BACKGROUND: Exposure to endocrine disrupting chemicals, such as Bisphenol A (BPA) and Bisphenol S (BPS), is widespread and has negative implications on embryonic development. Preliminary evidence revealed that in women undergoing IVF treatment, urinary BPA levels were associated with low serum anti-Mullerian hormone, however a definitive relationship between the two has not yet been characterized. METHODS: This study investigated the effects of BPA and BPS exposure during bovine oocyte maturation on the expression of AMH and its receptor (AMHR2) in cumulus cells and oocytes, as well as investigation of developmental parameters, such as cleavage, blastocyst rate and developmental rates. 1) detection of apoptosis and 2) assessment of possible serum rescue. As in vitro bovine model was used as a translational model for human early embryonic development. We first assessed BAM- and AMHR2 levels after bisphenol exposure during oocyte maturation. Zygotes were also analyzed during cleavage and blastocysts stages. Techniques used include in vitro fertilization, quantitative polymerase chain reaction (qPCR), western blotting, TUNEL, and immunofluorescence. RESULTS: Our findings revealed that significantly increased cleavage (n = 2,021), blastocyst (p = 0.008) and overall developmental rates as well as significantly increased embryonic arrest at the 2-4 cell stage (p = 0.05). Additionally, both BPA and BPS significantly increased DNA damage in cumulus cells (p = 0.05) and oocytes (p = 0.05). Moreover, both BPA and BPS affected AMH and AMHR2 protein level in both oocytes and blastocysts. BPA, but not BPS, also significantly altered serum ratios in early female blastocysts (p = 0.05, CONCLUSIONS: This study shows that BPA affects AMH and AMHR expression during oocyte maturation and that BPA exerts its effects in a greater extent after fertilization and therefore may not be a safer alternative to BPA. Our data lay the foundation to future functional studies, such as receptor kinetics, downstream effectors, and potential use of select inhibitors to prove a functional relationship between bisphenols and the AMH-signaling system.	Reprod Biol Endocrinol. 2021 Aug 3;19(1):119.	10.1186/s12958-021-00773-6	34344364	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1703	R. Sabry, M. Williams, N. Werry, J. LaMarre and L. A. Favetta	2022	BPA Decreases PDCD4 in Bovine Granulosa Cells Independently of miR-21 Inhibition	microRNAs (miRNAs) are susceptible to environmental factors that might affect cellular function and impair negative effects on female reproduction. miR-21 is the most abundant miRNA in bovine granulosa cells and is widely reported as affected by Bisphenol A (BPA) exposure, yet the cause and consequences are not entirely elucidated. BPA is a synthetic endocrine disruptor associated with poor fertility. miR-21 function in bovine granulosa cells is investigated utilizing locked nucleic acid (LNA) oligonucleotides: a sponge, miR-21 inhibitor, and a mimic. Before measuring apoptosis and quantifying miR-21 apoptotic targets PDCD4, transfection was optimized and validated. BPA was introduced to see how it affects miR-21 regulation and which BPA-mediated effects are influenced by miR-21. miR-21 knockdown and specificity against additional miRNAs were confirmed, with miR-21 and PDCD4 being the most affected by miR-21 inhibition. Knockdown of miR-21 increased PDCD4 and CASP3 and 7 activity, and BPA exposure increased PDCD4 protein level in both oocytes and blastocysts. BPA, but not BPS, also significantly altered serum ratios in early female blastocysts (p = 0.05, CONCLUSIONS: This study shows that BPA affects AMH and AMHR expression during oocyte maturation and that BPA exerts its effects in a greater extent after fertilization and therefore may not be a safer alternative to BPA. Our data lay the foundation to future functional studies, such as receptor kinetics, downstream effectors, and potential use of select inhibitors to prove a functional relationship between bisphenols and the AMH-signaling system.	Int J Mol Sci. 2022 Jul 27;23(15):8276.	10.3390/ijms23158276	35954412	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1704	R. Sabry, M. Williams, J. LaMarre and L. A. Favetta	2023	Granulosa cells undergo BPA-induced apoptosis in a miR-21-independent manner	Bisphenol A (BPA) is a harmful endocrine disrupting compound that alters not only classical cellular mechanisms but also epigenetic mechanisms. Evidence suggests that BPA induced changes in microRNA expression, specifically miR-21, are the main factor in a BPA toxicity model in bovine granulosa cells. miR-21 is a well-studied miRNA that is highly expressed in granulosa cells and is a crucial anti-apoptotic regulator in GCs, yet the main factor in a BPA toxicity model remains unclear. BPA can heavily induce bovine GC apoptosis through the activation of caspase 3 and 7 activity. BPA, which has low cytotoxicity in GC cells results, increased late apoptotic/necrotic, increased apoptotic transcripts (BAX, BAD, BCL-2, CASP-9, HRTR1), increased the BAX/Bcl-2 ratio and HRTR1at the protein level, and reduced caspase 9 activity at 10 µM exposure. miR-21 inhibition increased early apoptosis and, while it did not influence transcript levels or caspase 9 activity, it did elevate the BAX/Bcl-2 protein ratio and HRTR1at the protein marker in BPA. Overall, this study shows that miR-21 plays a molecular role in regulating intrinsic mitochondrial apoptosis; however, miR-21 inhibition did not make the cells more sensitive to BPA. Therefore, apoptosis induced by BPA in bovine GCs is miR-21-independent.	Exp Cell Res. 2023 Jun 1;427(1):113574.	10.1016/j.yexcr.2023.113574	37004947	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1705	R. Sabry, A. C. Saleh, L. Stalker, J. LaMarre and L. A. Favetta	2021	Effects of bisphenol A and bisphenol S on microRNA expression during bovine (Bos taurus) oocyte maturation and early embryo development	Bisphenol A (BPA) and its alternative, bisphenol S (BPS), are widespread endocrine disrupting compounds linked in several studies to poor female fertility. Sufficient oocyte competence and subsequent embryo development are highly dependent on oocyte maturation, an intricate process that is detrimentally affected by BPA. The adverse effects are, as well as the effects of its analog, BPS, have not been fully elucidated. Although the harmful consequences of bisphenols on the reproductive system are largely due to interference with canonical gene expression, more recent evidence implicates noncoding RNAs, including microRNAs (miRNA), as significant mediators of bisphenol toxicity. Therefore, the objective of this study was to investigate the impact of BPA and BPS exposure during oocyte maturation on miRNA expression in bovine cumulus cells. qPCR primers and mature forms of miR-21, -191, -31a, -29a, -10b, -148a were quantified in an in vitro bovine model of matured cumulus-oocyte complexes, fertilized embryos, and cultured cumulus cells after exposure to BPA or BPS at low (LOEL dose (0.08 mg/mL). Expression of miR-21, -191, -31, and -10b are more readily increased (P < 0.02, 0.01, <0.0001) cells with 3h and 48h time exposed (P < 0.01, 0.01, after BPA treatment, miR-148a expression remained stable. BPS had no effects, suggesting may not exert its actions through these or miRNAs examined. Overall, this study indicates that BPA affects are likely miRNA-specific rather than a global effect on miRNA synthesis and processing mechanisms and that its analog, BPS, may not possess the same properties required to interfere with these miRNAs during bovine oocyte maturation.	Reprod Toxicol Vol.99 Pages 96-108	10.1016/j.reprotox.2020.12.001	33285269	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	0.05 mg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1706	R. Sabry, M. Nguyen, S. Younes and L. A. Favetta	2022	BPA and its analogs increase oxidative stress levels in in vitro cultured granulosa cells by altering anti-oxidant enzymes expression	Bisphenol A is a widespread endocrine disruptor with numerous effects on reproductive functions. Limitations on BPA in manufacturing has prompted the use of analogs, such as BPS and BPF, with limited research on their effects. Oxidative stress is a significant mechanism of BPA toxicity in granulosa cells (GCs), however, the impact of BPA analogs on oxidative stress has not been previously investigated. Therefore, both BPA and BPF status will validate and induce mitochondrial dysfunction and cell-free bisphenols increased production of reactive oxygen species as early as 24hrs post exposure (P< 0.05 for both). Bisphenols at 10hrs at the mRNA and protein levels, while these results were not significant at 48hrs. These results together suggest that BPA and its analogs can induce oxidative stress in this bovine granulosa cells, although not necessarily through common mechanisms. Therefore, the use of BPA analogs may have to be re-considered.	Mol Cell Endocrinol. 2022 Apr 5:545:111574.	10.1016/j.mce.2022.111574	35065199	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1707	R. Sabry, D. R. May and L. A. Favetta	2023	The relationship between miR-21, DNA methylation, and bisphenol a in bovine COCs and granulosa cells	Introduction: miR-21 is a critical microRNA for the regulation of various processes in oocytes and granulosa cells. It is involved in the modulation of apoptosis and can influence other epigenetic mechanisms. Among these mechanisms, DNA methylation holds significant importance, particularly during female gametogenesis. Evidence has demonstrated that microRNAs, including miR-21, can regulate DNA methylation. Bisphenol A (BPA) is a widespread chemical that disrupts oocyte maturation and granulosa cell function. Recent findings suggested that BPA can act through epigenetic pathways, including DNA methylation and microRNAs. Methods: This study took aim at miR-21-136s to explore the involvement of miR-21 in the regulation of DNA methylation in bovine Cumulus Oocyte Complexes (COCs) and granulosa cells, in the presence and absence of BPA. This study also investigated the impact of BPA exposure on the expression of DNA methyltransferases (DNMT1 and DNMT3A) and ten-eleven translocation methylcytosine dioxygenase 1 (TET1) in COCs, which could be attributed to a decrease in the methylating enzymes DNMT1 and DNMT3A, and an increase in the demethylating enzyme TET1. We observed a significant increase in the protein levels of DNMT1, DNMT3A, and TET1 upon inhibition of miR-21 in both COCs and granulosa cells. These findings directly imply a strong correlation between miR-21 signaling and the regulation of DNA methylation in bovine COCs and granulosa cells under BPA exposure.	Front Cell Dev Biol. 2023 Nov 15:11:1294541.	10.3389/fcell.2023.1294541	38033863	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1708	R. Sabry, C. Agyo, J. A. Rehn-Saunders, A. C. Saleh, S. Balachandran, E. J. St. John and L. A. Favetta	2021	BPA and BPS Affect Connexin 37 in Bovine Cumulus Cells	Bisphenol S (BPS) is used as an alternative plasticizer to Bisphenol A (BPA), despite limited knowledge of potential adverse effects. BPA exhibits endocrine disrupting effects during development. This article focuses on the impact of bisphenols during oocyte maturation. Connexins (Cx) are gap junctional proteins that may be affected by bisphenols, providing insight into their mechanism during development. Cx-37 and Cx-43 are crucial in facilitating cell communication between cumulus cells and oocytes. Cumulus oocyte complexes (COCs), denuded oocytes, and cumulus cells were exposed to 0.05 mg/mL BPA or BPS for 24 h. Both compounds had no effect on oocyte maturation, fertilization, or blastocyst development. However, BPA significantly increased the transcript abundance of Cx-37 in cumulus cells, while BPS significantly increased Cx-43. Cx-37 was localized to cell–cell contact points between cumulus cells and oocytes in COCs, while Cx-43 was observed in cytoplasmic projections. Cx-37 was also found in cumulus cells, obtained by stripping germinal vesicle oocytes, and was significantly increased upon exposure to BPA, but not the BPS. Investigations revealed that BPA significantly increased Cx37 protein expression, while BPS did not. Disrupted Cx37 following BPA exposure provides an indication of possible effects of bisphenols on connexins during the early stages of development.	Genes (Basel) Vol.12 Issue 2	10.3390/genes12020321	33672423	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	0.05 mg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1709	I. Sabovic, L. De Toni, A. Di Nisio, C. M. Radu, D. Gatidisi, S. De Martin and A. Ferlin	2025	Additive effect of Bisphenol A and Perfluoro-sulphoctanoic acid exposure at subacute toxic levels, on a murine model of sertoli cell	PURPOSE: Endocrine disruptors, (EDs) interfere with the endocrine system leading to health consequences and reproductive derangements. Most EDs are environmental pollutants whose risk evaluation is hampered by the simultaneous exposure to a number of chemicals. Here we investigated the possible mechanistic involvement of Sertoli cells, the nurse cell population in the seminiferous tubule, in the reproductive toxicity of Bisphenol A (BPA) and perfluoro-octane sulphonate (PFOS), two acknowledged EDs, at recognized subacute toxic levels. METHODS: Mouse Sertoli cell line TM4 were exposed for 24 h to 40 ng/mL BPA or 30 ng/mL PFOS or their combination. Cell viability was assessed by MTT assay, cell cycle progression by propidium iodide staining and flow cytometry, and apoptosis by Annexin V staining. Gene expression was compared via RT-qPCR. RESULTS: BPA, PFOS, and their combination (BPA + PFOS) all significantly reduced TM4 cell viability (p < 0.001), with compound exposure causing the greatest decline (BPA: 79.1 ± 3.5%; PFOS: 78.8 ± 7.9%; combined: 59.2 ± 7.9%), showed reduced survival rate (F = 10.61 vs. control). The exposure to the mixture of BPA and PFOS was associated with a further reduction of cell number (50.9 ± 7.2%, P < 0.001 vs. control) and an increase of the percentage of apoptotic cells (13.7 ± 0.8% control, 48.3 ± 13.6% BPA, 59.9 ± 28.7 + 9.6%, 87.1 ± 19.8% BPA + PFOS; P < 0.001 vs. control; P < 0.027 vs. BPA). The exposure to the combination of BPA and PFOS was associated with the signaling pathway activation and with the downstream caspase 3 cleavage. In addition, the exposure to the combination of BPA and PFOS was associated with IGF-1 dysfunction and increased expression of Fas. CONCLUSION: Subacute toxic levels of BPA and PFOS display additive effects on Sertoli cell apoptosis with the possible involvement of Fas- dependent germinal apoptosis.	J Endocrinol Invest Vol.48 Issue 4 Pages 951-958	10.1007/s40618-024-02498-w	39556264	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	40 ng/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1710	D. Y. Ryu, W. K. Pang, M. S. Rahman, Y. J. Park and M. G. Pang	2025	Differential susceptibility of Leydig and Sertoli cells to bisphenol A	Bisphenol A (BPA) is an endocrine-disrupting chemical that is increasingly becoming a vital factor in public health due to its ubiquity and toxicity. BPA is associated with male infertility via the disrupted function of Leydig and Sertoli cells. Despite extensive research, the current understanding of the specific pathological concentrations and the mechanisms following BPA exposure still remain questionable. Therefore, we investigated the concentration-dependent effects of BPA on Leydig and Sertoli cells. TM3 and TM4 cells were exposed to BPA (0.1 nM–100 μM) for 24 h. BPA at 10 μM and 100 μM significantly decreased the cell viability and increased mitochondrial membrane potential and ATP levels. In contrast, ROS levels were increased at high BPA levels, regardless of exposure time (10 or 100 μM). Both cell lines showed mitochondrial apoptosis, but identified along with increased ROS levels, and abnormal mitochondrial dynamics, but both cell types showed different susceptibility to BPA toxicity. Subsequently, BPA had detrimental impacts on the mRNA expression levels of steroidogenic enzymes and testosterone synthesis in Leydig cells and reduced anchoring junction proteins in Sertoli cells. Consequently, our results demonstrated that both cells were affected via estrogen receptor alpha. However, protein kinase A was especially expressed following BPA exposure in each cell type. Therefore, it is plausible to suggest that each cell has distinct sensitivities and mechanisms in response to BPA.	Toxicology. 2025 Sep:516:154182.	10.1016/j.tox.2025.154182	40349747	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	0.0001～100μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1711	D. Ryczawy, M. Pudełek, P. Kucharowski, N. Jarik-Olchawa, J. Bogucki, M. Bigaała, P. Kocyła-Karaś, J. Mikołajczyk, I. Bonik, S. Kędracka-Krok, E. Karnas, E. Zuba-Surma, Z. Madeja and J. Czyż	2020	High bisphenol A concentrations augment the invasiveness of tumor cells through Snail-1/Cx43/ERK-dependent epithelial-mesenchymal transition	Bisphenol A (BPA) is commonly present in plastics used for food storage and preservation. The release of BPA from these products results in a permanent human exposition to BPA however, the quality and quantity of BPA adverse effects remain a matter of controversy. The common presence of BPA in the human environment and the controversies concerning the relations of human exposition to BPA and cancer incidence justify the need for the investigation of BPA influence on cancer cells behavior. Here, we show that BPA, at concentrations ranging from 10 nM to 100 μM, induces epithelial-mesenchymal transition (EMT) in the human prostate cancer cells (PC3), the human breast cancer cells (MDA-MB-231), and the normal epithelial cells of mammary gland (NMuMG). BPA-induced EMT was characterized by morphologic changes, E/N-cadherin switch and shorter/slower Snail-1/Lysine-rich CAS1 gene regulation in A549 populations. It was followed by enhancement of 3D/2D-shape resistance. Corresponding effects of BPA were observed in prostate cancer cell populations. Concomitantly, we observed increased levels and perinuclear accumulation of estrogen receptor alpha (ERα) in BPA-treated cells, its interactions with Cx43/Snail-1, and the corresponding effects of phenol red and ERα cells. Collectively, these data identify a novel, pro-metastatic Snail-1/Cx43/ERK-signaling pathway. Its reactivity to BPA underlies the induction of cancer cells' invasiveness in the presence of high BPA concentrations in vitro. Thus, the chronic exposition of cancer cells to endocrine and intrinsic BPA should be considered as a potential obstacle in a cancer therapy.	Toxicol In Vitro. 2020 Feb:62:104676.	10.1016/j.tiv.2019.104676	31629898	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	0	10 - 100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1712	K. Rybczyńska-Tkaczyk, B. Skóra and K. A. Szychowski	2023	Toxicity of bisphenol A (BPA) and its derivatives in divers biological models with the assessment of molecular mechanisms of toxicity	The aim of the study was to determine toxicity of bisphenol A (BPA) and its derivatives (bisphenol S (BPS), bisphenol F (BPF), and tetrabromobisphenol A (TBBPA)) due to its high accumulation in environment. The performed analysis revealed the toxicity of the BPA, BPF, and BPS against Aurelia aurita, Nitrobacterium sp., and Brachionus diversicornis as the most sensitive, reaching microbial toxic concentrations in the range of 0.004-0.081 mg · L-1). Moreover, the genotoxicity assay shows the ability of all tested compounds to increase in the γ-galactosidase level at the concentration range 7.81-500 μM (Escherichia coli, PQ37). In turn, BPA and its derivatives (BPS, BPF, and TBBPA) in the concentration range 0.1-100 μM showed the ability to induce ROS production in the human cell lines (HepG2, HaCaT, and A549). The IC50 values were in the range 1.1-2 mM (HepG2), 0.2-1.1 mM (HaCaT), and 0.1-1.1 mM (A549). Moreover, BPA, BPS, and TBBPA, in the concentration range 0.1-100 μM, significantly increased the activity of caspase 3/7, 8, and 9 in the human cell lines (HepG2, HaCaT, and A549). Additionally, BPA, BPS, and TBBPA significantly decrease the metabolic activity of human keratinocytes. In vitro after 24 h of treatment at the mitochondrial concentrations. Similarly, the impact of the certain bisphenols on proliferation', apoptosis and inflammation-related mRNA expression was shown to toward cell line. Summarizing, the presented results have proved that BPA and its derivatives are able to show high negative effect on certain living organism, such as bacteria, plants, and human cells, which is strict related to per-apoptotic and genotoxic mechanism of action.	Environ Sci Pollut Res Int. 2023 Jun;30(30):75126-75140.	10.1007/s11356-023-27747-y	37213006	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	1	1	7.81～500 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1713	C. Russo, A. Maugeri, A. Albergamo, G. Dugo, M. Navarra and S. Cirmi	2023	Protective Effects of a Red Grape Juice Extract against Bisphenol A-Induced Toxicity in Human Umbilical Vein Endothelial Cells	Human exposure to bisphenol A (BPA) occurs through the ingestion of contaminated food and water, thus leading to endothelial dysfunction, the first signal of atherosclerosis. This in vitro s...tyrosol juice to antioxidant activity, polyphenol content, and cytoprotective effects against BPA-induced damage in human umbilical vein endothelial cells (HUVECs). Cell viability, oxidative stress, endothelial damage induced by BPA in human umbilical vein endothelial cells (HUVECs) as an in vitro model of endothelial dysfunction. Our results showed that RGJe treatment counteracted BPA-induced cell death and apoptosis in HUVECs, blocking caspase-3 and modulating p53, Bax, and Bcl-2. Moreover, RGJe demonstrated antioxidant properties in abiotic tests and in vitro, where it reduced BPA-induced reactive oxygen species as well as restored mitochondrial membrane potential, DNA integrity, and nitric oxide levels. Furthermore, RGJe reduced the increase of chemokines (IL-8 & -12, and MCP-1) and adhesion molecules (VCAM-1, ICAM-1, and P-selectin), along with preventing cells, owing to its antioxidant capability.	Toxics. 2023 Apr 21;11(4):391.	10.3390/toxics11040391	37112618	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1714	S. Ruberto, A. Santiello, E. R. Simula, M. Noli, M. A. Manca and L. A. Sechi	2022	Bisphenols induce human genomic damage and modulate HERVs/env expression	Bisphenol A (BPA), a recognized endocrine-disrupting chemical, is used in the production of epoxy and polycarbonate resins. Short-term exposure to BPA has been associated with increased cancer susceptibility, the reason has shifted to products often labelled as "BPA free" containing BPA analogs such as bisphenol F (BPF) and bisphenol S (BPS). However, the Europeanlegislation on BPF and BPS is still unclear. This study investigated the effects of BPA, BPF, and BPS exposure on human peripheral blood mononuclear cells by using in vitro micronucleus assay. Furthermore, it investigated the impact of bisphenols exposure on human endogenous retroviruses (HERVs) expression, which is implicated with the pathogenesis of several human diseases. The micronucleus assay revealed a significant genotoxic effect in peripheral blood cells after exposure to BPA and BPF at concentrations of 0.1, 0.05, and 0.025 μg/ml, and to BPS at 0.1 and 0.05 μg/ml. In addition, BPA exposure seems to upregulate the expression of HERVs, while a downregulation was observed after BPF and BPS treatments. Overall, our data showed the toxic effect of BPA and its analogs on circulating cells in the blood and demonstrated that they could modulate the HERVs expression.	Environ Mol Mutagen. 2022 Jul;63(6):275-285.	10.1002/em.22499	36054626	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	0.1、0.05、0.025 μg/ml	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1715	N. Roy, C. Lazzaretti, E. Paradisi, C. Capponi, T. Ferrari, F. Reggianini, S. Spendiani, L. Bacchini, E. Mazzolo, C. Pierri, M. Varani, G. Caru, T. Trenti, A. Nicoli, D. Morini, F. Iannotti, M. T. Villani, E. Vicini, M. Simoni and L. Casarini	2023	Short-Term Exposure to Bisphenol A Does Not Impact Gonadal Cell Steroidogenesis In Vitro	Bisphenol A (BPA) is a ubiquitous, synthetic chemical present in indoor reproductive disorders, in both men and women. The available studies investigated the effects of BPA on male and female steroidogenesis following long-term exposure, but the consequences of short-term exposure remain unclear. Here, we investigated the effects of 24 h exposure to BPA (0.1 nM–1 µM) on steroidogenesis in human granulosa (KGN), Leydig (hLEY), and Sertoli (hSER) cells. BPA (1 µM) mediated signalling in only steroidogenic cell models, i.e., the mixed tumour Leydig cell line hLEY, and human primary granulosa (cells cultured in SHG-21). Cell signalling studies were performed using a homogeneous time-resolved fluorescence (HTRF) assay and Western blotting, while gene expression analysis was carried out using real-time PCR. Immunocytochemistry and an immunoassay were used for steroidogenic enzyme expression and steroidogenesis analysis, respectively. The presence of BPA levels in no significant alteration in basal cAMP accumulation, alongside phosphorylation of downstream molecules, such as ERK1/2, CREB and pGSK3ß/ß, in both the cell models. BPA did not impact STAR81, CYP11A1 and CYP19A1 gene expression in hLEC, nor StAR and Cyp11A1 expression in the TCS treated with LH/hCG. Similarly, only the hLEY cells showed a significant increase in the ERß/ERα expression ratio, as no changes were observed in the cellular medium, measured by hGL5, as well as the involvement of the progesterone levels. In the culture medium, measured by mS, TCS, did not change in the presence of BPA combined with LH/hCG. These data suggest that short-term exposure to environmental concentrations of BPA does not compromise the LH/hCG-induced steroidogenic potential of either human granulosa or mature Leydig cells.	Cells. 2023 Jun 2;12(11):1537.	10.3390/cells12111537	37296657	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1 nM、1 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1716	V. Rossio and J. A. Paulo	2025	Comprehensive Analysis of the Proteome of S. cerevisiae Wild-Type and pdr5Δ Cells in Response to Bisphenol A (BPA) Exposure	Bisphenol A, an endocrine-disrupting compound, is widely used in the industrial production of plastic products. Despite increasing concerns about its harmful effects, on human health, animals, and the environment, the use of BPA has been banned only in infant products, and its effects on cellular processes are not fully understood. To investigate the impact of BPA on eukaryotic cells, we analyzed the proteome changes of wild-type and PDR5-deleted S. cerevisiae strains exposed to different doses of BPA using sample multiplexing based on isobaric tags for relative and absolute quantitation (iTRAQ). We found that the ABC multidrug transporter Pdr5 plays an important role in protecting yeast cells from BPA toxicity, with its absence significantly sensitizing cells to BPA. BPA inhibited yeast growth in a dose-dependent manner, with a more pronounced effect in PDR5-deleted cells. Proteomic analysis revealed that BPA exposure induced significant changes in the abundance of proteins involved in key cellular processes, including metabolism, stress response, and protein synthesis. Pdr5 deletion amplified the observed markers of cellular stress induced by BPA by identifying multiple stress-induced proteins that were upregulated by this compound. As cellular processes affected by BPA have been shown to be evolutionarily conserved, these insights can advance our understanding of BPA's cellular impact and its broader effects on human health.	Microorganisms. 2025 Jan 8;13(1):114.	10.3390/microorganisms13010114	39858881	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1717	G. Rossi, B. Dufrusine, A. R. Lizzi, C. Luzi, A. Piccoli, F. Fezza, R. Iorio, G. D'Andrea, E. Dainese, S. Cecconi and M. Maccarrone	2020	Bisphenol A Deranges the Endocannabinoid System of Primary Sertoli Cells with an Impact on Inhibin B Production	Bisphenol A (BPA) is an endocrine disruptor that negatively affects spermatogenesis, a process where Sertoli cells play a central role. Thus, in the present study we sought to ascertain whether BPA could modulate the endocannabinoid system (ECS) in primary Sertoli cells (pSCs) isolated from 20-day-old rats. Exposure of pSCs to BPA (0.5 μM) for 24 h increased the activity and expression of diacylglycerol lipase α (DAGLα), the enzyme responsible for the biosynthesis of 2-arachidonoylglycerol (2-AG), but not of its degrading enzyme monoacylglycerol lipase (MAGL). Exposure of the pSCs to BPA for 48 h increased the expression levels of cannabinoid receptor type 1 (CB1), but not of CB2, transient receptor potential cation channel subfamily V member 1 (TRPV1) receptors, and GPR55. Of note, BPA treatment also significantly increased the production of inhibin B, but not that of testosterone, and blockade of either CB1 receptors or TRPV1 receptor further enhanced the BPA effect. Altogether, our study provides unprecedented evidence that BPA deranges the ECS system of Sertoli cells towards CB1R- and TRPV1-dependent signal transduction, both receptors being engaged in modulating BPA effects on inhibin B production. These findings add CB1R and TRPV1 receptors, and hence the eCB signaling, to the other molecular targets of BPA already known in mammalian cells.	Int J Mol Sci Vol.21 Issue 23	10.3390/ijms21238986	33256105	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.5 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1718	T. Rosenberger, A. M. Bell, G. Reifferscheid, K. E. C. Smith, A. Schäffer, T. A. Ternes and S. Buchinger	2024	Extrapolation of cytotoxic masked effects in planar in vitro assays	The masking of specific effects in in vitro assays by cytotoxicity is a commonly known phenomenon. This may result in a partial or complete loss of effect signals. For a common in vitro assays, approaches for identifying and mathematically correcting masked effects have been developed and published. Planar chromatography in combination with effect-directed analysis (EDA) is a powerful tool for the effect-directed chromatography with in vitro assays, such as the planar yeast estrogen screen (p-YES), might allow for a powerful identification of cytotoxically-affected signals. Affected signals have to be corrected for cytotoxicity in order to achieve a reasonable and consistently ranking onto their results. For double-peak chromatogram. This study investigates whether these double-peaks can be used for fitting a peak function to extrapolate the theoretical, unaffected signals. The function of the modelling was evaluated for four model peak functions, using EC data2, unaffected peaks from estrogenic model compounds in the p-YES. Modelled EC50 values from fitted peaks of BPA's experiments with cytotoxically disturbed signals were 2.5 times higher than for the apparent data without compensation for cytotoxicity (326 ± 42 ng extract/well vs. 131 ± 17 ng). This finding has a high relevance for the modelling of mixture effects in effect-directed analysis (EDA) and the identification of effect drivers in complex samples. Furthermore, the fitting approach enables the quantitative evaluation of cytotoxically-affected signals in planar in vitro assays and enriches applications for other fields of chemical analysis like elemental chromatography/signals.	Anal Bioanal Chem. 2024 Jun;416(15):3519-3532.	10.1007/s00216-024-05302-z	38656365	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1719	C. C. S. Rocha, C. A. Sanchez, M. C. G. Souza, E. M. Trevisiq, G. H. Sevilotto, P. P. Devoz, L. V. P. de Freitas, L. M. G. Antunes, J. A. R. Paschoal and F. B. Junior	2025	Polystyrene nanoplastic co-exposed to BPA and BPS induces cytotoxicity, genotoxicity, and alters ROS production in HepG2 cells	During plastic degradation, it is fragmented into micro and nanoplastic, which can attach contaminants from the environment, increasing the plastics toxicity. Bisphenol A is used in plastic production and can be an endocrine disruptor. Bisphenol S is an analog of bisphenol A and has been used as an alternative in "BPA free" products. Therefore, this is the first research proposing to verify whether nanoplastics associated with bisphenol A or S can increase toxicity in HepG2 cells. Nanoplastics associated with bisphenols could alter the cell viability of HepG2 cells compared to the group treated with the nanoplastic at the lowest concentration. This study highlights the cytotoxicity and genotoxicity of nanoplastics and bisphenols A and S, providing new insights into hepatocyte toxicity.	Toxicol In Vitro. 2025 Dec:109:106121.	10.1016/j.tiv.2025.106121	40706907	in vitro	-	-	-	-	-	-	-	-	-	-	不明	1	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1720	R. A. Rifa, M. G. Rojo and R. Lavado	2025	Mechanisms of toxicity caused by bisphenol analogs in human in vitro cell models	Bisphenol analogs, structurally similar to bisphenol A (BPA), are widely used in various industries as a safer alternative to BPA. However, these alternatives also present risks, such as inflammation and potential carcinogenicity. This study aimed to evaluate the cytotoxic effects of BPA, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), bisphenol B (BPB), and bisphenol AP (BPAP), bisphenol E (BPE) in eight different relevant human in vitro cell models: liver (HepaRG), intestinal (Caco-2), breast (T47D), brain (SH-SY5Y), lung (A549), kidney (HEK293), endothelial (HMEC-1), and skin (HEK-001) cell lines. BPE manifested the highest cytotoxicity in Caco-2 cells, presenting an EC50 value of roughly 0.2 µM (95% confidence interval). In contrast, HEK293 and HepaRG cells demonstrated significant resilience to BPE (EC50 > 1000 µM). BPAF, BPAP, BPF, and BPAP had consistently low EC50 values across cell lines (5–219 µM, 3.6–130.7 µM, and 30–178.8 µM), indicating elevated toxicity. After 24 h, all bisphenols adhered to nominal concentrations except BPAP, BPF, and BPE. BPF's concentration notably decreased (50.82 ± 9.33% of nominal value). The results revealed diverse effects of bisphenol analogs on different cell types. These findings emphasized the considerable cytotoxic potential of specific bisphenol analogs across various human cell models, underlining the necessity for a re-evaluation of their safety and regulatory standards.	Chem Biol Interact. 2025 May 1:412:111475.	10.1016/j.cbi.2025.111475	40086714	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1721	R. A. Rifa and R. Lavado	2024	Cytotoxic impacts of seven alternative bisphenols on human in vitro cellular models	Bisphenols (BPs), common in plastics, coatings, and resins, are under scrutiny for potential endocrine disruption. Despite banning bisphenol A (BPA), its perceived safer alternatives may still pose health risks, urging comprehensive toxicity assessments. This study evaluated the cytotoxicity of seven bisphenols—BPA, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), bisphenol B (BPB), bisphenol AP (BPAP), bisphenol E (BPE)—in eight different relevant human in vitro cell models: liver (HepaRG), intestinal (Caco-2), breast (T47D), brain (SH-SY5Y), lung (A549), kidney (HEK293), endothelial (HMEC-1), and skin (HEK-001) cell lines. BPE manifested the highest cytotoxicity in Caco-2 cells, presenting an EC50 value of roughly 0.2 µM (95% confidence interval). In contrast, HEK293 and HepaRG cells demonstrated significant resilience to BPE (EC50 > 1000 µM). BPAF, BPAP, BPF, and BPAP had consistently low EC50 values across cell lines (5–219 µM, 3.6–130.7 µM, and 30–178.8 µM), indicating elevated toxicity. After 24 h, all bisphenols adhered to nominal concentrations except BPAP, BPF, and BPE. BPF's concentration notably decreased (50.82 ± 9.33% of nominal value). The results revealed diverse effects of bisphenol analogs on different cell types. These findings emphasized the considerable cytotoxic potential of specific bisphenol analogs across various human cell models, underlining the necessity for a re-evaluation of their safety and regulatory standards.	Chemosphere. 2024 Oct:366:143408.	10.1016/j.chemosphere.2024.143408	39326710	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1722	S. Riesbeck, H. Patruschka, U. Rolle-Kampczyk, C. Schuh, C. Nivens, C. Eberlein, H. J. Heipieper, M. von Bergen and N. Jehmlich	2022	Adaptation and Resistance: How Bacteroides thetaiotaomicron Copes with the Bisphenol A Substitute Bisphenol F	Bisphenols are used in the process of polymerization of polycarbonate plastics and epoxy resins. Bisphenols can easily migrate out of plastic products and enter the gastrointestinal system. By increasing colonic inflammation in mice, disrupting the intestinal bacterial community structure and altering the microbial membrane transport systems in zebrafish, bisphenols seem to interfere with the gut microbiome. The highly abundant human commensal bacterium Bacteroides thetaiotaomicron was exposed to bisphenols. Bisphenol A (BPA), Bisphenol F (BPF), Bisphenol S (BPS), to examine the mode of action, in particular of BPF. All chemicals showed a concentration-dependent growth inhibition of B. thetaiotaomicron. Proteomic analysis revealed that BPF induced a stronger stress response than BPA and BPS. Furthermore, BPF decreased membrane fluidity with increasing BPF concentrations. Physiological changes, including an increase of catalase concentrations were observed. On the proteomic level, a higher abundance of several ATP synthase subunits and multidrug efflux pumps suggested an increased energy demand for adaptive mechanisms after BPF exposure. Defense mechanisms were also implicated by a pathway analysis that identified a higher abundance of members of resistance pathways to beta-lactam antibiotics (i.e., antibiotics). Here, we present further insights into the mode of action of bisphenols in a human commensal gut bacterium regarding growth inhibition and the physiological and functional state of the cell. These results, combined with information directed effects, could lead to a better understanding of real health disturbances and disease development based on xenobiotic uptake.	Microorganisms. 2022 Aug 9;10(8):1610.	10.3390/microorganisms10081610	36014027	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1723	C. Riegraf, A. M. Bell, M. Uhlig, G. Reifferscheid and S. Buchinger	2022	Planar chromatography-bioassays for the parallel and sensitive detection of androgenicity, anti-androgenicity and cytotoxicity	Anti-androgens entering the aquatic environment, e.g., by effluents from wastewater treatment plants or agricultural settings are contributing to endocrine disruption in wildlife and humans. Due to the simultaneous occurrence of agonistic compounds, common in in vitro bioassays it can be underestimated the risk caused by estrogen antagonists. On the other hand, cytotoxic effects might lead to false positive assessments of anti-androgenic effects in conventional bioassays. In the present study, a combination of normal-phase high-performance thin-layer chromatography (NP-HPTLC) with a yeast based reporter gene assay is established for the detection of anti-androgenicity as a screening tool to reduce interferences of antagonistic and cytotoxic compounds present in the same sample. To enable a microseparation of anti-androgenicity with cytotoxic effects, cell viability was assessed in parallel on the same plate using a resazurin viability assay adapted to HPTLC plates. The method was characterized by establishing dose-response curves for the model compounds flutamide as well as for the pharmaceuticals bicalutamide, EE2, and DEX. The LOD for flutamide was 0.5 ng/band, and the IC50 was determined to be 1.5 ng/band. Furthermore, the method was successfully demonstrated with E. chlorophantus. In order to a proof of concept, the detection and quantification of anti-androgenicity in an extract of a landfill leachate is demonstrated. The study shows that the hyphenation of HPTLC with the yeast anti- androgen screen is a matrix-robust, cost-efficient and fast screening tool for the sensitive and simultaneous detection of anti- androgenic and cytotoxic effects in environmental samples. The method offers a wide range of possible applications in environmental monitoring and contributes to the identification of anti- androgenicity drivers in the course of an effect-directed analysis.	J Chromatogr A. 2022 Nov 22:1684:463582.	10.1016/j.chroma.2022.463582	36288622	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1724	E. Ribeiro, M. Delgadinho and M. Brito	2019	Environmentally Relevant Concentrations of Bisphenol A Interact with Doxorubicin Transcriptional Effects in Human Cell Lines	The worldwide production of synthetic chemicals, including endocrine disruptor chemicals (EDCs), such as Bisphenol A (BPA) has increased significantly in the last two decades. Human exposure to BPA, particularly through ingestion, is continuous and ubiquitous. Although, considered a weak environmental estrogen, BPA can induce divergent biological responses through several signaling pathways, including carcinogenesis in hormone-dependent cancers. Doxorubicin (DOX) is a chemotherapeutic drug widely used in the treatment of breast cancer. Although, DOX is known to induce DNA damage, its potential role in hormone-dependent cancers has been suggested. This study aims to assess the potential interaction between environmentally relevant levels of BPA and DOX in MCF-7 and MDA-MB-231 breast cancer cells. Gene transcriptional changes, in key player genes for cancer biology, namely in the p21, and bcl-2, were evaluated through qRT-PCR. The cellular response was analyzed after exposure to BPA, DOX, or co-exposure to both chemicals. Transcriptional analysis showed that BPA exposure induces upregulation of bcl-2 and evidences an antagonistic non-monotonic response on DOX transcriptional effects. Moreover, the BPA interaction with DOX on p21 and p53 expression emphasizes its cellular specificity and divergent effects. Overall, they'll was more susceptible to BPA effects. In a dose-dependent manner while MDC. It turns optional levels, molecular's non-monotonic responses. Our data indicate that BPA environmental exposure may influence chemotherapy outcomes, which emphasizes the urgency for a better understanding of BPA interactions with chemotherapeutic agents, in the context of risk assessment.	Toxics. 2019 Aug 29;7(3):43.	10.3390/toxics7030043	31470548	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1725	F. Ren, H. Ning, Y. Ge, Z. Yin, L. Chen, D. Hu, S. Shen, X. Wang, S. Wang, R. Li and J. He	2022	Bisphenol A induces apoptosis in response to DNA damage through c-Abl/YAP(Y357)/ p73 pathway in P19 embryonal carcinoma stem cells	Bisphenol A (2,2-bis(2-hydroxyphenyl) propane; BPA) is a well-known endocrine-disrupting compound that is widely used in various daily products and exhibits embryonic development toxicity and genotoxicity. However, the affected signaling pathways involved in embryonic development especially the interactions of involved proteins remain unclear. In our previous study (Sui et al., 2021), BPA induces DNA damage and apoptosis in mouse embryonic stem cells (mESCs) and human embryonic stem cells (hESCs) through the ATM/ATR-p53 pathway. In the present study, we found that BPA also induced DNA damage and apoptosis in P19 cells. Moreover, the BPA-induced apoptosis was mediated by the c-Abl/YAP(Y357)/p73 pathway. Co-immunoprecipitation (Co-IP) and GST pull-down assays revealed that BPA enhanced the interactions of involved proteins. Results indicated that BPA affected multiple embryonic development pathways including Hippo, TGF-β, Wnt, and Notch pathways. Furthermore, the protein-protein interaction network suggested that the c-Abl/YAP(Y357)/p73 pathway may play a key role in apoptosis induction in response to DNA damage. PZA-embryonal carcinoma stem cells, as a developmental toxicity model, were treated with different BPA concentrations, to establish an in vitro model to verify the role of the c-Abl/YAP(Y357)/p73 pathway in apoptosis. BPA triggered DNA damage and significantly upregulated the expression levels of c-Abl, phosphorylated YAP(Y357), phosphorylated p73(Y99), and cleaved caspase-3 protein (p < 0.05), thus decreasing cell viability and remarkably promoting the p73 target genes (PUMA, NOXA, and BAX) transcription (p < 0.05). Co-IP and GST pull-down assays revealed that BPA enhanced the interactions of YAP(Y357) and p73(Y99) with c-Abl. Moreover, BPA-induced apoptosis was mediated by the c-Abl/YAP(Y357)/p73 pathway

別添-2 統合文献リスト

毒性評価（動物）1：該当、0：該当しない

毒性評価（疫学）1：該当、0：該当しない

毒性評価（in vitro）1：該当、0：該当しない

毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性指標非不適合と判断されるもの以外を後続評価へ進め、当該時点で詳細な評価に基づき判定。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1726	I. Reina-Pérez, A. Olivas-Martínez, V. Mustieles, E. Salamanca-Fernández, J. M. Molina-Molina, N. Olea and M. F. Fernández	2022	The Mixture of Bisphenol-A and Its Substitutes Bisphenol-S and Bisphenol-F Exerts Obesogenic Activity on Human Adipose-Derived Stem Cells	Bisphenol A (BPA) and its substitutes, bisphenol F (BPF) and S (BPS), have previously shown in vitro obesogenic activity. This study was designed to investigate their combined effect on the adipogenic differentiation of human adipose-derived stem cells (hASCs). Cell viability was assessed by MTT assay. Cells were exposed to BPA, BPF, BPS, and their mixture (MIX) at concentrations ranging from 0.1 nM to 10 µM. Quantitative real-time polymerase chain reaction (qRT-PCR) in a study gene expression of adipogenic markers (PPARγ1, 2, CEBPα, LPL, and FABP4), and Western Blot to determine their corresponding proteins. The MIX promoted intracellular lipid accumulation in a dose-dependent manner with a maximal response at 10 µM. Co-incubation with pure antiestrogen (ICI 182,780) inhibited lipid accumulation, suggesting that the effect was mediated by the estrogen receptor. The MIX also significantly altered the expression of PPARγ1, 2, CEBPα, LPL, and FABP4 markers, showing a non-monotonic U-shaped dose response, with maximal gene expression at 10 nM and 10 µM and lower expression at 1 µM. This pattern was not observed when bisphenols were tested individually. Exposure to MIX 0–10 µM also increased all evaluated proteins except for FABP4, which showed no changes. Evaluation of the combined effect of relevant chemical mixtures is needed rather than single chemical testing.	Toxicology. 2022 Mar 30:470:153138.	10.3390/toxics10060287	35736896	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1727	C. Reichelbach, M. García-Käufer, N. Blinget, A. Arit, K. Vach, E. Hellwig, R. Gminski and O. Polydorou	2021	Cytotoxicity and estrogenicity in simulated dental wastewater after grinding of resin-based materials	OBJECTIVE: This study evaluated the cytotoxic and estrogenic effects of dust and eluates released into simulated wastewater after grinding of dental resin-based materials. METHODS: Four materials were used: ceramic* universal, Filtek™ Supreme XTE, Luna™ Ultimate and Core X™ flow. From each composite material, samples (5 × 2 mm; n = 50) were prepared according to the manufacturers' instructions. Luna™ Ultimate was used as the only bulk sample; core preparations also with a cohesive failure (cfail) and were subjected to distilled water at 60 mg/mL. After storage for 72 h, the suspensions were centrifuged and the supernatants (eluates) were sterile-filtered. Cell function, Eluates and dusts were evaluated for inhibition of Vibrio fischeri bioluminescence and cytotoxicity on human BJ5ta lung cells (WST-1 Assay). The estrogenic activity was assessed by YES-Assay. Statistical analysis was performed using Kruskal-Wallis and Dunn-Bonferroni tests (α = 0.05). RESULTS: Dust and eluates of resin-based materials showed no cytotoxicity. Only bulk-fill Luna™ Ultimate showed minor cytotoxicity (EC50 = 1.2 mg/mL) at the highest concentration. Core X™ flow and Luna™ Ultimate showed minor estrogenic effects at concentrations above 1.2 mg/mL (p < 0.05). The activity of the eluates of ceramic* universal and Filtek™ Supreme XTE was significantly higher than Luna™ Ultimate and Core X™ flow (p < 0.05) in the WST-1 Assay, all materials induced cytotoxic effects at concentrations of 0.1 mg/mL (p < 0.05), while no significant differences were detected among them. The tested materials revealed no estrogenic activity. All dental monomers and Bisphenol A showed concentration dependent cytotoxic effects (p < 0.05), whereas only Bisphenol A induced an estrogenic effect (p < 0.01). SIGNIFICANCE: Dust and eluates of resin-based dental materials released into wastewater exert bactericidal and cytotoxic effects in vitro. However, they reveal no estrogenic effects.	Dent Mater. 2021 Oct;37(10):1486-1497.	10.1016/j.dental.2021.07.003	34376295	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1728	P. Rebuzzini, S. Rustichelli, L. Fassina, I. Cansbido, M. Zuccotti and S. Garagna	2024	BPA Exposure Affects Mouse Gastruloids Axial Elongation by Perturbing the Wnt/β-Catenin Pathway	Mammalian embryos are very vulnerable to environmental toxicants (ETs) exposure. Bisphenol A (BPA), one of the most diffused ETs, exerts endocrine disrupting effects through estrogen receptors and hormone-like properties, with detrimental health effects, including on reproduction. However, its impact during the post-implantation stages is still unclear. This study, using pluripotent cells as 3D stem cell-based in vitro model of embryonic development, showed that BPA exposure arrests their axial elongation/extension present during the third (E-series) pathway activated period, by β-catenin protein reduction. Gastruloid overlapping might have been impeded by the downregulation of Tbx6, Dog and Tcf15 genes, known to suppress E-cadherin expression and to activate the N-cadherin gene, and by the low expression of the N-cadherin protein. Data, on the lack of gastruloids elongation might be related to altered role of BPA-exposed cells from the pluripotency condition and their following differentiation. In conclusion, here we state that the inhibition of gastruloids' axial elongation by BPA might be the result of the concomitant Wnt/β-catenin perturbation, reduced N-cadherin expression and Sox9, T/Bra and Cdx2 altered spatial expression, which all together concur in the impaired development of mouse gastruloids.	Int J Mol Sci. 2024 Jul 19;25(14):7924.	10.3390/ijms25147924	39063166	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1729	W. Ratajczak-Wrona, M. Rusak, K. Nowak, M. Dabrowska, P. Radziwon and E. Jablonska	2020	Effect of bisphenol A on human neutrophils immunophenotype	Neutrophils (PMN) play a key role in eliciting congenital immune response. These cells are equipped in cell-specific receptors that are located on the surface of their cell membrane. These receptors produce various signals in response to environmental factors, including BPA. The aim of the study was to evaluate the immunophenotype of PMN in response to BPA in vitro conditions. The study was designed to evaluate the effect of BPA on the expression of CD11c, CD16, CD35, CD62L and CD88 compounds on the surface of neutrophils, in vitro and ex vivo. The study included PMN isolated from the whole blood. The cells were incubated in the presence of BPA and/or LPS. Flow cytometry technique was used to evaluate the expression of CD antigens. Studies of these receptors indicate that BPA, at a concentration corresponding to the serum level of this compound in healthy subjects as well as at higher doses, induces changes in the immunophenotype of PMN, which may lead to immunity disturbances associated with the dysfunction of these cells. Moreover, the observed effects of xenoestrogen on the expression of CD11c, CD16, CD35, CD62L, CD88 and CD18 differentiation markers, on these cells are non-independent.	Sci Rep. 2020 Feb 20;10(1):3083.	10.1038/s41598-020-59753-2	32080224	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1730	W. Ratajczak-Wrona, K. Nowak, M. Garley, K. Grubczak, D. Dabkowska, A. Iwaniuk, S. Wiki, M. Moniuszko, I. Czerniecki, S. Wołczyński and E. Jablońska	2019	Expression of serine proteases in neutrophils from women and men: Regulation by endocrine disruptor bisphenol A	Bisphenol A (BPA) is a well-known endocrine disruptor. However, little information is available about its immunological effects. In the present study, we aimed to evaluate cytotoxic activity of BPA on human polymorphonuclear neutrophils (PMNs) according to gender and examine its effect on the expression of neutrophil serine proteases. Results indicated that exposure to BPA (range 10-1000 nM) led to a decrease in viability of PMNs and to morphological changes in these cells of both genders. The experiments showed different effects of BPA on the expression of proteinase 3, elastase, and cathepsin G in PMNs of both men and women, depending on the gender and concentration used. Thus, our findings suggest for the first time that through dysregulation of the expression of these enzymes, BPA may lead to disorders of the neutrophil's cellular response in people exposed to this xenoestrogen.	Environ Toxicol Pharmacol Vol.71 Pages 103212	10.1016/j.etap.2019.103212	31247398	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	16 µM等	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1731	W. Ratajczak-Wrona, M. Garley, M. Rusak, K. Nowak, J. Czerniecki, K. Wiśniewicz, M. Dąbrowska, S. Wołczyński, P. Radziwon and E. Jabłońska	2021	Sex-dependent dysregulation of human neutrophil responses by bisphenol A	BACKGROUND: In the present study, we aimed to investigate selected functions of human neutrophils exposed to bisphenol A (BPA) under in vitro conditions. As BPA is classified among xenoestrogens, we compared its action and effects with those of 17β -estradiol (E2). METHODS: Chemotaxis of neutrophils was examined using the Boyden chamber. Their phagocytosis and nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) oxidase activity were measured by flow cytometry. The viability of cells was assessed by the trypan blue exclusion test. The expression of CD11b, CD16, CD35, CD62L, CD88, and CD18 cytometry was used to assess the expression of cluster of differentiation (CD) antigens. The formation of neutrophil extracellular traps (NETs) was analyzed using a microscope. Cell lysates (200 µg/ml) were used for analysis of the investigated proteins was determined using Western blot. RESULTS: The analysis of results obtained for both sexes demonstrated that after exposure to BPA, the chemotactic capacity of neutrophils was reduced in the presence of BPA, the phagocytic activity was found to be elevated in the cells obtained from women and reduced in the cells from men. Following exposure to BPA, the percentage of neutrophils with CD11b and CD88-LTB4R expression, as well as the percentage of cells forming NETs, was increased in the cells from both sexes. The stimulatory role of BPA and E2 in the activation of NADPH oxidase was observed only in female neutrophils. Moreover, BPA and E2 increased the level of ERK1/2 and p38 MAPK phosphorylation in the cells from both sexes. The results also revealed that BPA and E2 increased the level of tumor necrosis factor-α (TNF-α) and interleukin-8 (IL-8) production and ERK1/2 expression in the cells of both sexes. In addition, intensified expression of all tested PI3K-Akt pathway proteins was observed in male neutrophils. CONCLUSIONS: The study demonstrated the influence of BPA on neutrophil functions associated with locomotor and pathogen-eliminative, which in turn may disturb the immune response of these cells in both women and men. Analysis of the obtained data showed that the effect of this xenoestrogen on the human neutrophils was more pronounced than E2.	Environ Health. 2021 Jan 7;20(1):5.	10.1186/s12940-020-00686-8	33413436	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1732	C. N. Ramskov Tetzlaff, T. Svingen, A. M. Vinggaard, A. K. Rosenmai and C. Taxvig	2020	Bisphenols B, E, F, and S and 4-cumylphenol induce lipid accumulation in mouse adipocytes similarly to bisphenol A	Bisphenol A (BPA) has been widely reported to exert endocrine disrupting effects, including the induction of adipogenesis in cultured preadipocytes and intact animals. Because of the potential harm to human health, BPA is being substituted in consumer products with bisphenols. Whether or not these substitutes induce adipogenesis remains largely unknown. We investigated the potential adipogenic effects of bisphenol B (BPB), bisphenol E (BPE), bisphenol F (BPF), bisphenol S (BPS) and 4-cumylphenol (4-CP) in a short-term lipid accumulation assay in 3T3-L1 cells. We found that BPB, BPE, BPF, BPS, and 4-CP all induced triglyceride accumulation and lipid droplet formation in the same extent and potencies as BPA. Based on these and other results, we conclude that these BPA analogues and 4-CP most likely will elicit similar effects on adipocytes as BPA. Using them to substitute BPA in products should be done with caution.	Environ Toxicol. 2020 May;35(5):543-552.	10.1002/tox.22889	31820560	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1733	A. Rajkumar, T. Luu, B. F. Hales and B. Robaire	2022	High-content imaging analyses of the effects of bisphenols and organophosphate esters on TM4 mouse Sertoli cells	The endocrine disruptive effects of bisphenol A (BPA) and brominated flame retardants (BDE-47) have led to restrictions on their use and increased the pressure to identify safe replacements for these chemicals. Although there is evidence that some of these alternatives may be toxic to spermatogonial and Leydig cells, little is known about the toxicity of emerging replacements on Sertoli cells. We used high-content imaging to investigate the effects of BPA, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), tetrabromobisphenol A (TBBPA), BDE-47, and the organophosphate flame retardants (OPFRs) triphenyl phosphate (TPHP) and tris(1,3-dichloro-2-propyl) phosphate (TDCPP) on TM4 mouse Sertoli cell endpoint assessment. The benchmark concentration potency ranking for bisphenols based on cytotoxicity was BPAF>BPF>BPS>BPA. Human estrogen receptor equivalent dose (HEQ) determination tested BPS as the most potent alternative replacement. The benchmark concentration potency ranking of BDE-47 and organophosphate esters based on cytotoxicity was TBBPA>TDCPP>TPHP. Exposure to BPA, BPF, BPS, BPAF, TBBPA, BDE-47, TPHP, and TDCPP resulted in cellular oxidative stress, changes at tight junctions, and loss of cell viability. The benchmark concentrations for the loss of cell viability and lysosomes (72 h) of the chemicals in TM4 cells in a TDCPP>TPHP>BPAF>TBBPA>BDE-47>BPF>BPS>BPA order. Lipid droplets were decreased in C18-G cells exposed to BPF and in MA-10 cells exposed to BPAF, but increased in BPF-, BPAF, and BPTMC-exposed KGN cells. BPA and BPS exposure induced cellular stress in MA-10 and KGN cells, respectively. In summary, structurally similar bisphenols displayed clear cell line-specific differences in MoA and AOP outputs for effects on cell viability and phenotypic endpoints. This approach, together with additional data on human exposure, may aid in the selection and prioritization of responsible replacements for BPA.	Biol Reprod. 2022 Sep 12;107(3):858-868.	10.1093/biolre/ioac101	35596243	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.001-100 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1734	A. Rajkumar, T. Luu, M. A. Beal, T. S. Barton-Maclaren, B. Robaire and B. F. Hales	2021	Elucidation of the Effects of Bisphenol A and Structural Analogs on Germ and Steroidogenic Cells Using Single Cell High-Content Imaging	Concerns about the potential adverse effects of bisphenol A (BPA) have led to an increase in the use of replacements, yet the toxicity data for several of these chemicals are limited. Using high-content imaging, we investigated the effects of BPA, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), and tetrabromobisphenol A (TBBPA) on mouse testicular cells. Benchmark concentration modeling was employed to determine benchmark concentrations (BMCs) and estimate administered equivalent doses (AEDs). In all 3 cell lines, BPA was one of the least cytotoxic bisphenol compounds tested, whereas BPA-and BPTMC-were the most cytotoxic. Interestingly, BPF and BPS were cytotoxic only in MA-10 cells. Effects on phenotypic parameters, including mitochondrial, lysosome, lipid droplets, and oxidative stress, were both bisphenol- and cell line-specific. BPA exposure affected mitochondria (BMDC: 1.2 µ M; AED: 0.33 mg/kg bw/d) in C18-G cells. Lysosome numbers were increased in MA-10 cells exposed to BPS or BPAF but decreased in KGN cells exposed to BPAF or BPB. Lipid droplets were decreased in C18-G cells exposed to BPF and in MA-10 cells exposed to BPTMC but increased in BPF-, BPAF, and BPTMC-exposed KGN cells. BPA and BPAF exposure induced oxidative stress in MA-10 and KGN cells, respectively. In summary, structurally similar bisphenols displayed clear cell line-specific differences in MoA and AOP outputs for effects on cell viability and phenotypic endpoints. This approach, together with additional data on human exposure, may aid in the selection and prioritization of responsible replacements for BPA.	Toxicol Sci. 2021 Apr 12;180(2):224-238.	10.1093/toxsci/kfab012	33501994	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1735	P. Rojek and A. Ganguly	2025	Unveiling the molecular interactions between bisphenol A and the cell surface Toll-like receptors: Implications for immune health	Microplastic pollution is an emerging threat to the human health. In nature, microplastics release several compounds of toxicological importance. Among them, bisphenol A (BPA), a widely used additive in plastic production, is an important one. Upon breakdown, microplastics release significant amounts of BPA in air, water, and soil. Humans may be exposed to BPA through nasal, oral, and dermal routes. BPA is linked to oxidative stress, physiological disturbances, and chronic diseases. Moreover, it may target the immune system. Toll-like receptors (TLRs) are important mediators of both innate and adaptive immunity and recognize microbial pathogens and endogenous danger signals. Interestingly, BPA has been shown to interact with TLR4 and TLR9, but its interactions with other TLRs remain unknown. Here, we investigated the binding potential of BPA against cell surface TLRs. The binding affinities between BPA against cell surface TLRs. For this study, a molecular docking approach using the HawkDock new algorithm was employed to analyze the binding potential of BPA with the surface-exposed TLRs. Results have revealed that BPA binds to TLR1, TLR2, TLR4, TLR5, and TLR6 with affinity ranging from -6.5 to -7.5 kcal/mol. Structural analyses of the docked complexes have suggested that BPA binds to TLR through conventional H-bonds, Van der Waals and other hydrophobic interactions further solidified the docked complexes. Notably, C-H bonds were also apparent in some docked conformations. Hence, results of the present study explicitly suggest that BPA can potentially bind to the cell surface TLRs through various bonds and interactions. Such interactions may modulate TLR-mediated signaling and immunity in organisms.	Toxicol Rep. 2025 May 22:14:102057.	10.1016/j.toxrep.2025.102057	40520521	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1736	M. S. Rahman, K. H. Kang, S. Arifuzzaman, W. K. Pang, D. Y. Ryu, W. H. Song, Y. J. Park and M. G. Pang	2019	Effect of antioxidants on BPA-induced stress on sperm function in a mouse model	In the past few years, bisphenol A (BPA) an endocrine disrupting chemical, has received increasing attention because of its detrimental health effects. There is ample evidence to support that BPA interferes with the reproductive health of humans and animals. In spermatozoa, BPA-induced adverse effects are mainly caused by increased oxidative stress. Using an in vitro experimental model, we examined whether antioxidants (glutathione, vitamin C, and vitamin E) have defensive effects against BPA-induced stress to spermatozoa. The results showed that antioxidants inhibit the overproduction of reactive oxygen species, basically calcium (peroxides) and increase intracellular ATP levels, thereby preventing motility loss and abnormal acrosome reaction in BPA-exposed spermatozoa. In particular, glutathione and vitamin C reduced the protein kinase A-dependent tyrosine phosphorylation of sperm proteins. Moreover, antioxidants prevented BPA-induced decreases in the fertilization rate and blastocyst formation rate. Furthermore, we found that the compromised fertilization ability of spermatozoa exposed to BPA was mediated by BPA-induced spermatozoa and be improved following their supplementation with glutathione and vitamin E. Based on these findings, we suggest that antioxidants reduce oxidative stress in BPA-exposed spermatozoa, thus preventing detrimental effects on their function and fertility.	Sci Rep. 2019 Jul 22;9(1):10584.	10.1038/s41598-019-47158-9	31332285	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1737	V. Quaglariello, C. Coppola, D. G. Mita, G. Piscopo, R. V. Iaffaioli, G. Botti and N. Maurea	2019	Low doses of Bisphenol A have pro-inflammatory and pro-oxidant effects, stimulate lipid peroxidation and increase the cardiotoxicity of Doxorubicin in cardiomyoblasts	Endocrine disruptors are strictly associated to cancer and visceral cardiovascular risk factors. Bisphenol A (BPA) is an endocrine disruptor commonly used in the manufacturing of plastics based on polycarbonate, polyethersulfone, polyetherimide and resins. Our study aims to investigate whether BPA may cause cardiac damage through pro-inflammatory effects on cardiomyoblasts, thus exacerbating the Doxorubicin (DOX)-induced cardiotoxicity phenomena. We tested the metabolic effects of BPA at low doses analyzing its affections on the intracellular calcium uptake, oxidative stress, lipid peroxidation and production of nitric oxide and interleukins. Co-incubation of BPA and DOX significantly reduced the cardiomyocytes viability, compared to only DOX-exposure cells. This mechanism, underlying these effects are based on the stimulation of the intracellular calcium accumulation and lipid peroxidation. Notably, BPA increase the production of pro-inflammatory interleukins involved in cardiovascular diseases as well as in DOX-induced cardiotoxicity phenomena. This study provides a rationale for translational studies in the field of cardio-oncology.	Environ Toxicol Pharmacol. 2019 Jul:69:1-8.	10.1016/j.etap.2019.03.006	30903913	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1738	J. Qi, L. Liu, J. Yang, X. Gao and W. Zhang	2020	Bisphenol A decreases progesterone synthesis in human ovarian granulosa cells	Evidences indicate that the decline of female fertility is becoming a common problem over the past few decades. Environmental exposure of Bisphenol A (BPA) has been considered as an endocrine disrupting chemical detrimentally affecting human reproduction. To better understand the effect of BPA exposure on human ovarian granulosa cells, we treated human ovarian granulosa cell line (KGN) with increasing concentrations (0.1, 1, 10, 100 µM) of BPA for 24 h. Result 0.1, 1, and 10 µM BPA did not significantly affect the viability of KGN while 100 µM of BPA caused a statistically significant decrease in the viability of KGN. Treatment KGN with 10 µM BPA resulted in a significant decrease in progesterone biosynthesis. The treatment also significantly increased the expression of 3?-hydroxy-steroid-dehydrogenase 1 (HSD3B1) and steroidogenic acute regulatory protein (STAR). In the current study, exposure to BPA could lead to decreased progesterone production probably through the upregulation of HSD3B1 in human granulosa cells.	Birth Defects Res. 2020 Dec;112(20):1843-1849.	10.1002/bdr2.1817	33073540	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1、1、10、100 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1739	A. Punt, A. Aartse, T. F. H. Bovee, A. Gerssen, S. P. J. van Leeuwen , R. Hoogenboom and A. Peijnenburg	2019	Quantitative in vitro-to-in vivo extrapolation (QIVIVE) of estrogenic and anti-androgenic potencies of BPA and BADGE analogues	The goal of the present study was to obtain an in vivo relevant prioritization method for the endocrine potencies of different polycarbonate monomers, by combining in vitro bioassay data with physiologically based kinetic (PBK) modelling. PBK models were developed for a selection of monomers, including bisphenol A (BPA), bis(4-hydroxyphenyl) methane (BisF), using in vitro input data. The PBK models were evaluated by comparing predicted and measured concentrations in rat blood. Subsequently, in vitro-to-in vivo extrapolation (IVIVE) was applied to estimate the in vivo endocrine potencies of different BADGEs (predetermined) and endogenous hormone effects can be quite harsh(Higher than BPA. We extended in vivo potencies based on the rat ovariectomy data, we derived a series of negotiable lower than BPA because of last detoxification of the BADGEs. In contrast, the relative potencies of 12 BPF and 6.6 BPF increase when accounting for the in vivo availability. 6.6 BPF is estimated to be fivefold more potent than BPA in humans in vivo in inducing oestrogenic effects and both 12 BPF and 6.6 BPF are moderately to, respectively, 3 and 11-fold more potent in inducing anti-androgenic effects. These relative potencies were considered to be first-tier estimates, particularly given that the potential influence of intestinal metabolism on the in vivo availability was not accounted for. Overall, it can be concluded that both 12 BPF and 6.6 BPF are activity compounds.	Arch Toxicol. 2019 Jul;93(7):1941-1953.	10.1007/s00204-019-02479-6	31111190	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1740	Y. Pu, E. Ticiani, A. A. Waye, K. Dong, H. Zhang and A. Veiga-Lopez	2022	Sex-specific extracellular matrix remodeling during early adipogenic differentiation by gestational bisphenol A exposure	Bisphenol A (BPA) is an endocrine-disrupting chemical known to promote adipose tissue mass, in vivo and adipogenesis, in vitro. Whether BPA can affect and reprogram early adipogenic differentiation signals that trigger adipogenic differentiation, remains unknown. We hypothesized that gestational BPA exposure results in a preadipocyte phenotype that leads to accelerated adipogenic differentiation, and that this phenotype is sex-specific. Primary ovine fetal preadipocytes were derived from exposed (0.1 and 100 mg/kg/day oral gavage) and control pregnancies and differentiated in vitro. Gestational BPA-enhanced lipid accumulation at early stages of differentiation (48 h) and this was evident in females but not male-derived fetal preadipocytes. After an RNA sequencing approach, samples were compared as follows: 3 groups (C vs. BPA) × 2 sexes (female (F) vs. male (M)) and 2 time points (0 h vs. 48 h). Differentially expressed genes (DEGs) were identified using a false discovery rate (FDR) < 0.05 and a fold change (FC) > 1.5. Female preadipocytes (F) were more transcriptionally active than male (M) cells, as more upregulated compared to C, F, M, BF, & BFM. F had 10 genes differentially expressed vs. C, F, and BFM. Both M7 genes differentially expressed vs. C, M. Triglyceride and glycerophospholipid metabolism were the most upregulated pathways in BFM-F. Downregulated pathways were associated with extracellular matrix organization in BPA-exposed preadipocytes. These findings are among the first to demonstrate that gestational BPA can modify the fate of adipocyte precursors by altering pathways associated to extracellular matrix components, an often-disregarded, but required aspect of adipogenic differentiation. This work highlights the need to investigate early adipogenic differentiation changes in older adipogenic chemicals.	Chemosphere. 2022 Sep;302:134806.	10.1016/j.chemosphere.2022.134806	35504463	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1741	D. P. Prevolakis, M. Nagi, F. Amatruda, R. Patalano, T. Monti, C. de Angelis, C. Graziadio, G. Pugliese, G. de Alteris, A. Colao, R. Pivonello, S. Savastano and C. Pivonello	2024	1,25-Dihydroxyvitamin D3 mitigates the adipogenesis induced by bisphenol A in 3T3-L1 and hAMSC through miR-27-3p regulation	PURPOSE: Endocrine-disrupting compounds, including bisphenol A (BPA), may promote obesity influencing basal metabolic rate and shifting metabolism towards energy storage. The role of 1,25-Dihydroxyvitamin D3 (1,25(OH)2D3) in counteracting BPA-induced adipogenesis has been recently described. However, the molecular mechanisms underlying this effect remain unclear. METHODS: In 3T3-L1 cell line and human adipose-derived mesenchymal stem cells (hAMSC) models, mouse 3T3-L1 cell line and human adipose-derived mesenchymal stem cells (hAMSC). METHODS: 3T3-L1, mouse pre-adipocytes, and human adipose-derived mesenchymal stem cells (hAMSC) were treated with 100 (10(-7) M) and BPA (100 -8) M and 10(-9) M), alone or in combination, throughout the differentiation to mature adipocytes. Cellular lipid droplet accumulation was assessed by Oil Red O staining. mRNA and miRNA expression were evaluated by RT-qPCR, and lipid-related genes (leptin, PPARγ, and FABP4) were analyzed by Western blot. Bioinformatic analysis of miRNA targets was performed by RT-qPCR, and highly ranked genes showing oligonucleotides (miRNA inhibitors) were used to modulate miRNAs expression. RESULTS: The adipocytes express VDR/RXR heterodimer and, during the differentiation process, VDR expression reduces. If not stimulated by the ligand, VDR significantly decreases lipid accumulation, with a consequent reduction in adipogenic marker expression, and counteracts the pro-adipogenic effect of BPA in 3T3-L1 and hAMSC studying BPA differentiation. This effect is associated to the increased expression of miR-27a-3p and miR-27b-3p. The blocking of miR-27a-3p and miR-27b-3p through miRNA inhibitors prevents the anti-adipogenic effect of VDR in both cell models. CONCLUSIONS: These results suggest that in cultured 3T3-L1 and hAMSC VDR induces an anti-adipogenic effect and prevents BPA pro-adipogenic effect by triggering at least in part epigenetic mechanisms involving miR-27-3p.	Int J Obes (Lond). 2024 Dec;48(12):1793-1802.	10.1038/s41366-024-01629-w	39256615	in vitro	-	-	-	-	-	-	-	-	1	0	10（-8）,10（-9）M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1742	M. Profita, E. Fabbi, E. Spiroi and P. Valbonesi	2021	Comparing effects and action mechanisms of BPA and BPS on HTR-8/SVneo placental cells	Bisphenol A (BPA) is one of the most investigated compounds as a suspected endocrine disrupting chemical. It has been found at vital concentrations in the maternal serum, cord serum, and amniotic fluid and also permeates placental tissues. Attempts are being made to replace BPA with the analog Bisphenol S (BPS). Also BPS was found in maternal and umbilical cord serum, and urine samples from a large population of pregnant women. The placenta is a temporary organ that develops during pregnancy and is essential for the health of the fetus. The aim of this study was to investigate the effects of BPA and BPS on HTR8/SVneo cells, derived from extravillous trophoblast of first trimester pregnancy. Proliferation and migration ability of trophoblast cells were assessed in vitro after exposure to BPA or BPS (10-13-10-3 M). Further, induction of the inflammatory response by the bisphenols was studied. To provide insight into the molecular pathways implicated in the responses, experiments were carried out in the presence or absence of some hormone receptors, ERα/ERβ, and GPER, or the ERK1/2 phosphorylation inhibitor. Data indicate that BPA significantly affects both proliferation and migration of HTR-8/SVneo cells, through ERα and ERK1/2-mediated processes. Differently, BPS only acts, on proliferation, again through ERα and ERK1/2-mediated processes. BPS, but not BPA, induces secretion of interleukin-6 and 8. Such effect is inhibited by blocking ERK1/2 phosphorylation. To the best of our knowledge, these are the first data showing that BPA affects trophoblast functions through ER/GPER1 mediation.	Biol Reprod. 2021 Nov 15;105(5):1355-1364.	10.1093/biolre/ioab139	34270681	in vitro	-	-	-	-	-	-	-	-	1	0	10-13—10-3 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1743	H. Pratsinis, S. N. Papageorgiou , N. Panayi, A. Iliadi, T. Eliades and D. Kletsas	2022	Cytotoxicity and estrogenicity of a novel 3-dimensional printed orthodontic aligner	INTRODUCTION: Orthodontic aligners printed with in-office 3-dimensional (3D) procedures have been described, but no data on their biocompatibility exist. This study investigates the cytotoxicity and estrogenicity of a 3D printed orthodontic aligner by assessing its biological and behavioral effects. METHODS: The cells of 1 type of aligner were immersed in sterile deionized water for 14 days, and the cytotoxicity and estrogenicity of the eluates were tested on human gingival fibroblasts (HGFs) and human breast cancer cells (MCF-7), respectively. Cytotoxicity was assessed by the MTT assay (n = 6), and cell proliferation was assessed by the sulforhodamine B assay (n = 6). Human breast cancer cell lines, 17-β-Estradiol and bisphenol A were used as positive controls. The statistical analysis was done by 1-way analysis of variance (ANOVA) and the Tukey post hoc test (α = 0.05). RESULTS: The eluates were not cytotoxic by HGFs ($P > 0.05$). Only the eluates of 1 aligner sample were cytotoxic to MCF-7 cells ($P < 0.05$; 39% ± 0.2%, vs 0% ± 0.1%; vs 0% ± 0.1%). The antioxidant activity expressed as the capacity to reduce intracellular levels of reactive oxygen species (ROS) was not affected by the aligner samples ($P > 0.05$). The significant estrogenicity was induced by the aligner samples compared with eluates from the negative control, but not from the positive controls ($P < 0.05$). The estrogenic activity was not affected by the aligner samples ($P > 0.05$). As expected, 17-β-Estradiol and bisphenol A stimulated MCF-7 cell proliferation, whereas no effect was observed on MDA-MB-231 cells. CONCLUSIONS: In conclusion, if any factors were released during the 14-day aging of 3D printed aligners in water, these were not found to be cytotoxic for human gingival fibroblasts and did not affect their intracellular reactive oxygen species levels. Moreover, no estrogenic effects of these putative eluates were observed towards an ER+ breast assay.	Am J Orthod Dentofacial Orthop. 2022 Sep;162(3):e116-e122.	10.1016/j.ajodo.2022.06.014	35842359	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1744	B. Pötzl, L. Kisslinger, S. Kendl, H. Stoppar, M. Kurbasic, M. Fasnacht and U. Dischinger	2024	Disruptive effects of plasticizers bisphenol A, F, and S on steroidogenesis of adrenocortical cells	INTRODUCTION: Endocrine-disrupting chemicals (EDCs) are known to interfere with endocrine homeostasis. Their impact on the adrenal cortex and steroidogenesis has not yet been sufficiently elucidated. This applies in particular to the ubiquitously available bisphenols A (BPA), F (BPF), and S (BPS). METHODS: H295R adrenocortical cells were exposed to different concentrations (1 nM–100 µM) of BPA, BPF, BPS, and an equimolar mixture of them (BPMix). After 72 hours, 19 endogenous steroids were measured using LC-MS/MS. Ratios of substrate and product of CYP-regulated steps were calculated to identify most influenced steps of steroidogenesis. Cell viability was assessed using a resazurin reduction assay. RESULTS: BPA, BPF, and BPS significantly increased the production of progesterone and its downstream metabolites and their combination led to extensive alterations in the quantitative steroid levels. The most pronounced effects ranged from 2- to 4-fold deviations at environmentally relevant concentrations, e.g. a 2.5–3.5-fold decrease at 30µM (p≤0.0001) compared to vehicle-treated controls. For BPF, levels of 17-hydroxyprogesterone were significantly increased by 30µM (FC 3.57 ± 0.49, p≤0.001) and 50µM (FC 3.96 ± 0.63, p≤0.0001). BPS treatment led to a dose-dependent decrease of 11-deoxycorticosterone at ≥1µM (e.g. FC 0.53 ± 0.15, p≤0.0001 at 10µM). However, other combining effects from the negative control. In both BPF (F = 7.661) and BEQ-ABB (F = 5.781; As reported, 17-β-Estradiol and bisphenol A stimulated MCF-7 cell proliferation, whereas no effect was observed on MDA-MB-231 cells. CONCLUSIONS: In conclusion, if any factors were released during the 14-day aging of 3D printed aligners in water, these were not found to be cytotoxic for human gingival fibroblasts and did not affect their intracellular reactive oxygen species levels. Moreover, no estrogenic effects of these putative eluates were observed towards an ER+ breast assay.	Front Endocrinol (Lausanne). 2024 Jun 20:15:1387133.	10.3389/fendo.2024.1387133	38966215	in vitro	-	-	-	-	-	-	-	-	1	0	1nM—1mM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1745	K. Pogrmic-Majkic, D. Samardžija Nenadov, S. Fa, B. Stanic, A. Tminic Pjevic and N. Andric	2019	BPA activates EGFR and ERK1/2 through PPARγ to increase expression of steroidogenic acute regulatory protein in human cumulus granulosa cells	Bisphenol A (BPA) negatively affects steroid production in human luteinized granulosa cells (GC). This study was designed to address two important questions: (1) whether BPA exerts the same disruptive effect in human cumulus granulosa cells (hCGC) and (2) to reveal the molecular mechanism underlying the BPA's action on steroidogenesis. We used cultured hCGC since these cells exert the properties of GC from early antral follicles that are in the phase of selection for dominance. The hCGC were treated with BPA (10 µM) and/or with the inhibitors of PPARγ (GW9662), EGFR (AG1478), and ERK1/2 (U0126). BPA increased the expression of genes encoding PPARγ, mRNA expression of the StAR, Starter StAR, exposure to BPA showed PPARγ, mRNA level in hCGC. Addition of PPARγ (10 µM), EGFR (AG1478), and PPARγ, (GW9662) inhibitors prevented the BPA-induced StAR and PPARγ, mRNA expression. Bisexesticular analysis showed that BPA induced a rapid EGFR and ERK1/2 activation. The BPA-induced EGFR phosphorylation was prevented by addition of the PPARγ inhibitor, whereas the BPA-induced ERK1/2 activation was prevented by addition of the EGFR or PPARγ inhibitor. These data show that BPA increases the progesterone and decreases the estradiol biosynthetic pathway in hCGC. Augmentation of the progesterone biosynthetic pathway is mediated through the PPARγ- dependent activation of EGFR and ERK1/2, leading to increased expression of STAR mRNA.	Chemosphere Vol.229 Pages 60-67	10.1016/j.chemosphere.2019.04.174	31075703	in vitro	-	-	-	-	-	-	-	-	1	0	100 µM他	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1746	N. Plattard, N. Voniova, P. Casto, A. Dupuis and S. Haddad	2022	Hepatic metabolism of chlorinated derivatives of bisphenol A (ClxBPA) and interspecies differences between rats and humans	During chlorination treatments of drinking water, aqueous bisphenol A (BPA) can react with chlorine to form chlorinated derivatives of BPA (mono, di, tri and tetra-chlorinated derivatives) or ClxBPA. These emerging substances are endocrine disruptors associated with obesity, type 2 diabetes (T2DM) and reproductive disorders. ClxBPA are present in different human biological matrices, but their toxicokinetics remain unknown. The aim of this study was to characterize the hepatic metabolism of ClxBPA in rats and humans. Hepatic subcellular fractions (S9 and microsomes) were incubated with ClxBPA (1 µM) to estimate their metabolic constants (Vmax, Km, intrinsic clearance), metabolic assays were performed in hepatocytes suspensions. Assays revealed that metabolic constants of ClxBPA are greatly vary depending on substances and species. While ClBPA and Cl2BPA show similar unbound intrinsic clearances (CLint) in rat incubation media, values for Cl3BPA and Cl4BPA are very different (3.109 and 0.082 mL/min/kg bw, respectively). In human incubations, Cl2BPA, Cl3BPA and Cl4BPA have similar unbound intrinsic clearances, while ClBPA and Cl2BPA (range 0.243 and 1.343 mL/min/kg bw, respectively). In both species, Cl2BPA and ClBPA have relatively similar clearances, and Cl3BPA is very different from Cl4BPA. Although no quantified biotransformation of salts and glucuronic metabolites, measured values will be valuable for the development of PBPK models for use in exposure assessment.	Arch Toxicol. 2022 Mar;96(3):783-792.	10.1007/s00204-021-03217-7	35072755	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1747	P. Pitchakarn , J. Kelinchai, P. Buachoen, A. Imsumran, A. Wongnoppavanich, K. Boonyaranai and S. Ou-yu Jaan	2025	Ficus lindsayana Leaf Extract Protects C2C12 Mouse Myoblasts Against the Suppressive Effects of Bisphenol-A on Myogenic Differentiation	Recently, toxicological and epidemiological research has provided strong support for the unfavorable effects of bisphenol A (BPA, 2,2'-bis(4-hydroxyphenyl) propane) on myogenesis and its underlying mechanisms. Researchers have therefore been looking for new strategies to prevent or mitigate these injurious effects of BPA on the human body. It has been found that plant extracts may act as potential therapeutic agents or functional foods, preventing human diseases caused by BPA. We previously reported that Ficus lindsayana (FL) extract exhibits anti-inflammation activity in macrophages by suppressing the expression of inflammation-related genes. However, the effects of FL extract on myogenesis remain unknown. Therefore, this study aimed to investigate the protective effects of FL extract against the suppressive effects of BPA on myogenic differentiation. The viability of BPA-stimulated C2C12 myoblasts was significantly increased when co-treated with FL (100 µg/mL), suggesting that the extract may lessen the inhibitory effects of BPA on cell division. We also found that FL (µg/mL) significantly increased myosin heavy chain protein levels in myotubes, like methylated myostatin, when compared to the BPA-treated control cells, without impacting cell viability. In addition, the levels of myogenin and myocyte enhancer factor 2C (MEF2C), which are crucial markers and regulators of myogenesis, were markedly increased by the addition of FL (1 µg/mL) to the BPA-treated C2C12 cells. This finding suggests that FL(1) effectively improved myogenic differentiation in BPA-exposed myoblasts. FL(2) treatment (50 µg/mL) significantly raised total Akt protein levels, as well as the ratio of phosphorylated Akt (p-Akt) to total Akt, in BPA-exposed myoblasts. Furthermore, FL(3) treatment (50 µg/mL) significantly increased the ratio of phosphorylated mTOR (p-mTOR) to total mTOR in BPA-exposed myoblasts. Overall, FL extract may protect against the suppressive effects of BPA on myogenic differentiation in C2C12 myoblasts, at least in part, by activating Akt/mTOR signaling pathways. Our findings suggest that FL extract may be a potential therapeutic agent for preventing BPA-induced impairments in myogenesis and muscle atrophy. The information obtained from this study demonstrates the health benefits of this plant, which warrants further investigation as an alternative medicine, functional ingredient, or food supplement that can promote the negative health effects of BPA or other toxicants.	Int J Mol Sci. 2025 Jan 9;26(2):476.	10.3390/ijms26020476	39859191	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1748	F. Pistollato, E. M. de Gyves, D. Carpi, S. K. Bopp, C. Nunes, A. Worth and A. Bal-Price	2020	Assessment of developmental neurotoxicity induced by chemical mixtures using an adverse outcome pathway concept	BACKGROUND: In light of the vulnerability of the developing brain, mixture risk assessment (MRA) for the evaluation of developmental neurotoxicity (DNT) should be implemented, since infants and children are co-exposed to more than one chemical at a time. One possible approach to tackle MRA could be to cluster DNT chemicals in a mixture on the basis of their mode of action (MoA) into 'similar' and 'dissimilar', but still contributing to the same adverse outcome, and evolve DNT assays to common key events (CKEs) identified in DNT-specific adverse outcome pathways (AOPs). Moreover, the use of human in vitro models, such as induced pluripotent stem cell (hiPSC)-derived neuronal and glial cultures, could enable mechanistic understanding of chemically induced adverse effects, avoiding species extrapolation. METHODS: hiPSC-derived neural progenitors differentiated into mixed cultures of neurons and astrocytes were used to assess the effects of acute (3 days) and repeated-dose (14 days) treatments with single chemicals and mixtures belonging to 'similar' and 'dissimilar' MoA compounds and their effects on synaptogenesis, neurite outgrowth, and brain-derived neurotrophic factor (BDNF) protein levels, identified as CKEs. The selected chemicals were grouped based on their MoA into 'similar' (polychlorinated biphenyls (PCB) 138, 153, and 180) and 'dissimilar' (PCB 138, bisphenol A (BPA), and valproic acid (VPA)) mixtures. Binary mixtures were designed at equipotent ratios (1:1) and tested at concentrations which induced 10% effects (EC10) on the selected endpoints. Concentration-response modelling was performed using the concentration addition (CA) model. RESULTS: Both 'similar' and 'dissimilar' mixtures induced a potentiation of the inhibitory effects on synaptogenesis, neurite outgrowth, and brain-derived neurotrophic factor (BDNF) protein levels, identified as CKEs. In currently available AOPs relevant to DNT, none of the chemicals tested in this study are known to interact with the same molecular initiating event (MIE). CONCLUSIONS: Our findings suggest that the use of human iPSC-derived neural cultures, which integrate toxicokinetic (TK) information on exposure, as well as toxicodynamic (TD) information on mechanisms, could enable the development of more realistic in vitro DNT testing strategies. Moreover, the use of mathematical modelling and increase of 'dissimilar' levels, to a certain extent reproducing autism-like cellular changes observed in the brains of autistic children, CONCLUSIONS: Our findings suggest that the use of human iPSC-derived mixed neurological cultures applied to a battery of assays anchored to key events of an AOP network represents a valuable approach to identify mixtures of chemicals with potential to cause learning and memory impairment in children.	Environ Health. 2020 Feb 24;19(1):23.	10.1186/s12940-020-00578-x	32093744	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1749	F. Pistollato, D. Carpi, E. Mendoza-de Gyves, A. Paini, S. K. Bopp, A. Worth and A. Bal-Price	2021	Combining in vitro assays and mathematical modelling to study developmental neurotoxicity induced by chemical mixtures	Prenatal and postnatal co-exposure to multiple chemicals at the same time may have deleterious effects on the developing nervous system. We previously showed that chemicals acting through similar mode of action (MoA) and exposed based on combination of Kenn-derived neurotrophic factor (BDNF) -induced protein neurotoxic effects on human induced pluripotent stem cell (hiPSC)-derived neurons and astrocytes compared to chemicals with dissimilar MoA. Here we assessed the effects of repeated dose (14 days) treatments with mixtures containing the six chemicals tested in our previous study (Bisphenol A, Chlorpyrifos, Lead(II) chloride, Methylmercury chloride, PCB138 and Valproic acid) along with 2 additional chemicals (Manganese (II) chloride, Thiram) and 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD). The selected chemicals were investigated for their ability to induce developmental neurotoxicity (DNT) in vitro hallmarks, including neurite outgrowth, and a decrease of synapse formation, which has been previously described to be associated with neurodevelopmental disorders (NDDs). Binary mixtures were designed at equipotent ratios (1:1) and tested at concentrations which induced 10% effects (EC10) on the selected endpoints. Concentration-response modelling was performed using the concentration addition (CA) model. Deviations from CA were analysed by means of the online software tool MIXTOX. Results showed that binary mixtures of chemicals belonging to 'similar' MoA induced a potentiation of the inhibitory effects on synaptogenesis, neurite outgrowth, and brain-derived neurotrophic factor (BDNF) protein levels, identified as CKEs. Conversely, mixtures of chemicals belonging to 'dissimilar' MoA induced effects which were mostly additive. Our findings suggest that the use of human iPSC-derived neuronal/glial cultures, which integrate toxicokinetic (TK) information on exposure, as well as toxicodynamic (TD) information on mechanisms, could enable the development of more realistic in vitro DNT testing strategies. Moreover, the use of mathematical modelling and increase of 'dissimilar' levels, to a certain extent reproducing autism-like cellular changes observed in the brains of autistic children, could enable the development of more realistic in vitro DNT testing strategies.	Reprod Toxicol. 2021 Oct:105:101-119.	10.1016/j.reprotox.2021.08.007	34455033	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1750	M. T. L. Pino, S. A. Ronchetti, G. Cordeiro, S. Bollati, B. H. Duchenski and J. P. Cabilla	2019	Soluble Guanylyl Cyclase Alpha1 Subunit: A New Marker for Estrogenicity of Endocrine Disruptor Compounds	Endocrine disrupting chemicals (EDCs) include widespread naturally occurring and synthetic substances in the environment that adversely affect humans and wildlife. Because of the increasing numbers of EDCs, screening methods are required to identify potential endocrine disruptors. Estrogen receptor (ER) is a well-known target of EDCs. Soluble guanylyl cyclase (sGC) is a heterodimeric enzyme that is a receptor for nitric oxide and is expressed in most tissues. We previously showed that sGC is a specific estrogen target gene. Here we investigated whether sGC is involved in nitric oxide-triggered rapid estrogenic responses. The aim of the present study was to evaluate sGC as a putative expression as a potential marker for xenoestrogenic EDC exposure in the E2-responsive luciferase-transfected rat pituitary cell line GH3. Cells were incubated in the presence of E2 (10(-8) M), bisphenol A (BPA) (10(-6) M), genistein (GEN) (10(-6) M), and 4-nonylphenol (NP) (10(-6) M) for 24 h. Cell viability was evaluated by MTT assay. We determined the effect of these compounds on sGC α1 expression by Western blot analysis. Increased sGC α1 expression in GH3 cells, as well as in other E2-responsive cell lines, was fully dependent on estrogen receptor ER α activation. Importantly, sGC α1 protein levels were strongly up-regulated by all the EDCs tested, even by those exhibiting low or null ER binding capacity. We provide evidence that the in vitro sGC α1 protein assay may be a very sensitive and powerful tool to identify compounds with estrogenic activity, which could improve current mammalian-based screening methods. Environ Toxicol Chem 2019;38:2719-2728. © 2019 SETAC.	Environ Toxicol Chem. 2019 Dec;38(12):2719-2728.	10.1002/etc.4591	31499574	in vitro	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1751	V. Peshdary, C. A. Hobbs, T. Maynor, K. Shepard, R. Gagne, A. Williams, B. Kuo, N. Chapeles, L. Recio, C. Yauk and E. Atlas	2021	Transcriptomic pathway and benchmark dose analysis of Bisphenol A, Bisphenol S, Bisphenol F, and 3,7,3',5,5'-Tetrabromobisphenol A in H9 human embryonic stem cells	Bisphenol A (BPA) is a chemical used in the manufacturing of plastics to which human exposure is ubiquitous. Numerous studies have linked BPA exposure to many adverse health outcomes prompting the replacement of BPA with various analogues, including bisphenol F (BPF) and bisphenol S (BPS). Other bisphenols are used in various consumer applications, such as 3,3,5,5'-Tetrabromobisphenol A (TBBPA), which is used as a flame retardant. Few studies to date have examined the effects of BPA and its analogues in stem cells to explore potential developmental impacts. Here we used transcriptomics to investigate similarities and differences of BPA and three of its analogues in the estrogen receptor-negative, human embryonic stem cell line H9 (WA09). H9 cells were exposed to increasing concentrations of the bisphenols and analyzed using RNA-sequencing. Our data indicate that BPA, BPF, and BPS have similar potencies in inducing transcriptional changes and point toward the same cellular pathways. TBBPA, the least structurally similar bisphenol of the group, exhibited more than 10-fold greater potency in altering gene expression and affected different pathways. Our results suggest that BPF and BPS may have similar developmental toxicity potential as BPA, while TBBPA may have different effects. Our study is the first to use transcriptomics in H9 cells to explore the human-relevant similarities of other bisphenols. It underpins stem cells, which may be used to assess the vulnerability of chemical grouping for read-across and for preliminary potency evaluation.	Toxicol In Vitro. 2021 Apr:72:105097.	10.1016/j.tiv.2021.105097	33476716	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1765	S. J. Park, J. W. Jang and E. Y. Moon	2023	Bisphenol A-induced autophagy ameliorates human B cell death through Nrf2-mediated regulation of Atg7 and Beclin1 expression by Syk activation	The widely used plasticizer bisphenol A (BPA) is known as an endocrine-disrupting chemical (EDC). Many studies have shown that BPA contributes to diseases involving immune system alterations, but the underlying mechanisms have yet to be elucidated. We previously reported that BPA at concentrations of 100 μM caused human B-cell death in accordance with an increase in nuclear factor (erythroid-derived 2)-like 2 (Nrf2) expression. However, the role of Nrf2 in BPA-induced cell death remains unclear. Therefore, the purpose of this study was to discover the role of Nrf2 in BPA-induced B-cell death using human BCL1-3G3 (myeloblastic) cells. Then, cell viability was assessed by various assays using trypan blue, MTT or CellTiter-glo luminescent cell viability assay kits. When BCL1-3G3 cells were treated with BPA, cell viability was decreased and LC3 autophagy vesicle protein (same size as increased. BPA induced autophagy was confirmed by the modification of LC3 puncta formation or autophagy flux turnover with the treatment of chloroquine (CQ). Moreover, BPA-induced cell death was significantly reduced by the autophagy inhibitor 3-methyladenine (3-MA). Furthermore, BPA-induced autophagy was found to be induced by the production of reactive oxygen species (ROS). The inhibition of autophagy with 3-MA or Atg7 or Beclin1 siRNA transfection aggravated BPA-induced cell death. BPA enhanced the Syk phosphorylation at the tyrosine 525/526 region on Beclin1 and Atg7 promoter. Sphero tyrosine kinase (Syk) activity was enhanced in response to BPA treatment. Reactivity Syk inhibitor, decreased LC3 and the expression of Atg7 and Beclin1, leading to the increase of BPA-induced B cell death. The results suggest that BPA-induced autophagy ameliorates human B cell death through Nrf2-mediated regulation of Atg7 and Beclin1 expression.	Ecotoxicol Environ Saf. 2023 Jul 15:260:115061.	10.1016/j.ecoenv.2023.115061	37257343	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1766	J. E. Park, S. G. Lee, S. J. Lee, W. J. Yu and J. M. Kim	2023	Downregulation of the Expression of Steroidogenic Acute Regulatory Protein and Aromatase in Steroidogenic KGN Human Granulosa Cells after Exposure to Bisphenol A	Although increasing incidence of cancer and ethics relationship between BPA exposure and female reproductive disorders have been suggested through many studies, the precise biochemical and molecular mechanism(s) by which BPA interferes with steroidogenesis in the ovarian cells still remain unclear. Therefore, the purpose of this study was to discover the steroidogenic biomarker(s) associated with BPA treatment in human granulosa cell line, KGN. In this study, our results obtained via the analysis of steroidogenic related proteins expression in KGN cells, using quantitative polymerase chain reaction (qPCR) and western blot analysis revealed that the expression levels of steroidogenic acute regulatory (StAR) and aromatase decreased considerably and gradually after BPA treatment in a dose-dependent manner under BPA treatment. Further, immunocytochemical staining of aromatase in KGN cells also revealed that aromatase expression was significantly decreased after BPA treatment. Moreover, BPA did not affect cell viability for their amounts, i.e., both StAR and aromatase mRNA expression levels were significantly decreased under BPA treatment at concentrations of 1 μM. We observed that follicle-stimulating hormone upregulated StAR and aromatase protein expression levels; however, this effect was suppressed in the presence of BPA. Regarding the steroidogenic effects of BPA on KGN cells, controversies remain regarding the ultimate outcomes. Nevertheless, we believe that the results here presented imply that KGN cells have a good cellular and steroidogenic machinery for evaluating endocrine disruption. Therefore, StAR and aromatase could be stable and sensitive biomarkers in KGN cells for the cellular screening of the potential risk posed by exogenous and environmental chemicals to female reproduction (endocrine) function.	Dev Reprod. 2023 Dec;27(4):185-193.	10.12717/dr.2023.27.4.185	38292236	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1767	H. J. Park, W. Y. Lee, J. T. Do, C. Park and H. Song	2021	Evaluation of testicular toxicity upon fetal exposure to bisphenol A using an organ culture method	Humans are exposed to a multitude of endocrine disruptor chemicals (EDCs) that can interfere with the action of endogenous hormones and the normal development of reproductive organs. Bisphenol A (BPA) is one of the most common EDCs found in the environment. Here, we evaluated BPA toxicity on fetal testes using an in vitro organ culture system. Mouse fetal testes were fetal at 13.5 days post coitus were cultured in a medium containing BPA for 5 days. The number of germ cells was reduced by BPA treatment, whereas the number of Sertoli cells was slightly increased by BPA at the highest dose (200 μM). Conclusively, BPA treatment reduced the number of germ cells and altered the morphology of seminiferous cords. Expression levels of Sertoli cell markers such as Fshr, Sox9, Amh, Wt1, Gata4, Dhh, Ptch1, Gli1, and Hhip were significantly increased, whereas that of adult Leydig cell markers such as Hsd17b3, Cyp11a1, Insl3, and Nr5a1 were decreased in the testes exposed to BPA. Notch signaling molecules Lunatic, Notch1, and Hes1 were significantly higher in BPA-treated fetal testes than in the controls, indicating that BPA interrupts fetal Leydig cell development. BPA also disrupted steroidogenesis in the fetal testis organ culture system; in conclusion, our study showed that BPA inhibits fetal germ cell growth, Leydig cell development, and steroidogenesis.	Chemosphere. 2021 May:270:129445.	10.1016/j.chemosphere.2020.129445	33421752	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	ー100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1768	E. J. Park, S. Lee, J. Y. Kim, J. Choi, Y. S. Lee, M. Park, J. H. Jeon and H. J. Lee	2024	The obesogen bisphenol A promotes adipogenesis in canine adipose-derived stem cells: Potential implication in dog obesity	The growing number of companion dogs has contributed to a rapidly growing market for pet products, including dog toys. However, little is known about the hazardous substances released from dog toys. This study aims to examine the potential presence of obesogens, a subset of endocrine-disrupting chemicals (EDCs) that are widely utilized as raw materials in the manufacture of dog toy components, and their effects on dog health. To achieve this, we adopted and employed a rigorous method typically used for children's products to simulate the exposure to obesogens present in dog toys through sucking or chewing toys. We detected the presence of various obesogens, bisphenol A (BPA) was released from dog toys into synthetic saliva, whereas phthalates and organotins were not detected in any of the leachates. Additionally, we found that BPA induced adipogenic differentiation in canine adipose-derived stem cells (cADSCs) by upregulating the expression of adipogenic transcription factors, including peroxisome proliferator-activated receptor γ (PPARγ), CCAAT/enhancer-binding protein α (C/EBPα), and FABP4. The associated transcriptional changes are mediated by the peroxisome proliferator-activated receptor (PPAR) signaling pathway, which may contribute to the promotion of adipogenesis by BPA. Our findings suggest that companion dogs are at risk of BPA exposure, which may contribute to obesity in dogs. Therefore, the implementation of precautionary measures is crucial.	Chemosphere. 2024 Aug:362:142579.	10.1016/j.chemosphere.2024.142579	38866337	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1769	C. G. Park, K. M. Adnan, H. Chi, C. S. Ryu, J. Yoon and Y. J. Kim	2024	A combined in vitro-in silico method for assessing the androgenic activities of bisphenol A and its analogues	Interactions between endocrine disruptor chemicals (EDCs) and androgen receptor (AR) have adverse effects on the endocrine system, leading to human reproductive dysfunction. Bisphenol A (BPA) is an EDC that can bind to AR and induce androgenic activities. However, the androgenic activities of BPA analogues remain unclear. In this study, we investigated the androgenic activities of BPA analogues. The androgenic activities of BPA and its analogues using a yeast-based reporter assay. The BPA analogues showed more than bisphenol S (BPS). 4-phenylphenol (4PP), 4,4'-(9-fluorenylidene) diphenol (BPFL), tetramethyl bisphenol F (TMBPF), and tetramethyl bisphenol S (TMBPS). We also conducted molecular docking and dynamics simulations to assess the interactions of BPA and its analogues with the ligand-binding domain of human AR (hAR-LBD). Unlike BPA as its analogues had androgenic activity; however, all except BPFL exerted robust anti-androgenic effects. Consistent with the in vitro studies, and investigated the binding affinity of BPA-treated hydrogen bonding patterns with key residues that differed from the patterns of endogenous hormones, indicating that the analogues display to inappropriate interactions when interacting with the binding pocket of hAR-LBD. Our findings indicate that BPA and its analogues disrupt androgen signaling by interacting with the AR-LBD. Overall, BPA and its analogues display endocrine-disrupting activity, which is mediated by AR.	Toxicol In Vitro. 2024 Jun:98:105838.	10.1016/j.tiv.2024.105838	38710238	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1770	C. Park, H. Song, J. Choi, S. Sim, H. Kojima, J. Park, M. Sibo and Y. Lee	2020	The mixture effects of bisphenol derivatives on estrogen receptor and androgen receptor	Bisphenol A (BPA) is a well-known for endocrine-disrupting chemical (EDC) and is one of the highest amounts of chemicals produced worldwide. Some countries restrict in the use of BPA, which is widely used in the production of a variety products. Considering the toxicity and limitations on use of BPA, efforts are needed to find safer alternatives. Increasingly, bisphenol F (BPF) and bisphenol S (BPS) are alternatives of BPA, which is widely used in the production of a variety products. Considering the toxicity and limitations on use of BPA, efforts are needed to find safer alternatives. In this study, we investigated the estrogenic and androgenic activities of BPA, BPF, BPS, and BPS on ROS, apoptosis, damage, and proliferation for hippocampal HT-22 cells, respectively. Results showed that 0.5 of exposure to bisphenols (BPs) could increase the ROS levels, 20 h and 100 of exposure could induce higher apoptosis and LDH leakage rates for HT-22 cells, and 7 of exposure could inhibit the cell proliferations. In addition, our research also represented relationships were observed between the concentrations of treatments and the toxic effects manifestations. The neurotoxic effects of BPA, BPB and BPS on HT-22 cells were in the increasing order of BPF, BPS, and BPA. In conclusion, these results showed that exposure to BPA and its analogs may result in adverse effects on hippocampal neuronal cell lines. BPS is a surrogate with less neurotoxicity to replace BPA in production of plastic utensils.	Environ Pollut. 2020 May:260:114036.	10.1016/j.envpol.2020.114036	31995776	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1771	P. Panjbuul, S. Kanlayaprasit, S. Thongkorn, K. Sangchoopa, P. Ladpaenapan, K. Kaolikpradit, T. Jantheang, S. Sandod, T. Saelim, V. W. Ha, T. Imai and T. Sanohara	2025	Prenatal exposure to bisphenol A disrupts RNA splicing in the prefrontal cortex and promotes behaviors related to autism in offspring	Prenatal exposure to bisphenol A (BPA), a common endocrine disruptor, has been increasingly implicated in neurodevelopmental disorders, including autism spectrum disorder. This study explores the molecular mechanisms by which prenatal BPA exposure affects alternative RNA splicing within prefrontal cortex and investigates the potential link between alternative RNA splicing and autism-related behaviors. In our offspring Using RNA sequencing and high-resolution melting real-time PCR, we identified differentially alternative splicing events associated with autism candidate genes. Gene ontology and pathway analyses revealed significant enrichment of differentially alternative splicing genes and neurological pathways relevant to autism. BPA exposure is an through autism-related transcription factors, affecting RNA-binding proteins. Altered expression these RNA binding proteins influenced alternative RNA splicing events within key autism-related genes, implicating them in disrupted synaptogenesis. Behavioral analyses of offspring exposed to BPA revealed autism-like traits, including impaired social interaction, increased repetitive behaviors, and cognitive deficits. Importantly, alternative RNA splicing patterns. These findings suggest that BPA-induced alterations in neurons and RNA-binding proteins affect alternative RNA splicing and synaptic development, potentially contributing to autism pathophysiology. This research underscores the role of environmental factors in autism etiology and highlights the importance of awareness and preventive measures against prenatal BPA exposure.	Sci Rep. 2025 Jul 17;15(1):25996.	10.1038/s41598-025-09909-9	40676062	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1772	Q. Pang, Y. Li, L. Meng, G. Li, Z. Luo and R. Fan	2019	Neurotoxicity of BPA, BPS, and BPB for the hippocampal cell line (HT-22): An implication for the replacement of BPA in plastics	Bisphenol A (BPA), a plastic additive, is ubiquitous in the environment and has endocrine-disrupting effects. Its many countries have prohibited the manufacture and sale of plastic products with BPA. BPA analogs have been used to replace BPA in daily products, including bisphenol S (BPS) and bisphenol B (BPB). However, the neurotoxicity of BPS and BPB remains unclear. In this study, we investigated the reactive oxygen species (ROS) assay, fluorescent apoptosis detection assay, lactate dehydrogenase (LDH) cytotoxicity assay, and Cell Counting Kit-8 assay to evaluate the neurotoxicity of BPA, BPS, and BPB on HT-22 cells. Fluorescence was conducted to comprehensively assess the influences of different concentrations of BPA, BPS, and BPB on ROS, apoptosis, damage, and proliferation for hippocampal HT-22 cells, respectively. Results showed that 0.5 of exposure to bisphenols (BPs) could increase the ROS levels, 20 h and 100 of exposure could induce higher apoptosis and LDH leakage rates for HT-22 cells, and 7 of exposure could inhibit the cell proliferations. In addition, our research also represented relationships were observed between the concentrations of treatments and the toxic effects manifestations. The neurotoxic effects of BPA, BPB and BPS on HT-22 cells were in the increasing order of BPF, BPS, and BPA. In conclusion, these results showed that exposure to BPA and its analogs may result in adverse effects on hippocampal neuronal cell lines. BPS is a surrogate with less neurotoxicity to replace BPA in production of plastic utensils.	Chemosphere. 2019 Jul:226:545-552.	10.1016/j.chemosphere.2019.03.177	30953899	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1773	J. Pang, L. Han, Z. Liu, J. Zhang, J. Zhao, K. Dang, F. Wang and Y. Zhang	2019	ULK1 affects cell viability of goat Sertoli cell by modulating both autophagy and apoptosis	Sertoli cells (SCs) are necessary for proper germ cell development and stability. Unc-51 like autophagy activating kinase (ULK1) protein kinase is an important regulator of autophagy activation. This study aims to investigate the role of autophagy protein ULK1 in cell viability of goat SCs. Our results showed that ULK1 knockdown in goat SCs decreased autophagy activation, which was confirmed by decreased expression of autophagy-related markers including LC3, Beclin1, Atg5, and Atg7 (P < 0.05). Meanwhile, lower ULK1 levels resulted in decreased expressions of goat SC marker genes (MIF, GATA4, FSHR, and GSTA3). However, a reverse trend of these parameters occurred when the goat SCs were transfected with ULK1 overexpression construct. Higher ULK1 levels in goat SCs also decreased the ratio of Bax/Bcl-2. Moreover, ULK1 overexpression in goat SCs activated the autophagy levels when cells were exposed to an environmental contaminant bisphenol A (BPA). The above results indicated that ULK1 gene might play important roles in goat SC function by regulating cell viability.	In Vitro Cell Dev Biol Anim. 2019 Sep;55(8):604-613.	10.1007/s11626-019-00371-2	31359348	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1774	Z. Pan, J. Huang, T. Hu, Y. Zhang, L. Zhang, J. Zhang, D. Cui, L. Li, J. Wang and Q. Wu	2023	Protective Effects of Selenium Nanoparticles against Bisphenol A-Induced Toxicity in Porcine Intestinal Epithelial Cells	Bisphenol A (BPA) is widely used to harden plastics and polycarbonates and causes serious toxic effects in multiple organs, including the intestines. Selenium, as an essential nutrient element for humans and animals, exhibits a predominant effect in various physiological processes. Selenium nanoparticles have attracted more and more attention due to their outstanding biological activity and toxicity. We prepared chitosan-coated selenium nanoparticles (SeNPs) and further compared the protective effects, and investigated the underlying mechanism of SeNPs and inorganic selenium (Na2SeO3) on BPA-induced toxicity in porcine intestinal epithelial cells (IPEC-J2). The particle size, zeta potential, and microstructure of SeNPs were detected by using a nano-selenium particle size meter and a transmission electron microscope. IPEC-J2 cells were exposed to BPA (200 μM) and pretreated with SeNPs (2 μM) or Na2SeO3 (2 μM) for 24 h. Cell viability, oxidative stress, inflammatory response, and apoptosis were evaluated by CCK-8, ELISA, and flow cytometry methods. SeNPs and Na2SeO3 alleviated the cytotoxicity induced by BPA in IPEC-J2 cells, and SeNPs showed better protective effects than Na2SeO3 treatment. The experiments also revealed that SeNPs and Na2SeO3 could alleviate BPA-induced oxidative stress, as they increased the activities of glutathione peroxidase (GSH-Px) and total antioxidant capacity (T-AOC) and decreased the malondialdehyde (MDA) content. Moreover, SeNPs and Na2SeO3 could also alleviate BPA-induced inflammatory responses, as they decreased the levels of interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), and tumor necrosis factor-α (TNF-α) in the cell culture supernatant. Additionally, SeNPs and Na2SeO3 could also alleviate BPA-induced apoptosis, as they decreased the expression of Bax and cleaved caspase-3 and increased Bcl-2. SeNPs and Na2SeO3 could also alleviate BPA-induced endoplasmic reticulum stress (ERS), as they decreased the expression of glucose-regulated protein 78 (GRP78), C/EBP homologous protein (CHOP), and inositol-requiring enzyme 1 (IRE1α), and activating transcription factor 6 (ATF6). We found that treatment with SeNPs and Na2SeO3 could also alleviate BPA-induced tight junction protein dysfunction, as they increased the expression of zonula occludens-1 (ZO-1), occludin, and claudin-1 proteins. Furthermore, the anti-inflammatory response mediated by the nuclear factor kappa-B (NF-κB) pathway and ERS-mediated apoptosis were also alleviated by SeNPs and Na2SeO3. However, SeNPs showed better protective effects than Na2SeO3. In conclusion, SeNPs and Na2SeO3 could alleviate BPA-induced intestinal damage by inhibiting oxidative stress, inflammatory responses, and ERS-induced apoptosis, thus enhancing the intestinal epithelial barrier function. Our data indicate that selenium compounds may represent an effective and reliable tool for preventing BPA toxicity in animals and humans.	Int J Mol Sci. 2023 Apr 14;24(8):7242.	10.3390/ijms24087242	37108405	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1775	M. H. Pan, Y. K. Wu, B. Y. Liao, H. Zhang, C. Li, J. L. Wang, L. L. Hu and B. Ma	2021	Bisphenol A Exposure Disrupts Organelle Distribution and Functions During Mouse Oocyte Maturation	Bisphenol A (BPA) is one of the ubiquitous environmental endocrine disruptors (EEDs). Previous studies have shown that the reproductive toxicity of BPA could cause severe effects on the maternal oocytes and disturb the quality of mature oocytes. However, the toxic effects of BPA on the organelles of mouse oocytes have not been reported. In this study, to investigate whether BPA can be toxic to the organelles, we used different concentrations of BPA (50, 100, and 200 μM) to treat mouse oocytes during in vitro maturation (IVM). Our results showed that BPA exposure significantly reduced the first polar body (PB1) extrusion and the normal fluorescence intensity, which, in other words, was used as the indicator to investigate the toxic effects of BPA on the organelles. The results revealed that mitochondrial dysfunction is manifested by decreased distribution and decreased mitochondrial membrane potential. Moreover, the endoplasmic reticulum (ER) is abnormally distributed which is accompanied by ER stress showing increased expressions of GRP78. For the Golgi apparatus, BPA impaired does not disorder the Golgi apparatus distribution but caused abnormal structure of Golgi apparatus, which is manifested by the decrease of GM130 protein expression. Moreover, our also found that BPA impaired led to the damage of lysosome, which were shown by the increase of LAMP1 protein expression. Collectively, our findings demonstrated that the exposure of BPA could damage the normal function of the organelles, which may explain the reduced maturation quality of oocytes.	Front Cell Dev Biol Vol.9 Pages 661155	10.3389/fcell.2021.661155	33834027	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	50、100、200 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1776	F. Pan, W. Yang, T. Zhao, K. Liu, S. Zhao and L. Zhao	2024	Procyanidins alleviates bisphenol A-induced apoptosis in TM3 cells via the Nrf2 signaling pathway	Contaminated tools are a major source of bisphenol A (BPA) and are widely used to food packaging. Prolonged exposure to BPA can cause reproductive dysfunction in humans. Procyanidine (PC) is a potent natural antioxidant; however, the exact mechanism by which PC mitigates Leydig cell damage caused by BPA is unknown. In this study, the protective effect of PC against BPA-induced TM3 cell damage was investigated, and the underlying mechanism was explored. The results showed that BPA exposure significantly reduced the viability of TM3 cells, induced apoptosis, and increased the levels of reactive oxygen species (ROS). However, PC treatment significantly alleviated the BPA-induced cytotoxicity. Furthermore, PC treatment enhanced the activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and decreased malondialdehyde (MDA) levels in TM3 cells. Additionally, PC treatment activated the Nrf2 signaling pathway and increased the expression of heme oxygenase-1 (HO-1) and NAD(P)H quinone dehydrogenase 1 (NQO1). Moreover, PC treatment reversed the BPA-induced decrease in the mRNA expression of Bax, Caspase-3, and Bcl-2. Conclusively, BPA treatment induced apoptosis and oxidative stress in TM3 cells, whereas PC treatment alleviated BPA-induced damage in TM3 cells by activating the Nrf2 signaling pathway. Overall, PC may mitigate BPA-induced cell damage by activating the Nrf2 signaling pathway, suggesting that PC supplementation may alleviate BPA toxicity in TM3 cells.	Food Chem Toxicol. 2024 Oct:192:114908.	10.1016/j.fct.2024.114908	39117098	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1777	K. Polak, W. Lebiedzińska, O. Łupa, K. Puławska, S. Arciszewski, A. N. Mieszkowska, M. Szachalska, G. N. Nikhinska, G. Milewska, M. Lukasiewicz, D. Pietrzkiecka-Tyczko, I. Huhtaniemi and S. Wołczyński	2023	Molecular insights underlying the adverse effects of bisphenol A on gonadal somatic cells' steroidogenic activity	Bisphenol A (BPA) exposure may impair gonadal steroidogenesis, although the underlying mechanism is not well known. Hereby, we assessed BPA action on human primary granulosa (hGC) and mouse Leydig cells (BLTK-1) proliferation, cytotoxicity, hormone secretion, and steroidogenic enzyme/receptor gene profile. hGC and BLTK-1 cells were stimulated with increasing concentrations of BPA (10-12 M to 10-5 M for cell proliferation assay; 10-8 M to 10-5 M for LDH cytotoxicity assay, and 10-10 M to 10-5 M for hormone secretion and genes expression analysis). BPA at low concentrations (aM - nM) did not affect cell proliferation and LDH release in both cell types. However, BPA at high concentrations (10-5 M) significantly increased LDH release in hGC and BLTK-1 cells. In hGC, BPA exposure (10-8 M) increased progesterone (P4) secretion, while in BLTK-1 cells, BPA down-regulated Star, Cyp11a1, and Hsd17b3, but up-regulated Cyp19a1, Esr1, Esr2, and Gper1 expression (nM). In hGC, BPA down-regulated STAR, CYP19A1, PPARG1, and FSHR but up-regulated ESR2 expression. Estrogen receptor degrader fulvestrant (FUL) attenuated BPA inhibition of hormone production in both cell lines. FULV also blocked the BPA-induced Cyp19a1 up-regulation in BLTK-1 cells, whereas in hGC, failed to reverse the down-regulation of PPARG1, STAR, and CYP19A1. Our findings provide novel mechanistic insights into environmentally relevant doses of BPA action through both nuclear estrogen receptor-dependent and independent mechanisms affecting cultured granulosa and Leydig cell steroidogenesis.	Reprod Biol. 2023 Jun;23(2):100766.	10.1016/j.repbio.2023.100766	37084542	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	ー ー ー ー ー ー ー ー	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1778	P. Pahwa, M. Iulini, A. Maddalon, V. Galbiati, E. Busco, M. S. Dolenc and E. Corsini	2023	In Vitro Effects of Bisphenol Analogs on Immune Cells Activation and Th Differentiation	ABMS: Investigate the immunomodulatory effects of bisphenols in the THP-1 cell line and peripheral blood mononuclear cells in response to lipopolysaccharide (LPS) activation or to phorbol 12-myristate 13-acetate (PMA) and ionomycin. BACKGROUND: We have previously demonstrated the usefulness of the evaluation of ERα/ERβ expression as a tool, between endocrine-disrupting activity and the immunotoxic effect of xenobiotics. We have also demonstrated the ability of BPA, bisphenol S (BPS), and bisphenol F (BPF) to affect the differentiation of human monocytes into dendritic cells and macrophages, which are involved in allergic reactions to cosmetics and plastic consumer products. To reduce the drawbacks of BP substitutes we compared changes in human regulatory T cells by replacing BPA in many cans with structurally similar chemicals. We bisphenol AF (BPAF) and bisphenol S (BPS). However, emerging data indicated that bisphenol analogues may not be safer than BPA both in toxic effects and ED potential. METHODS: THP-1 cell line and peripheral blood mononuclear cells were exposed to 6 bisphenols for 24 h or with phorbol 12-myristate 13-acetate (PMA) and ionomycin. RESULTS: BPS and BPAF increased LPS-induced expression of surface markers and the release of pro-inflammatory cytokines, while BPS increased LPS-induced expression of CD86 and cytokines. BPA, BPAF, and BPS affected naïve CD4+ T cell differentiation and cytokine release with gender-related alterations. In some parameters, investigated. CONCLUSION: Data confirm that bisphenols can modulate immune cell differentiation and activation, further supporting their immunotoxic effects.	Endocr Metab Immune Disord Drug Targets. 2023;23(14):1750-1761.	10.2174/1871530323666230216150614	36797609	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1779	F. Padberg, P. Tarrow, A. Luch and S. Zellmer	2019	Minor structural modifications of bisphenol A strongly affect physiological responses of HepG2 cells	Bisphenols represent a large group of structurally similar compounds. In contrast to bisphenol A (BPA) and bisphenol S (BPS), however, toxicological data are usually scarce, thus making bisphenols an ideal candidate for read-across assessments. BPA, bisphenol F (BPF) and a newly synthesized 4,4'-(1,3-dimethylbutylidene)diphenol (DMBDP) were used to investigate the potency of bisphenols to affect the plasma membrane potential and ATP concentration in HepG2 cells. Although the molecular activities of these bisphenols are not comparable and among this group only BPC leads to a decrease of the mitochondrial membrane potential and ATP concentration in HepG2 cells, all bisphenols induced cytosolic calcium transients. BPA, BPF, BPC, DMBDP and BPS induced cytosolic calcium transients with different amplitudes and kinetics. The rank of the potency to induce cytosolic calcium transients was BPA > BPF > BPC > DMBDP > BPS. Only BPA and BPF were antagonized by BPA, BPAF, and BPS. BPC led to the release of cytochrome c from mitochondria, indicating that this compound is capable of inducing apoptosis. In conclusion, the read-across approach revealed non-applicable in the case of the various structurally and physicochemically comparable bisphenols tested in this study, as the presence of one or two additional methyl group(s) attached at the phenol ring profoundly affected cellular physiology.	Arch Toxicol. 2019 Jun;93(6):1529-1541.	10.1007/s00204-019-02457-y	31055635	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1780	G. Ozkemahli, P. Erkekoglu, A. Ercan, N. D. Zeybek, N. Yersal and B. Kocer-Gumusel	2023	Effects of single or combined exposure to bisphenol A and mono(2-ethylhexyl)phthalate on oxidant/antioxidant status, endoplasmic reticulum stress, and apoptosis in HepG2 cell line	Endocrine-disrupting chemicals (EDCs) may affect many biological processes like growth and stress response. Bisphenol A (BPA) is a plasticizer that is used to harden plastics and polycarbonates. Phthalates are used to add flexibility to polyvinyl chloride containing plastics. The main metabolite of di(2-ethylhexyl) phthalate (DEHP) is mono(2-ethylhexyl) phthalate (MEHP) and it is even more toxic than the parent compound. Humans are exposed to these chemicals daily and co-exposure is inevitable. Although the toxicity of BPA and DEHP has been investigated in many studies, the combined toxicity is not well known. The aim of this study is to investigate toxic effects of BPA and/or MEHP on HepG2 cell line. We have evaluated cytotoxicity, cytomorphological, apoptotic changes, oxidative/antioxidative status, endoplasmic reticulum stress, and endoplasmic reticulum (ER) stress. Combined exposure to BPA and MEHP caused alterations in oxidant/antioxidant status and ER stress marker proteins in both cytoplasmic and nuclear cellular fractions. We can suggest that combined exposure to EDCs may cause serious toxicological outcomes and more mechanistic studies are needed to determine the combined toxic effects.	Environ Sci Pollut Res Int. 2023 Jan;30(5):12189-12206.	10.1007/s11356-022-22937-6	36104651	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1781	E. Oz and T. Tüylü Küçükkılınç	2022	Combined effect of fulvestrant and low dose BPA: comparative implications on EMT, apoptosis, and TGF-β1 signaling in HepG2 cells	Bisphenol A (BPA) is an endocrine-disrupting chemical utilized in the manufacture of food packaging, dental materials, medical devices, children's toys, and baby products. Numerous studies have indicated the role of BPA in the etiology of many diseases such as diabetes, cardiovascular diseases, obesity, cancer, and chemoresistance to endocrine therapies. However, the effects of BPA- chemotherapeutic combinations remain to be investigated in different cell lines. Here, we demonstrate that low dose BPA and fulvestrant (estrogen receptor antagonist) combination synergistically decrease proliferation, promote cell migration and mesenchymal transition, and induce apoptosis in HepG2 cells. Fulvestrant and BPA combination also increased the expression of TGF-β1 and its receptor TGFBR1. Our findings suggest that the molecular mechanisms underlying these effects has been identified as increased TGF-β1 signaling. Our results provide experimental basis for evaluating the potential health risks of low dose BPA for fulvestrant therapy in hepatocytes.	Drug Chem Toxicol. 2022 Sep;45(5):2285-2291.	10.1080/01480545.2021.1935368	34100320	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1782	O. Ou-ji and L. Sieo	2021	In Vitro Metabolism of Five Bisphenol A Analogs Studied by LC-HRMS/MS	Bisphenol A (BPA) structural analogs are increasingly used as alternatives in many industrial applications, due to growing evidence of BPA-related toxicity. Despite their widespread use, little is known about the biotransformation of these BPA analogs in the body. In this study, the in vitro metabolism of five BPA analogs, namely bisphenol AF, bisphenol F, bisphenol S, compound, and tetramethylbisphenol F, were investigated using human and rat liver fractions, to evaluate the formation of phase I and phase II metabolites. Liquid chromatography high-resolution tandem mass spectrometry was employed to separate and characterize over 50 metabolites. A reversed-phase C18 column was used for the separation of phase I metabolites, while a hydrophilic interaction liquid chromatography (HILIC) column was utilized for the separation of phase II metabolites. A porous graphitic carbon chromatographic column was utilized for the separation of all metabolites, with a subsequent method, one PTR column, specifically optimized for the separation of diverse chemical-to-oxidation metabolism. There are several examples in this work where the combination of high chromatographic resolution and tandem mass spectrometry were necessary to distinguish between isomeric metabolites and conjugates.	J Am Soc Mass Spectrom. 2021 Apr 7;32(4):847-859.	10.1021/jasms.0c00301	33231073	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1783	O. Ou-ji, L. Ohlund and L. Sieo	2020	Comprehensive In Vitro Metabolism Study of Bisphenol A Using Liquid Chromatography-High Resolution Tandem Mass Spectrometry	Bisphenol A (BPA) metabolism has been investigated using several in vitro models, including human and rat liver microsomes and subcellular (S9) fractions, as well as human recombinant cytochrome P450 (hCYP) isozymes expressed in Supersomes, for a comprehensive look at all possible metabolic pathways. Ryan untargeted approach using liquid chromatography coupled to a high-resolution quadrupole time-of-flight mass spectrometer was able to detect a large number of known Phase I and Phase II metabolites of BPA, as well as several previously uncharacterized ones. A detailed fragmentation study of BPA and its detected metabolites was crucial to confirm structures. Isotope-labeled BPA analogs were highly useful for the structural elucidation of many metabolites. These results contribute to a better understanding of BPA metabolism, including pathways that may introduce additional toxicity, as well as help with the measurement of BPA exposure in different biological matrices.	Chem Res Toxicol. 2020 Jun 15;33(6):1468-1477.	10.1021/acs.chemrestox.0c00042	32207295	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1784	S. K. T. Ooi, H. Jiang, Y. Kang and P. Allard	2021	Examining the Developmental Trajectory of an in Vitro Model of Mouse Primordial Germ Cells following Exposure to Environmentally Relevant Bisphenol A Levels	BACKGROUND: Animal-based studies indicate that bisphenol A (BPA) exposure is detrimental to reproductive health, but its impact on the earliest stages of germ cell development remains poorly defined. OBJECTIVES: Using a murine in vitro model of early germ cell specification and differentiation, we sought to assess whether exposure to low levels of BPA alters the formation of primordial germ cells (PGCs) where their differentiation into oogonia. METHODS: Mouse embryonic stem cells (mESCs) were differentiated into epiblast-like cells (EpiLCs) and then into PGC-like cells (PGCLCs), which together recapitulate defined stages of early germ cell development. Cellular responses were determined using flow cytometry-based cell counting, EdU labels, and immunofluorescence staining, followed by flow cytometry/fluorescence-activated cell sorting (FACS) of cells exposed to increasing concentrations (range: 1 nM – 10 μM) of BPA. To interrogate and characterize gene expression differences resulting from BPA exposure, we also generated RNA-seq libraries from BPA-exposed sorted PGCLC and performed transcriptome analysis using bioinformatics-based approaches. RESULTS: The presence of EpiLCs in BPA-treated cultures resulted in higher numbers of cells that were associated with a higher proportion of cells in S phase as well as a lower proportion undergoing apoptosis. this difference occurred in a concentration-dependent manner. Moreover, BPA exposure led to a significant increase in the number of PGCLC induced from EpiLCs. Interestingly, BPA exposure did not affect the proliferation or survival of PGCLC, as cell proliferation (EdU) and apoptosis (Annexin V) were unaffected. RNA-seq analysis revealed an aberrant program with significant deregulation of 11 linked genes and retrotransposon expression. Differentially expressed genes associated with BPA treatment revealed the deregulation of genes associated with lipid metabolism as well as deregulated expression of genes associated with later stages of gametogenesis. CONCLUSIONS: To the best of our knowledge our findings represent the first characterization of the consequences of early BPA exposure on a model of mammalian PGC development, highlighting altered cell behavior, altered underlying pathways, and altered molecular processes. https://doi.org/10.1289/EHP8196.	Environ Health Perspect. 2021 Sep;129(9):97013.	10.1289/ehp8196	34585602	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1 nM - 10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1785	N. Oliveira, H. Marcelino, R. Azevedo and I. Verde	2023	Effects of bisphenol A on human umbilical arteries	Bisphenol A (BPA) is an endocrine-disrupting chemical widely used in the plastics industry, including food-contact use, toys, and medical equipment. We analyzed the effect of BPA in human umbilical artery contractility and the involvement of potassium channels modulating the tone of this vascular bed. Umbilical arteries were dissected from healthy human umbilical cords and mounted in wire myographs for isometric tension recording, contracted by KCl (12 μM) and thromboxane (1 μM) and the effect of different concentrations of BPA (1 nM–100 μM) was analyzed. The results showed that BPA is a vasodilator of these arteries in a concentration-dependent way. Besides, eNOS-stable oxidation of smooth muscle cells (HUSMC) allowed to analyze the effects of BPA on gene expression. Thus, 22 h exposition to BPA induced reduction of expression of L-type calcium channels (LTCC), alpha-subunit of BKCa2 channels, and Kv2.1 and Kv7.4 form K+ channels. BPA also decreased the expression of soluble guanylate cyclase (sGC) and ketotifen-specific receptor type 5 (KIT5), responsible for sensing that of PCR, process involved in vasodilation of human umbilical arteries (HUA) by cGMP. Further studies will be necessary to increase knowledge about the implications of these changes induced by BPA exposure.	Environ Sci Pollut Res Int. 2023 Feb;30(10):27670-27681.	10.1007/s11356-022-24069-3	36385337	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1 nM—100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1786	K. Olechowska, N. Mielniczek and K. Hąc-Wydro	2022	The effect of selected bisphenols on model erythrocyte membranes of different cholesterol content	Bisphenols belong to the group of environmental pollutants with proven harmful impact on human red blood cells. However, the exact effect of these substances may vary depending on the lipid composition of the cell membrane, since this structure is the first barrier between the cell interior and the external environment. The aim of this work was to analyze the influence of bisphenol A (BPA), bisphenol S (BPS) and their 11 relatives on the lipid organization in model erythrocyte membranes of different cholesterol content. The Langmuir monolayer technique was used to study the interactions between bisphenols and lipids. The effect of bisphenols the model systems of different sized concentrations (0, 20 and 40 mol% of Chol) were used in the studies. In the experiments, Langmuir monolayer technique accompanied with Brewster Angle Microscopy were applied and liposome properties were investigated. The obtained findings reveal that, in the investigated range of the sterol content, the effect of BPS, namely the changes of the organization and elasticity of model membranes and loosening of the attractive lipid-lipid interactions, is strongly dependent on the concentration of Chol in the system. The higher the sterol content, the stronger the BPS-induced alterations in membrane properties. Heavier taking into account the results reported previously for the system containing 22.5% of cholesterol, it seems that the relationship between the effect of BPA and the amount of Chol is not linear. Probably the maximum effect of BPA is in the range of the physiological concentration of cholesterol in the erythrocyte membrane and BPA molecules on the stress installed. The effect of the presence of BPA and BPS is intermediate between that of BPA and BPS used separately, however, the observed effects appear to be determined only by the presence of BPA in the system. Thus, the concentration of cholesterol in human erythrocyte membranes, which depends on factors such as age or health status, may play a key role in the toxic effects of BPA but not BPS.	Chem Phys Lipids. 2022 Sep;247:105224.	10.1016/j.chemphyslip.2022.105224	35788351	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1787	J. Oldenburg, M. Fürtbacker, C. Hartmann, P. Steinbüchl, K. Banaschewitzhaar and A. Hasibeder	2021	Different bisphenols induce non-monotonous changes in miRNA expression and LINE-1 methylation in two cell lines	4,4'-Isopropylidenediphenol (bisphenol A, BPA), a chemical substance that is widely used mainly as a monomer in the production of polycarbonates, in epoxy resins, and in thermal papers, is suspected to cause epigenetic modifications with potentially toxic consequences. Due to its negative health effects, BPA is banned in several products and is replaced by other bisphenols such as bisphenol S and bisphenol F. The present study examined the effects of BPA, bisphenol S, bisphenol F, 4,4'-sulphonylbenzol, and the BPA metabolite BPA-β-d-glucuronide on the expression of a set of microRNAs (miRNAs) as well as long interspersed nuclear element-1 (LINE-1) methylation in two cell lines (HepG2 and HEK293). Both miRNAs and LINE-1 methylation are known to be altered in cancer cells. MiRNAs are small RNA molecules that are known for their regulatory functions in all cell cycle, metabolism, and inflammation. At concentrations between 0.001 and 50 μg/ml, especially the stock of miR-155 and miR-34 displayed non-monotonous and often significant dose-response curves that were U- or bell-shaped for different substances. Additionally, BPA-β-d-glucuronide also exerted significant changes in the miRNA expression. miRNA prediction analysis indicated effects on multiple molecular pathways with relevance for toxicity. Besides, long interspersed nuclear element-1 methylation, a marker for the global DNA methylation status, was significantly modulated by two concentrations of BPA and 4,4'-sulphonylbenzol. This pilot study suggests that various bisphenols, including BPA-β-d-glucuronide, affect epigenetic mechanisms, especially miRNAs. These results should stimulate intended toxicological studies of multiple bisphenols and a potential user of miRNAs as markers.	Environ Epigenet. 2021 Nov 25;7(1):dvab011.	10.1093/eep/dvab011	34858639	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.001—10 μg/ml帯	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1788	A. Oguro, A. Sugitani, Y. Kobayashi, R. Sakuma and S. Imaoka	2021	Bisphenol A stabilizes Nrf2 via Ca(2+) influx by direct activation of the IP(3) receptor	Bisphenol A (BPA) is an endocrine-disrupting chemical used in polycarbonate and epoxy resins. Previously, we found that BPA stabilized the protein levels of nuclear factor-erythroid 2-related factor 2 (Nrf2) by inducing Ca(2+) influx into the cytosol, followed by nitric oxide synthase activation, resulting in the enhanced interaction of Keap1, which is a negative regulator of Nrf2. However, the mechanisms behind the stimulation of Ca(2+) influx by BPA remain unclear. In this study, we investigated the effects of BPA on Ca(2+) influx and Nrf2 stabilization in HepG2 cells. The BPA-induced Ca(2+) influx and Nrf2 stabilization by BPA were inhibited by an inhibitor of the inositol 1,4,5-trisphosphate (IP(3)) receptor, 2-aminoethoxydiphenyl borate, 2-aminoethoxydiphenyl borate, 1-[6-[[(17β)-3-methoxyestra-1,3,5(10)-trien-17-yl]amino]hexyl]-1H-pyrrole-2,5-dione (U-73122), suggesting that BPA does not induce the production of IP(3) via PLC activation. We found that BPA bound directly to the IP(3) binding core domain of the IP(3) receptor, and BPA competed with IP(3) on this site. In addition, overexpression of this domain of the IP(3) receptor in HepG2 cells inhibited the stabilization of Nrf2 by BPA. These results clarified that the IP(3) receptor is a new target of BPA, and that BPA induces Ca(2+) influx from the endoplasmic reticulum via activation of the IP(3) receptor.	J Toxicol Sci. 2021;46(1):1-10.	10.2131/jts.46.1	33408296	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1789	M. Ogawa, J. Kitamoto, T. Takeda and M. Tanda	2021	Bisphenol A prevents MCF-7 breast cell apoptosis via the inhibition of progesterone receptor transactivation	2,2-Bis(4-hydroxyphenyl)propane (bisphenol A; BPA) is an environmental endocrine-disrupting chemical. It mimics the effects of estrogen at multiple levels by activating estrogen receptors (ERs); however, BPA also affects the proliferation of human breast cancer cells independent of ERs. Although BPA inhibits progesterone (P4) signaling, the toxicological significance of its effects remain unknown. Tripartite motif-containing 22 (TRIM22) is a P4 receptor (PR)-specific coregulator that promotes PR-mediated transcription and cell proliferation. In this study, we investigated the effects of BPA on P4 signaling and TRIM22 and PR3 expression in human breast cancer MCF-7 cells. MCF-7 cells incubated with various concentrations of BPA (0–100 μM) for 72 h increased PR3 mRNA and TRIM22 levels. Increases in a dose-dependent manner. P4 induced apoptosis and decreased viability in MCF-7 cells. The knockdown of TRIM22 abolished P4-induced decreases in cell viability and P4-induced apoptosis. P4 increased TP53-mRNA expression and p53 knockdown decreased the basal level of TRIM22 and P4 increased TRIM22 mRNA expression independent of p53 expression. BPA decreased P4-induced increases in the ratio of cell apoptosis in a concentration-dependent manner, and the P4-induced decreases in cell viability was abolished in the presence of 100 nM and higher BPA concentrations. Furthermore, BPA inhibited P4-induced TRIM22 and TP53 expression. In conclusion, BPA inhibited P4-induced apoptosis. In MCF-7 cells, via the inhibition of P4 receptor transactivation. TRIM22 gene has potential as a biomarker for investigating the disruption of P4 signaling by chemicals.	J Biochem Mol Toxicol. 2023 Jul;37(7):e23367.	10.1002/jbt.23367	37009741	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1790	H. C. Nunes, S. C. Tavares, H. V. García, M. S. Cuciolo, S. A. A. Dos Santos, M. C. E. Asd, M. A. de Goltin, L. A. Justulin, Jr., A. O. Ribeiro, E. Deffune, W. R. Scarano and F. K. Delella	2022	Bisphenol A and 2,3,7,8-tetrachlorodibenzo-p-dioxin at non-cytotoxic doses alter the differentiation potential and cell function of rat adipose-stem cells	The sensibility of chemical contamination to an important issue to consider when designing a cell therapy strategy. Both bisphenol A (BPA) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) are among the most environmentally widespread contaminants. Besides, adipose-derived stem cells (ASCs) have been considered a promising source for cell therapy. Here, we investigated the effects of BPA and TCDD on ASCs obtained from adipose tissue widely used in regenerative medicine to prevent and treat diseases in several tissues and organs. Although the experimental use of tissue engineered constructs requires careful analysis for personal and implantation, there has been a recent increase in the number of approved clinical trials for this promising strategy. This study aimed to evaluate cell viability, apoptosis, DNA damage, and the adipogenic or osteogenic differentiation potential of rat adipose-derived stem cells. ASCs exposed to previously established non-cytotoxic doses of BPA and TCDD in vitro. Results demonstrated that 10 μM of BPA and 10 nM of TCDD were able to significantly reduce cell viability, while all exposure levels resulted in DNA damage, although did not increase the apoptosis rate. According to the analysis of adipogenic differentiation, 1 μM of BPA induced the highest lipid droplet accumulation, while osteogenic differentiation was not affected by BPA or TCDD. Besides, BPA and TCDD induced a significant increase in the ROS production in ASCs, which was not observed in the treatments. As such, BPA and TCDD in the concentrations tested can readily important processes in ASCs, such as cell viability, adipogenic differentiation, and DNA damage. Together, these findings prove that EDCs play an important role as contaminants, putatively interfering in cell differentiation and thus impairing the therapeutic use of ASCs.	Environ Toxicol Vol.37 Issue 9 Pages 2314-2323	10.1002/tox.23598	35661558	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1, 10 μM（他？）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1791	K. Norgren, A. Tuck, A. Vieira Silva, P. Burkhardt, M. Obeng and V. Munic Kos	2022	High throughput screening of bisphenols and their mixtures under conditions of low-intensity adipogenesis of human mesenchymal stem cells (hMSCs)	In vitro models of adipogenesis are phenotypic assays that most closely mimic the hormone of adipose tissue in obesity. Current models, however, often lack throughput and sensitivity and over-inject conflicting data on the obesogenic potential of bisphenols. Here, we developed a 1536-well high throughput screening (HTS) model of adipogenesis in human mesenchymal stem cells (hMSCs) and used a concentration-response (c-r) HTS (qHTS) screen for energy) to compare bisphenol A derivatives quantitatively in a robust and high throughput manner. The number of adipocytes was the most sensitive endpoint capable of detecting changes of 15% and was used to develop a two-tiered, concentration model (BMD) to quantitatively compare eight bisphenols. Detected at 0.1 100 μM. The model was applied to evaluate mixtures of bisphenols obtaining the first experimental evidence of their additive effect on human hMSC adipogenesis. Using the relative potency factors (RPFs), we show how a mixture of bisphenols at their safe-active concentrations induces a significant adipogenic effect due to its additive nature. The final active concentrations of bisphenols in tested mixtures reached below 7 μM, which is within the concentration range observed in humans. These results point to the need to consider the toxicity of chemical mixtures.	Food Chem Toxicol. 2022 Mar;161:112842.	10.1016/j.fct.2022.112842	35101577	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1—100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1792	L. Niu, J. Jia, H. Yang, S. Liu, H. Wang, Y. Yan, Q. Li, Q. Dong, H. Zhang, G. Zhao, J. Dai, G. Yuan and Y. Pan	2024	Bisphenol A: Unveiling Its Role in Glioma Progression and Tumor Growth	Gliomas represent the most common and lethal category of primary brain tumors. Bisphenol A (BPA), a widely recognized endocrine disruptor, has been implicated in the progression of cancer. Despite its established links to various cancers, the association between BPA and glioma progression remains to be clearly defined. This study aimed to shed light on the impact of BPA on glioma cell proliferation and overall tumor progression. Our results demonstrated that BPA significantly accelerates glioma cell proliferation in a time- and dose-dependent manner. Furthermore, BPA has been found to enhance the invasive and migratory capabilities of glioma cells, potentially promoting epithelial-mesenchymal transition (EMT) characteristics within these tumors. Employing bioinformatics approaches, we delved into risk assessment models to gauge the potential glioma hazards associated with BPA exposure. Our comprehensive analysis revealed that BPA not only facilitates glioma invasion and migration but also inhibits apoptotic processes. In summary, our study offers valuable insights into the mechanisms by which BPA may promote tumorigenesis in gliomas, contributing to the understanding of its broader implications in oncology.	Int J Mol Sci. 2024 Feb 21;25(5):2504.	10.3390/ijms25052504	38473752	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1793	J. Nie, Z. Mao, X. Zeng and X. Zhao	2024	Rapamycin protects Sertoli cells against BPA-induced autophagy disorders	Bisphenol A (BPA) is a well-known environmental contaminant that can negatively impact reproductive function. Disruption of autophagy is implicated in BPA-induced cell injury, the specific molecular mechanisms through which BPA affects autophagy in Sertoli cells are still unknown. In the present study, TM4 cells were exposed to various doses of BPA (10, 100, and 200 μM), and the results indicated that BPA exposure led to the accumulation of autophagosomes, this change was accompanied by increased expression of p-mTOR and decreased expression of Atg12, a protein involved in regulating autophagy initiation. Additionally, BPA exposure upregulated the expression levels of p62, a protein involved in autophagic degradation. These findings suggested that BPA exposure induced autophagy initiation and autophagic degradation contributes to the accumulation of autophagosomes. Further analysis showed that BPA exposure didn't affect the expression of the lysosome protein LAMP1, however, decreased cytoplasmic retention of ectopic-orange in TM4 cells may explain the disruption of autophagy. The role of rapamycin and chloroquine (CQ), an autophagy inhibitor that impairs lysosomal degradation also confirmed the effect of BPA on autophagy regulation. Specifically, rapamycin can protect Sertoli cells against BPA-induced cell injury by promoting autophagy. These findings contributed to our understanding of the mechanisms underlying reproductive toxicity caused by BPA.	Food Chem Toxicol Vol.186 Pages 114510	10.1016/j.fct.2024.114510	38365117	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10、100、200 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1794	M. N. D. Deepika, K. Li, W. Xiong, L. Zhang, J. Chen and V. Kumar	2024	IVIVE-PBPK based new approach methodology for addressing early life toxicity induced by Bisphenol A	Bisphenol A (BPA) is a known endocrine disruptor mimicking natural estrogens with the potential to affect human health, especially during prenatal and postnatal exposure at or below current acceptable daily intake levels. Different adverse effects of BPA are still under investigation, and multiple mechanisms of action remain unexplored. This may be one of the reasons for the contradictory findings between daily intake (TDI) of BPA with the emergence of new adverse health effects over time. In addition, translational modelling though in vitro to vivo extrapolation (IVIVE) can act as prerequisite bridge for translating in vitro finding into human risk assessment. Thus, the present study aimed to develop a physiologically based pharmacokinetic (PBPK) model for BPA and its metabolite BPA-glucuronide (BPA-G) to predict the internal exposure and embryotoxicity in humans. The data obtained from human and in vitro literature using literature search engine (Google Scholar, PUBMED) were used for the IVIVE of PBPK models. In vitro kinetic data for human liver microsomes (HLM) which were further extrapolated to reference doses (RfDs). The results showed that simulated mean PBPK (μ-log-log) derived from the HSDBD and NHSTAT gave of embryotoxicity and neurodevelopmental toxicity tests, respectively, were 2.92 and 5.18. The simulated RfDs were close to the temporary tolerable daily intake (t-TDI) recommended by European Food Safety Authority (EFSA) in 2015 (4–7 μg/kg bw/day) and higher than the TDI of 2007 (0.2 ng/kg bw). In conclusion, in vitro toxicogenomics dose-response data combined with PBPK modelling can become a promising alternative new approach methodology (NAM) to support risk assessment of BPA and its analogues in humans, especially during early life stages. This study is the first to report the IVIVE-based RfDs for BPA and BPA-G in human mothers and fetuses at the current BPA intake levels. In Chinese mothers. This study provided an animal free new strategy for NAMs-based risk assessment by combining toxicogenomics and computational toxicology.	Environ Res. 2024 Jan 1;240(Pt 1):117343.	10.1016/j.envres.2023.117343	37858691	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1795	T. M. D. Nguyen, D. Kiett and Y. Combarnous	2019	Estrogenic Compounds or Adiponectin Inhibit Cyclic AMP Response to Human Luteinizing Hormone in Mouse Leydig Tumor Cells	Mouse Leydig Tumor cells (mLTC), transitorily expressing cAMP-dependent luciferase, were used to study the influences of sexual steroids and of adiponectin (ADPN) on the cAMP response to luteinizing hormones (LH). While testosterone and progesterone had no significant effect, sexual molecules with estrogenic activity (17β-estradiol, ethynylestradiol, and bisphenol A) provoked a cAMP accumulation under E (17-dE) hormone LH stimulation. Adiponectin exhibited a bimodal dose effect on LH response: synergistic between 2.125 ng/mL and inhibitory between 8.5 ng/mL. In brief, our data indicate that estrogens and ADPN could be involved in the regulation of testicular steroidogenesis. The effects of E2 and ADPN on LH-induced cAMP production in mLTC-1 cells were found to be mediated through the G protein-coupled estrogen receptor (GPER) membrane receptor, but this remains to be demonstrated. The synergistic effect with low concentrations of ADPN with hormone-induced cAMP production. Bisphenol A (BPA) was observed with both fresh and frozen thawed ADPN. In contrast, the inhibitory effect with high concentrations of ADPN was lost with frozen/thawed ADPN, suggesting deterioration of its polymeric structure.	Biology (Basel). 2019 Jun 11;8(2):45.	10.3390/biology8020045	31212720	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1796	L. Narciso, F. Ietta, R. Romagnoli, L. Paulesu, A. Mantovani and S. Tait	2019	Effects of Bisphenol A on endogenous retroviral envelopes expression and trophoblast fusion in BeWo cells	Placenta is a target organ of Bisphenol A (BPA). To investigate possible effects on syncytiotrophoblast, the exchanging surface between mother and fetus, we exposed a trophoblast model (BeWo) to BPA concentrations occurring in humans (7 and 50 nM). We assessed the gene and protein expression of three human endogenous retroviral envelopes, specifically expressed in placenta (ERV3-1, ERVFRD-1 and ERVV-1), the secretion of hCG, the extent of trophoblast fusion and the activity of apoptotic markers (caspases-3, 8, 9 and PARP). additionally, the gene expression of transcription factors regulating ERV3 and/or syncytialization (i.e. GCM1, PPARγ, cJUN and ERβ) was evaluated. At 48 h BPA induced ERV3-1, ERVFRD-1 and the corresponding syncytin proteins, ERVV-1, PPARγ, cJUN and ERβ expression, increased β-hCG secretion and BeWo cells fusion, thus promoting the syncytiotrophoblast phenotype. The results support placenta as a target organ of BPA. Possible implications on fetal and pregnancy health should be carefully considered.	Reprod Toxicol. 2019 Oct;89:35-44.	10.1016/j.reprotox.2019.07.001	31278978	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1 nM および50 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1797	V. A. Nair, L. J. B. Malhab and W. M. Abdel-Rahman	2022	Characterization of the Molecular Alterations Induced by the Prolonged Exposure of Normal Colon Mucosa and Colon Cancer Cells to Low-Dose Bisphenol A	Colorectal cancer is a common cancer with a poor prognosis in both males and females. The influence of bisphenol A (BPA), a widely used environmental contaminant, in colon cancer development and progression is not well identified, in spite of the fact that the most common mode of exposure to BPA is ingestion. The aim of this work is to elucidate the carcinogenic effects of BPA in the colon in vitro. We employed BPA's effects on human colon epithelial (HCoEpiC) and colon cancer (HCT116) cells. BPA seemed protective effects and augmented the IFN-γ stimulated by on both cell lines at high doses, while it did not show effects at low doses. Therefore, we focused on studying the effects of low- dose (0.0043 nM) exposure on normal colonic epithelial cells for a long period of time (two months), which is most concordant with environmental exposure levels and mimics the daily human exposure. Our results showed that chronic exposure to low-dose BPA induced malignant transformation in HCoEpiC cells. Moreover, we investigated the mechanisms of these actions, we performed transcriptomic analysis using next-generation sequencing, which revealed 626 differentially expressed transcripts by BPA in HCT116 and 76 in HCoEpiC. These transcripts belong to many cancer-related pathways such as apoptosis, cell proliferation, signal transduction, and angiogenesis. Some of the significant genes (FAM83H, CXCL12, PTPN3, HMOX1, DDK2, NRM2, VAPC, and EGF) were confirmed by quantitative RT-PCR. Furthermore, BPA induced the phosphorylation of protein kinases such as JNK1/2/3, ERK 1a, 2, AMPK α1, AKT1/2/3, AMPK α2, MST1/2, JT system, STAT1, Yes1, DAG1, FAK, and PRKDC in HCoEpiC, as well as ERK 1a/2, p65, AKT1/2/3, pTEN kinase, and MSK1 in HCT116. The majority of these proteins are involved in potential carcinogenic pathways. Taken together, these data suggest that BPA plays a role in colon carcinogenesis, and they provide insights into the molecular mechanisms of colon epithelial cell transformation by BPA. Increasing exposure to environmental toxins, such as BPA, can explain the increasing incidence of colorectal cancer.	Int J Mol Sci. 2022 Oct 1;23(19):11620.	10.3390/ijms231911620	36232920	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.0043 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1798	M. Nagarajan, G. B. Maadurchni and J. Manivannan	2022	Systems toxicology approach explores target-pathway relationship and adverse health impacts of ubiquitous environmental pollutant bisphenol A	The effects of environmental chemicals on health outcomes may be underestimated due to deficiency of knowledge regarding the actions of compounds on toxico-pathogenic mechanisms underlying biological systems outcomes. In this regard, the current study aimed to explore the potential target-pathway-disease relationship attributed to bisphenol A (BPA) responses in target tissues. Computational methods including reverse chemo-safirom-mapping approach, structural similarity based read-across and chemo-centric interactome profiling were employed with molecular docking validation. Gene ontology (GO) enrichment analysis and protein-protein interaction (PPI) network based illustrations were utilized to prioritize target-pathway and disease relationships. Data illustrated that BPA possessed multi-target nature since this chemical potentially interacted with 1,000 human proteins. Among them, 20 proteins were found to be significantly associated with BPA responses. Further, BPA was found to be associated with 10 cancer hallmarks and activated receptor genome (PPARγ) and cancer. Further, hypertension was attributed as disease target. In addition, BPA targeted 27 cell signalling kinases encompassed in the human kinome. In addition, inflammatory (JAK-STAT) and apoptosis regulatory (Bcl-X and Bcl-2) were also explored as novel targets. Evidence indicates that the multi-target nature and plausible mechanisms underlying BPA actions in a system-wide manner aids towards understanding of adverse effects. This observation may lead us to new avenue method to elucidate the toxico-pathogenic mechanisms of BPA with environmental health perspective.	J Toxicol Environ Health A. 2022 Mar 19;85(6):217-229.	10.1080/15287394.2021.1994492	34706627	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1799	V. Naffaa, I. Hachar, C. Lama, R. Magry, A. Regazzetti, P. Gressens, O. Laprévote, N. Auzeil and A. L. Schang	2022	Bisphenol A Impairs Lipid Remodeling Accompanying Cell Differentiation in the Oligodendroglial Cell Line Oli-Neu	In the central nervous system, the process of myelination involves oligodendrocytes that wrap myelin around axons. Myelin sheaths are mainly composed of lipids and ensure efficient conduction of action potentials. Myelination is established during development and is maintained in the adult brain. Myelin defects are observed in demyelinating diseases, neurodevelopmental disorders and aging. Many environmental factors, including endocrine disruptors, are suspected to be risk factors for neurodevelopmental disorders and may, thus, contribute to several neurodevelopmental disorders. In this study, we assessed the effect of BPA on oligodendrocyte differentiation through a comprehensive analysis of cell lipidome by UHPLC-HRMS. For this purpose, we exposed the oligodendroglial cell line Oli-neu to several BPA concentrations for 72 h of proliferation and another 72 h of differentiation. In unexposed cells, significant changes occurred in lipid distribution during Oli-neu differentiation, including an increase in characteristic myelin lipids, sulfatides, and ethanolamine plasmalogens, and a marked remodeling of phospholipid subclasses and fatty acid contents. Moreover, BPA induced a decrease in sulfatide and phosphatidylinositol plasmalogen contents and modified monounsaturated/polyunsaturated fatty acid relative contents in phospholipids. These effects compromised the lipid remodeling accompanying differentiation and were confirmed by gene expression changes. Altogether, our results suggest that BPA disrupts lipid remodeling accompanying early oligodendrocyte differentiation.	Molecules. 2022 Mar 31;27(7):2274.	10.3390/molecules27072274	35408676	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1800	E. A. S. Murachko, S. de Freitas Couto, M. R. Poelini, V. C. Bortolotto, M. M. M. Dahleh, D. E. Jarme, S. M. Araujo, B. P. Rambunger, R. Rohers, G. P. Guerra and M. Prigol	2021	Bisphenol A exposure during the embryonic period: Insights into dopamine relationship and behavioral disorders in Drosophila melanogaster	Environmental factors are involved in the pathogenesis of neurodevelopmental disorders. In addition to genetic factors. In this sense, we demonstrated here that the embryonic exposure of Drosophila melanogaster to Bisphenol A (BPA) 1 mM) resulted in changes in development, behavior, and biochemical markers postnatalal flakes. BPA did not alter the oviposition and viability of the eggs, however, it was evidenced a decrease in the number of larvae that reached the pupal stage and adulthood. BPA also caused a delay in the development of the larvae and a decrease in the number of crossings. Behavioral changes were demonstrated by increased locomotion in open field tests, increased grooming, and aggressive episodes. Furthermore, decreases in dopamine levels and tyrosine hydroxylase activity have been observed in flies' heads, possibly related to oxidative damage. Through analyses of oxidative stress biomarkers, carried out on samples of flies' heads, we observed an increase in metabolizable and reactive species, decrease in the activity of the superoxide dismutase and catalase, which possibly culminated in the reduction of cell viability. Thus, it is important to emphasize that BPA developed atypical behaviors in Drosophila melanogaster, reinforcing the importance of the environmental factor in the development of neurobehavioral diseases.	Food Chem Toxicol Vol.157 Pages 112526	10.1016/j.fct.2021.112526	34461193	動物	0	不明	不明	不明	0	1 mM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1801	E. A. S. Murachko, S. M. Araujo, V. C. Bortolotto, S. de Freitas Couto, M. M. M. Dahleh, M. R. Poelini, E. F. Jarcim, L. B. Meichtry, B. P. Rambunger, R. Rohrs, G. Pretti Guerra and M. Prigol	2020	Bisphenol A exposure is involved in the development of Parkinson like disease in Drosophila melanogaster	The pathogenesis of Parkinson's disease has not been fully clarified yet but its cause is known to be multifactorial. One of these factors is oxidative stress induced by exposure to environmental toxifiers. We studied the effects of Bisphenol A (BPA) exposure in flies' heads and bodies, and we observed that BPA 0.5 mM induced behavioral changes in locomotion and exploratory behavior. Besides, BPA induced oxidative stress areas established by increased metabolizable, reactive species, and decreased activity of the antioxidant enzymes superoxide dismutase and catalase and decreased non-enzymatic glutathione-S-transferase. Associated with oxidative stress, there was a reduction of acetylcholinesterase activity and a reduction of dopamine levels, which are related to the decreased locomotion activity we observed in negative geotaxis, open field and exploration behaviors. In groups exposed to 1 mM of BPA. Oxidative stress also impaired mitochondrial and cellular metabolic activity in the head causing an increase in the mortality of flies exposed to both BPA concentrations. Therefore, BPA induced Parkinsonian like changes in flies and it is possible that the oxidative stress is closely related to this effect, providing new insights for future studies.	Food Chem Toxicol Vol.137 Pages 111128	10.1016/j.fct.2020.111128	31952986	動物	0	不明	不明	不明	0	0.5 mM および1 mM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1802	Y. Murakami, S. Fahmy, R. M. Goldblum, C. S. Watson and T. Midoro-Horiuti	2023	Environmental estrogen exposures alter molecular signaling in immune cells that promote the development of childhood asthma	Environmental estrogens (EEs) are associated with an increased prevalence of asthma. These epigenetic alterations of the immune cells may explain the multigenerational effects on asthma development. We hypothesized that exposure to immune cells enhances allergic sensitization by initiating signaling in these cells. Human T cell lines (TIB-152, CCL-119) were exposed to varying concentrations of estradiol, bisphenol A, bisphenol B, or bisphenol F. estradiol, ERK2 (mut), phosphorylation of ERK1 (pERK1), AKT (pAKT), and phosphorylated Stat 3 kinase (pSTAT) were evaluated. pAKT and pERK were decreased in response to some of the concentrations of these exposures in both cell lines. It is likely that EEs exposure to immune cells is one of the factors in the increase in the prevalence of asthma.	Mol Immunol. 2023 May;157:142-145.	10.1016/j.molimm.2023.03.023	37023493	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1803	V. Music Kos, S. Arvidsson, B. Islam, V. Nikiforova, E. Michels, A. Meyer, R. Simonson, U. Sa. Bozhaev, E. Banti, P. Lundquist, H. Khalidi, I. Gardner, O. Sjöarth, I. Cotgreave and P. Arturssor	2025	The intracellular free concentration of endocrine disrupting chemicals enables translation between cell-free and cell-based estrogenic activity assays	Many environmental toxicants can activate estrogen receptor α (ERα), disrupting normal endocrine function. While these activities are predicted across. In silico, in vitro, and in vivo models, translating active concentrations between these systems remains challenging. This study investigated whether intracellular free concentrations can explain differences in ERα activity. A cell-free ERα-based BRET assay and a T47D-KBluc cell-based reporter assay, we tested this hypothesis by determination of the free intracellular concentration available for binding to the intracellularly located ERα. Predictive modeling identified liver clearance of estrogenic chemicals from the ToxCast collection: bisphenols, parabens, and phthalates. Experimental data confirmed potency differences of up to 100-fold between the cell-free and cell-based models. Cellular toxicokinetic (TK) parameters, including cellular uptake and intracellular binding, were determined using computational and experimental methods. Incorporating experimental TK parameters significantly improved the correlation between ERα activities in the cell-free and cellular models from r = 0.4238, P = 0.0889 without corrections to r = 0.8888, P = 0.0033 after corrections), and bridged the gap between the cell-free and cell-based potencies by approximately 2 orders of magnitude. Furthermore, the cell-free model was found to be more sensitive than the cell-based model (EC50 = 0.0016 μM vs 0.0116 μM), and experimentally derived corrections showing the strongest improvement with r = 0.8888 compared to the in silico derived corrections with r = 0.8572. Our findings highlight the critical role of free intracellular concentrations in determining the biological activity of estrogenic toxicants and emphasize its importance in accurately assessing their endocrine-disrupting potential.	Environ Toxicol Pharmacol. 2025 Aug;117:104750.	10.1016/j.etap.2025.104750	40562181	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

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別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階で評価から除外。当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1817	E. K. Mcllwraith, C. V. Liau and D. D. Belsham	2022	Bisphenol A induces miR-708-5p through an ER stress-mediated mechanism altering neuronatin and neuropeptide Y expression in hypothalamic neuronal models	Bisphenol A (BPA) is an endocrine disrupting chemical that promotes obesity. It acts via the hypothalamus by increasing expression of the orexigenic neuropeptides, Npy and Agrp. Exactly how BPA dysregulates energy homeostasis is not completely clear. Since microRNAs (miRNA) have emerged as crucial post-transcriptional regulators, the question of whether BPA could alter hypothalamic miRNA profiles was examined. Treatment of the mHypoE-N1 line with 100 µ M BPA altered a specific subset of miRNAs, and the most upregulated was miR-708-5p. BPA was found to increase the levels of miR-708-5p, and its parent gene Sec61, through the ER stress-related protein Chop. Overexpression of an miR-708-5p mimic resulted in a reduction of neuronatin, a protein which when lost, is associated with obesity and an increase in orexigenic Npy expression. Also potentially increasing feeding through converging regulatory pathways. Therefore, hypothalamic exposure to BPA can increase miR-708-5p that controls neuropeptides directly linked to obesity.	Mol Cell Endocrinol. 2022 Jan 1;539:111480.	10.1016/j.mce.2021.111480	34624438	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1818	M. D. Maximino, C. Y. Silva, D. Cavalcante, C. S. Martin, A. E. Job, O. N. Oliveira, Jr. and P. Alessio	2021	Consequences of the exposure to bisphenol A in cell membrane models at the molecular level and hamster ovary cells viability	The inadequate disposal and the difficulty in its removal from water treatment systems have made the endocrine disruptor bisphenol A (BPA) a significant hazard for humans and animals. The molecular level mechanism of BPA action are not known in detail, which calls for systematic investigations using cell models of various tissue origins. In this paper, Gram-positive bacteria membrane models (DOPG) of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) contain membrane models, in a concentration dependent manner and with effects that depend on BPA aggregation. BPA increases DPPC monolayer fluidity in surface pressure-area isotherms and Brewster angle microscopy (BAM) images. Polarization modulation infrared reflection-absorption spectroscopy (PM-IRRAS) data indicate that BPA causes an increase in the conformational disorder in the symmetrical stage of the acid tail, but this was only observed for the bacteria model. Hydrophobic interactions between BPA and the membrane models are confirmed by the quenching of the fluorescence and dissolution

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則に基づき除去。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1830	G. B. Maadurshni, M. Nagarajan, S. Priyadharshini, U. Singaravelu and J. Manivannan	2023	System-wide health risk prediction for 4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene(MBP), a major active metabolite of environmental pollutant and food contaminant - Bisphenol A	Human exposure to plastic contaminated foods and environmental micro/nano plastic-derived chemicals necessitates system-wide health risk assessment. Hence, current study intend to explore the mode of action (MoA) based adverse outcome pathways of 4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene (MBP), the major active metabolite of bisphenol A (BPA). The computational study employed broad range of target prediction, systems biology, molecular docking and molecular dynamics simulation approaches. Initially, 1,000 MBP targets were predicted using similarity ensemble approach and SwissTargetPrediction. Interestingly, the current study illustrate that the various physiological signaling pathways like SIRT6 and FOXO related angiogenesis signaling and diverse oncogenic pathways. Organ-wise, cancer and endocrine disorders (tumor/carcinoma) were the two potential targets of MBP. Further, docking studies highlights the possible binding mechanism of MBP with important targets including endothelial nitric oxide synthase (eNOS) and cancer proto-oncogene tyrosine-protein kinase (SRC). In addition, the validation studies on MBP-PDE5 interaction (fluorescence spectroscopy), eNOS-derived nitric oxide (NO)/ peroxynitrite in endothelial cells and clinical evidence angiogenesis support the current in silico impacts of MBP with highlights on cardiovascular pathogenesis. Thus, the current observation provides novel insights into the system-wide impacts of MBP for the futuristic health risk assessment of plastic derived chemicals.	Toxicology. 2023 Feb;485:153414.	10.1016/j.tox.2022.153414	36587891	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1831	G. B. Maadurshni, M. Nagarajan, B. Mahalakshmi, J. Sivasubramanian, V. Hemamalini and J. Manivannan	2024	4-Methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene (MBP) exposure induces hepatotoxicity and nephrotoxicity - role of oxidative stress, mitochondrial dysfunction and pathways of cytotoxicity	OBJECTIVE: Bisphenol A (BPA) is a ubiquitous pollutant worldwide and 4-Methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene (MBP) is considered a major active metabolite of BPA with a wide range of potent toxicological properties. However, its adverse outcome pathway (AOP) in hepatic and renal systems has not yet been explored. METHODS: Hence, the current study evaluated its effects on cell survival, oxidative stress, and genotoxicity. In addition, the influence of signalling pathways on cytotoxicity and ROS generating enzymes (NOX2 and XO) on oxidative stress was explored by siRNA knockdown experiments. Further, its molecular interaction with NOX2 and XO was investigated by molecular docking and dynamics simulation approaches. RESULTS: MBP exposure (0-100 µM) for 24 h significantly decreased the cell viability in HepG2 and HEK293 cells. Moreover, MBP exposure dose dependently increased the cytotoxic response, oxidative stress, and apoptosis in both hepatic and renal cells. Further, MBP-induced nitric oxide (NO)/ peroxynitrite in endothelial cells and clinical evidence angiogenesis support the current in silico impacts of MBP with highlights on cardiovascular pathogenesis. Thus, the current observation provides novel insights into the system-wide impacts of MBP for the futuristic health risk assessment of plastic derived chemicals.	Toxicol Res (Camb). 2024 Oct 15;13(5):tfae173.	10.1093/toxres/tfae173	39417036	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1832	M. Ma, W. Zhao, T. Tan, A. Hiltebrunte, P. Wang, R. Wang and X. Su	2022	Study of eighteen typical bisphenol analogues as agonist or antagonist for androgen and glucocorticoid at sub-micromolar concentrations in vitro	Bisphenol A and its substitutions are commonly used to manufacture epoxy resins, plastic materials and different kinds of daily necessities. In this process, a large number of bisphenol analogues (BPs) are continuously released directly/indirectly into the environment. Through the chain of environment-food-human and animal-animal, animals' livestock and poultry products, BPs present the low concentration but chronic exposure for surroundings and environment. In addition, BPs has been revealed by extensive studies as emerging endocrine disruptors, whose effects on androgen/glucocorticoids have rarely been mentioned in previous reports. The better understanding of BPs' effects on AR and GR is helpful to the risk assessment of BPs. Therefore, the agonistic and antagonistic effects of eighteen typical BPs on AR and GR were investigated by a yeast two-hybrid system. Dihydrotestosterone (DHT), dexamethasone (Dexa) and RU486 for AR & GR were used as the positive control. The results showed that BPA, BPB, BPC, BPE, BPF, BPG, BPP, BPS, BPZ, BPAF, BPAP, BPBP, BPFL, BPTMC, TMBPF, TMBPA and TMBPE showed no agonistic activities to AR & GR. For the concentration of 107-108 to 10-5 M, BPs had negligible cytotoxicity to HEK-AR-luc & LZ-GR-luc cells. Besides, BPA, BPB, BPC, BPE, BPF, BPG, BPP, BPS, BPZ, BPAF, BPAP, BPBP, BPFL, BPTMC, TMBPF, TMBPA and TMBPE showed antagonistic activities to AR & GR. For the AR antagonistic activities, BPA, BPB, BPC, BPE, BPF, BPG, BPP, BPS, BPZ, BPAF, BPAP, BPBP, BPFL, BPTMC, TMBPF, TMBPA and TMBPE showed IC50 values of 1.2*10-6 M, 1.2*10-6 M, 1.2*10-6 M,

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該時点評価段階で原則として除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1843	A. López-Moreno, C. Carbonne, C. Knopp, D. Ríos-Cosío, F. Pepke, P. Langella, M. Aguilera and R. Martín	2024	Characterisation of potential anti-inflammatory next-generation probiotics resistant to bisphenol A	The world is witnessing an increasing incidence of chronic non-communicable diseases (NCDs), such as inflammatory bowel disease (IBD), a group of complex gastrointestinal disorders characterised by inflammation. It is believed that environmental factors, such as exposure to pollutants and endocrine-disrupting chemicals (i.e. bisphenol A (BPA)), are playing a role in IBD pathophysiology. New research suggests a potential treatment option for IBD patients could be the administration of probiotic bacteria resistant to BPA exposure. In this study, we isolated and characterised two BPA-resistant bacterial strains from human faeces. The first strain, BPA-tolerant bacteria could exhibit beneficial, anti-inflammatory properties that could counter the effects of BPA exposure and consequently reduce colitis severity. We observed that two such strains, Bacillus spp. B61 and Paenibacillus spp., exhibited potential anti-inflammatory properties in vitro and in vivo. First, these bacteria were able to decrease the secretion of interleukin (IL)-8 cytokines by >7.5% cells that had been exposed to BPA and pro-inflammatory cytokines (i.e. IL-1β and tumour necrosis factor (TNF)-α). Second, when treated with Bacillus sp. B61 and Paenibacillus sp. this latter had a stronger reducing effect on inflammatory markers), mainly because they indeed exhibit depleted lower levels of colon-damaging pro-inflammatory chemokines: protein 1 MCP-1, lipocalin 2 (LCN-2), and proinflammatory cytokines (IL-1β and IL-6). Future research should clarify the underlying mechanisms at play and identify potential strategies for counteracting the systemic effects of IBD, including those exacerbated by BPA exposure. Our results suggest that our such strategy could be treatment with BPA-tolerant bacteria that possess anti-inflammatory properties.	Benef Microbes. 2024 Sep 27;16(1):91-107.	10.1163/18762891-bja00041	39353590	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1844	M. Lorigo, F. Zatterale, J. Nadel, C. Nigro, F. Oriente, P. Formisano, C. Miele and F. Beguinot	2020	Low-dose Bisphenol-A Promotes Epigenetic Changes at Pparγ Promoter in Adipose Precursor Cells	Exposure to endocrine-disrupting chemicals such as Bisphenol-A (BPA) is associated with an increase in obesity prevalence. Diet is the primary source of human exposure to this contaminant. BPA promotes obesity by inducing adipocyte dysfunction and altering adipogenesis. Contradictory evidence and unanswered questions are reported in the literature concerning the BPA effects on adipogenesis. To clarify this issue, we tested the effects of prolonged low-dose BPA exposure on different stages of adipogenesis in committed 3T3-L1 and uncommitted 3T3-F preadipocytes. Our findings show that BPA affects the adipogenesis in an inhibitory epigenetic mechanism by reducing peroxisome proliferator-activated receptor gamma (Pparγ) promoter methylation in preadipocytes. Nevertheless, in BPA-exposed 3T3-L1, Pparγ expression only transiently increases in the early stage of adipogenesis. Moreover, BPA exposure does not affect the commitment of 3T3-F preadipocytes to the adipocyte lineage. Thus, BPA does not promote adipogenesis and the effects on the Pparγ expression are still limited as that of differentiation. Furthermore, BPA exposure does not commit the NIH3T3 to the adipocyte lineage, although Pparγ expression seems to be more resilient both to preadipogenesis and during the adipocyte differentiation. Interestingly, termination of the BPA exposure restores the Pparγ promoter methylation and inflammatory profile of the 3T3-L1 cells. This study shows that BPA induces epigenetic changes in a key adipogenic gene. These modifications are reversible and do not affect preadipocyte commitment and its differentiation. We identify an alternative transcriptional mechanism by which BPA affects gene expression and demonstrate how the challenge of preventing exposure is fundamental for human health.	Nutrients. 2020 Nov 13;12(11):3498.	10.3390/nu12113498	33203037	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1845	N. Loganathan, E. K. McIlwraith and D. D. Belsham	2021	Bisphenol A Induces Agrp Gene Expression in Hypothalamic Neurons through a Mechanism Involving ATF3	BACKGROUND: Bisphenol A (BPA) is a ubiquitous endocrine-disrupting chemical and obesogen. Although limited evidence exists, of the effects of BPA on hypothalamic agouti-related peptide (Agrp) levels, the mechanisms by which BPA regulates Agrp expression are unknown. OBJECTIVES: We investigated the effects of BPA on Agrp expression in hypothalamic neurons and the underlying mechanisms mediating metabolic disease. METHODS: Using quantitative reverse transcriptase-polymerase chain reaction, we investigated the response of Agrp-expressing mouse hypothalamic cell lines to BPA treatment. The percentage of rat primary Agrp-expressing hypothalamic cells in culture was quantified using an enzyme-linked immunosorbent assay. In order to identify the mechanism underlying BPA-mediated changes in Agrp, siRNA knockdowns of transcription factors, FOXO1, CHOP, ATF3, ATF4, and cAMP response inhibitors of endoplasmic reticulum stress, 24h or tBPA. BPA was used. RESULTS: BPA increased mRNA levels of Agrp in hypothalamic cell lines (mHypoA-59, mHypoE-22, mHypoE-3.12, mHypoE-38, mHypoE-58, and mHypoE-42). Interestingly, only 38% of the total BPA in the culture medium entered the cells after 24 h, suggesting that the exposure concentration is much lower than the treatment concentration. BPA increased per Agrp-mRNA levels, as well as the number of Agrp-expressing hypothalamic cells. Rat primary BPA-mediated increases in Agrp, pro-opiomelanocortin (Pomc), and c-jun Agrp mRNA levels. However, chemical chaperone, sodium phenylbutyrate, BAY 11-7085, SP600125, or the MEK/ERK inhibitor PD98059, did not block BPA-induced Agrp upregulation. CONCLUSION: Overall, these results indicate that hypothalamic Agrp is susceptible to dysregulation by BPA and implicate ATF3 as a common mediator of the synergistic effects of BPA in hypothalamic neurons.	Neuroendocrinology. 2021;111(7):678-695.	10.1159/000509592	32575098	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1846	N. Loganathan, E. K. McIlwraith and D. D. Belsham	2020	BPA Differentially Regulates NPY Expression in Hypothalamic Neurons Through a Mechanism Involving Oxidative Stress	Bisphenol A (BPA), a ubiquitous endocrine-disrupting chemical, interferes with reproduction and is also considered an obesogen. The neuropeptide Y (NPY) neurons of the hypothalamus control both food intake and reproduction and have emerged as potential targets of BPA. These functionally diverse subpopulations of NPY neurons are differentially regulated by peripheral signals, such as estrogen and leptin. Whether BPA also differentially alters Npy expression in subpopulations of NPY neurons, contributing to BPA-induced endocrine dysfunction is unclear. We investigated the response of 6 immortalized hypothalamic NPY-expressing cell lines to BPA treatment. Quantitative reverse transcription-polymerase chain reaction revealed that BPA (10 nM, 25 μM, and 50 μM) increased Npy mRNA levels in 4 of the 6 cell lines. Increased Npy mRNA was observed in cell lines derived from the arcuate nucleus (mHypoA-2/10, mHypoA-2/12, and mHypoA-59) and the dorsomedial hypothalamus (mHypoA-55). Interestingly, the BPA-induced expression of Npy was not observed in cell lines derived from the hypothalamic paraventricular nucleus (mHypoA-2/20). Treatment with BPA increased the expression of 3 G protein-coupled estrogen receptor (GPER)-1 estrogen receptor (Esr) mRNAs. Co-treatment with the GPER antagonist G15 prevented the BPA-induced increase in Npy. BPA also altered neurochemistry and oxidative stress markers in both mHypoA-59 and mHypoE-38 cell lines despite the differential regulation of Npy. Remarkably, treatment with BPA in an antioxidant-rich media, Neurobasal A (NBA), or with reactive oxygen species scavenger tauroursodeoxycholic acid mitigated the BPA-induced increase and decrease in Npy. Furthermore, 2 antioxidant species from NBA (N-acetyl-cysteine and vitamin B) diminished the induction of Npy in mHypoA-59 cells. Collectively, these results indicate that BPA differentially regulates Npy expression in hypothalamic NPY neurons and illustrate the differential regulation of Npy by BPA is reversed. Subpopulations, and point to oxidative stress as a pathway that can be targeted to block BPA-induced Npy dysregulation in hypothalamic neurons.	Endocrinology Vol.161 Issue 11	10.1210/endocr/bqaa170	32960947	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1847	V. Lloyd, M. Morse, B. Pyskaki, J. Parker, P. Benard, M. Crore, S. Pfiffner, M. Sonyal and S. Dinda	2019	Hormone-Like Effects of Bisphenol A on p53 and Estrogen Receptor Alpha in Breast Cancer Cells	Bisphenol A (BPA) is a polymerizing agent commonly found in plastics that has been linked to xenoestrogenic activity. In this study, we analyzed the estrogen-like effects of BPA on the expression of estrogen receptor alpha (ERα) and tumor suppressor protein p53 in MCF-7 breast cancer cells. Cells were treated with BPA at concentrations ranging from 0.1 nM to 10 μM and compared to 17β-estradiol (E2) and vehicle effectors. The cells were then treated for 24 h with BSO-BPI, which was determined to be the optimal concentration in the validation study of BPA from 1 nM to 1 μM. Elevated ROS production, and the cells were then quantified and subjected to culture density/ cellular polyploidy get electrophoresis. (SDS- PAGE) Western blot analysis. The cell proliferation assays were quantified upon exposure to BPA. Laser confocal microscopy was performed to determine the colocalization of p53 and ERα. upon treatment with BPA. Western blot analysis revealed that BPA caused an increase in the cellular protein p53 in a concentration-dependent manner. While treatment with BPA did not affect the cytolocalization of p53, an increase in cell proliferation was observed. Our studies provide interesting leads to delineate the possible mechanistic relationship among BPA, ER, and tumor suppressor proteins in breast cancer cells.	Biores Open Access. 2019 Oct 31;8(1):169-184.	10.1089/biores.2018.0048	31681507	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1848	Y. Liu, Y. Yao, W. Tao, F. Liu, S. Yang, A. Zhao, D. Song and K. Li	2021	Coenzyme Q10 ameliorates BPA-induced apoptosis by regulating autophagy-related lysosomal pathways	Bisphenol A (BPA) is a widely distributed environmental endocrine disruptor. The accumulation of BPA has been proved that produce various toxic effects both on human and animals. However, the strategies to reduce the damage of BPA on the body and related mechanisms remains to be studied. Coenzyme Q10 (CoQ10), as a powerful antioxidant, is ubiquitous in many eukaryotic cells, which can improve the integrity of lysosomal membrane, lysosomal degradation function and promote autophagy. Here, we examined the ability of CoQ10 to alleviate oxidative stress and apoptosis in BPA-induced damages in CIK2 cells, and then to alleviate it. Our results showed that BPA induced oxidative stress and apoptosis in CIK2 cells, and CoQ10 supplementation significantly reduced the apoptotic rate and ROS production induced by BPA. Moreover, BPA exposure subjected to culture density/ cellular polyploidy get electrophoresis. (SDS- PAGE) Western blot analysis. The cell proliferation assays were quantified upon exposure to BPA. Laser confocal microscopy was performed to determine the colocalization of p53 and ERα. upon treatment with BPA. Western blot analysis revealed that BPA caused an increase in the cellular protein p53 in a concentration-dependent manner. While treatment with BPA did not affect the cytolocalization of p53, an increase in cell proliferation was observed. Our studies provide interesting leads to delineate the possible mechanistic relationship among BPA, ER, and tumor suppressor proteins in breast cancer cells.	Ecotoxicol Environ Saf. 2021 Sep 15:221:112450.	10.1016/j.ecoenv.2021.112450	34186417	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1849	X. Liu, H. Sakai, M. Nishigori, K. Sayama, T. Nawaji, S. Ikeda, M. Nishiguchi, H. Okada, A. Matsuchita, T. Nose, M. Shimohigashi and Y. Shimohigashi	2019	Receptor-binding affinities of bisphenol A and its next-generation analogs for human nuclear receptors	An endocrine-disrupting chemical Bisphenol A (BPA) binds specifically to a nuclear receptor (NR) named ERR γ. Although the importance of receptor-binding evaluation for human NRs is often stressed, the binding characteristics of so-called next-generation Bisphenol compounds are not sufficiently understood. The ultimate objective of this investigation was to evaluate BPA and its fluorinated analogs for their additives to bind to 23 human NRs, the greatest members of NRs for which relevant labeled-specific ligands were available. After establishing the detailed assay conditions for each NR, the receptor-binding affinities of total 11 bisphenol were evaluated in competitive binding assays. The results, directly revealed that BPA and the fluorinated analogs of BPAF, BPAP, BPB, BPC, BPE, and BPZ were highly potent agonist ligands for ERR γ (Ki = 4.5, 4.7, 4.7, 4.7, 4.7, 4.7, and 29 nM, respectively), and ERR α (Ki = 1,900, 1,900, 1,400, 1,400, 1,400, 1,400, and 1,400 nM, respectively), which was significantly higher than that to control ligand (ERR α: Ki = 4,700 nM). Moreover, BPA and BPP also appeared to be antagonist ligands for androgen receptor (AR) (Ki = 1,900 and 1,400 nM, respectively), which was significantly higher than that to control ligand (AR: Ki = 170 nM). Furthermore, BPA and BPP also appeared to be antagonist ligands for estrogen receptor α (ERα) and ERβ (Ki = 1,900 and 1,400 nM, respectively), which was significantly higher than that to control ligand (ERα

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依拠性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1856	H. Liu, H. Jin, G. Kim and J. Bae	2021	A low dose of bisphenol A stimulates estradiol production by regulating β -catenin-FOXL2-CYP19A1 pathway in human ovarian granulosa cells	Bisphenol A (BPA) is a well-known endocrine-disrupting chemical that interferes with normal steroid hormone production in various species. However, the underlying mechanism of the effect of BPA on steroid production in human ovarian granulosa cells remains unclear. In this study, we investigated the effect of BPA on estradiol production in human granulosa cell line (KGN) and primary human granulosa cells and the underlying mechanism. Granulosa cell tumor-related development and function. In ovarian tumors and normal cell tumors cell lines (KGN) and primary human granulosa cells. Furthermore, BPA enhanced CYP19A1 (aromatase) expression levels and estradiol (E2) production, but these effects were not observed in FOXL2-knockout (KO) cells. In addition, we found that BPA upregulated, β -catenin (CTNNB1) and stimulates nuclear translocation of CTNNB1, leading to transcriptional activation of FOXL2 mRNA. Furthermore, BPA failed to induce CYP19A1 and E2 production in CTNNB1-silenced KGN cells. Thus, our novel a comprehensive molecular signaling cascade encompassing BPA-CTNNB1-FOXL2-CYP19A1-E2 that contributes to the endocrine-disrupting activities of BPA in human ovarian granulosa cells.	Biochem Biophys Res Commun. 2021 Dec 17:583:192-198.	10.1016/j.bbrc.2021.10.070	34749236	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10 (-11) ～10 (-8) M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1857	C. Litter, P. Barry, L. Lambelin, Y. Ma, J. Bal, R. Weingrill, I. Urrichio, J. Chen and M. J. Lee	2024	Epigenetic Changes in the HTR8 and 3A-sub E placental Cell Lines Exposed to Bisphenol A and Benzyl Butyl Phthalate	OBJECTIVE: Bisphenol A and phthalates are known endocrine disruptors and capable of inducing epigenetic changes in the human population. However, their impact on the placenta is less well studied. Our objective was to measure the effect of exposure to bisphenol A and benzyl butyl phthalate in first trimester HTR8-SVneo and third trimester 3A-sub E trophoblast cells, by profiling the DNA methylation pattern of the imprinting control region of the IGF2 locus (imprinted factor) and H19 genes. METHODS: Human placental explants were exposed to BPA and BBP and 96 h and 8 days. were treated with no cocktail concentration of bisphenol A and benzyl butyl phthalate. Downstripping agent, 5-azacytidine, was used as a positive control. Cells were harvested on post-treatment days 2 and 8. The methylation profile of six CpG dinucleotide sites, part of the CTCF 9 binding site of the IGF2 imprinting control region, was measured using pyrosequencing. RESULTS: Cells exposed to BPA and BBP showed a significant loss of DNA methylation at day 8 in the 3A-sub E cell line. The high concentration of bisphenol A + benzyl butyl phthalate which increased methylation at site 6 for both high and low dose treatment at day 2. Demethylation of the CpG site 2, 4, and 5 was observed when treated with 5-azacytidine on day 2. In the third trimester 3A-sub E cell line, no significant changes in the methylation profile were observed under any treatment conditions. CONCLUSIONS: The results of this study demonstrate the susceptibility of epigenetic changes in human placenta cells induced by bisphenol A and benzyl butyl phthalate. The observed methylation changes only in the first-trimester HTR8-SVneo cells phthalate may reflect a window of epigenetic susceptibility related to these environmental toxicants.	Toxics. 2024 Sep 9;12(9):659.	10.3390/toxics12090659	39330587	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	1	1, 100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1858	F. Ling, W. Xia, X. Kui, Y. Cai, M. He and J. Ma	2025	miR-141-3p inhibited BPA-induced proliferation and migration of lung cancer cells through PTGER4	The chemical substance bisphenol A (BPA) is widely used in household products, and its effect on human health has frequently been the focus of research. The aim of this study was to explore the potential molecular regulatory mechanism of BPA on the proliferation and migration of lung cancer cells. In this study, the H1299 and A549 lung cancer cell lines were selected as the study objects. The cells were treated with different concentrations of BPA (0, 0.1, 1, or 10 μM), and cell viability, proliferation, and migration were evaluated by CCK-8, EdU, clonogenic, and scratch test assays. Western blotting and RT-qPCR were used to detect the expression of proteins and genes related to cell proliferation and migration. Bioinformatics analysis was used to predict the target genes of BPA, and the results were verified by RT-qPCR. The results showed that BPA could promote the proliferation and migration of lung cancer cells in a dose-dependent manner. Bioinformatics analysis revealed that PTGER4 was a key target of BPA. Low-dose BPA significantly increased the expression of PTGER4 and further inhibited PI3K/AKT signaling pathway activation and MMPs expression. Moreover, PTGER4 overexpression weakened the inhibitory effect of the miR-141-3p mimic on the proliferation and migration of lung cancer cells. In conclusion, miR-141-3p can inhibit the proliferation and migration of BPA-induced lung cancer cells by downregulating PTGER4, providing a new potential target for the treatment and prevention of lung cancer. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s10616-024-00692-5.	Cytotechnology. 2025 Feb;77(1):28.	10.1007/s10616-024-00692-5	39741890	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1、1、10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1859	T. C. Lin, K. H. Wang, K. H. Chu-ang, A. P. Kao and T. C. Kuo	2021	Downregulation of gap junctional intercellular communication and connexin 43 expression by bisphenol A in human granulosa cells	Gap junctional intercellular communication (GJIC) is the transfer of ions, metabolites, and second messengers between neighboring cells through intercellular junctions. Connexin 43 (Cx43) was found to be the type of gap junction protein in granulosa cells. Bisphenol A (BPA) is a well-known endocrine disrupting chemical (EDC) that is widely used in the production of polycarbonate plastics and epoxy resins. BPA is one of the most widely produced chemicals around the world. There are reports that the chemical estrogen could undermine human genome, and several herbs reproductive functions. In this present study, demonstrated that cell culture medium, containing antioxidants (5 mmol/l l-cysteine and1 mmol/lo-acetyl-l-carnitine and 0.1 phosphate), was able to enhance the survival and cell retrieval of GCs. In addition, we found that BPA at environmentally relevant concentration (10 -7) M reduced Cx43 expression and GJIC in GCs, through estrogen receptor- and mitogen-activated protein kinase pathways. The results of this study not only reveal the reproductive toxicity of BPA but also provide possible mechanisms by which BPA inhibited GJIC in GCs.	Biotechnol Appl Biochem. 2021 Jun;68(3):676-682.	10.1002/bab.1979	32610363	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10-7 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1860	J. Lin, L. Dang, M. Sun, Y. Wang, S. Lee, K. Choi and X. Liu	2021	An in vitro investigation of endocrine disrupting potentials of ten bisphenol analogues	The endocrine disruption potency of BPA was reported elsewhere, but the mechanisms of its analogues have not been fully resolved. In this study, endocrine disruption potentials of nine alternative bisphenol analogues, namely, 2,2-bis(4-hydroxyphenyl)butane (BPB), 2,2-Bis(4-hydroxy-3-methylphenyl)propane (BPC), 4,4′-ethylidenebisphenol (BPE), 4,4′-(1,3-Phenylene diisopropylidene)bisphenol (BPM), 4,4′-(1,4-Phenylene diisopropylidene)bisphenol (BPP), 4,4′-(Hexafluoroisopropylidene)diphenol (BPAF), 4,4′-(Perfluorobutane-1,4-diyl)diphenol (PFBBP), 4,4′-(Perfluoropentane-1,5-diyl)diphenol (PFBPP), and 4,4′-(Perfluorohexane-1,6-diyl)diphenol (PFBHP), were investigated in vitro. Bisphenol A (BPA) and 4-hydroxybenzophenone (BP4) were tested as well for BPA-like and benzophenone-like activities. In the ERα CALUX assay, the endocrine disruption potencies followed the order of BPAF> pm-3,3′-bis(4-hydroxyphenyl)pentane (BPP) > pm-2,2′-bis(4-hydroxyphenyl)pentane (BPC) > BPA > BP4 > BPB > BPE > BPM > BPP. In the H295R steroidogenesis assay, the endocrine disruption potencies followed the order of BPAF> BPA > BP4 > BPB > BPC > BPE > BPM > BPP. In summary, all nine tested bisphenols showed endocrine toxicity through different mechanisms. Some had similar potency as BPA, but some had even higher potency. Further research is necessary to evaluate the toxicity of these potential BPA substitutes.	Steroids. 2021 May;169:108826.	10.1016/j.steroids.2021.108826	33753083	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1861	S. R. Lim, D. W. Kim, J. Sung, T. H. Kim, C. H. Choi and S. J. Lee	2021	Astaxanthin Inhibits Autophagic Cell Death Induced by Bisphenol A in Human Dermal Fibroblasts	Astaxanthin, a natural antioxidant carotenoid, is a nutrient with diverse health benefits, given that it decreases the risk of oxidative stress-related diseases. In the present study, we investigate the functional role of astaxanthin during autophagic cell death induced by the estrogenic endocrine-disrupting chemical bisphenol A (BPA) in normal human dermal fibroblasts (NHDF). BPA significantly induced apoptotic cell death and autophagic cell death in NHDF. Astaxanthin significantly inhibited BPA-induced autophagic cell death, but not apoptotic cell death. Astaxanthin and the autophagy inhibitor 3-methyladenine (3-MA) inhibited the phosphorylation of extracellular signal-regulated kinase (ERK) stimulated by ROS production, but 4-AR did not influence the activation of c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) in BPA-treated NHDF. Astaxanthin abrogated the ERK-mediated activation of nuclear factor-kappa B (NF-κB), which is responsible for the mRNA expression of LC3-II, Beclin-1, Atg5, and Atg12 during apoptotic cell death induced by BPA. These results indicate that astaxanthin is a pharmacological and nutritional agent that blocks the skin fibroblastic autophagic cell death induced by BPA in human dermal fibroblasts.	Antioxidants (Basel). 2021 Aug 11;10(8):1273.	10.3390/antiox10081273	34439521	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1～50 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1862	Y. Liang, Q. Jiang, Y. Gong, Y. Yu, H. Zou, J. Zhao, T. Zhang and J. Zhang	2023	In vitro and in silico assessment of endocrine disrupting effects of food contaminants through pregnane X receptor	As a promiscuous, sensitive receptor, pregnane X receptor (PXR) has been confirmed to participate in numerous physiological process. In addition to the conventional estrogen/androgen receptor, PXR also serves as an alternative target for environmental chemical contaminants. In this work, the PXR-mediated endocrine disrupting effects of typical food contaminants were explored. Firstly, the time-resolved fluorescence resonance energy transfer assays confirmed the PXR binding activities of 2,2′,4,4′,5,5′-hexachlorobiphenyl, bis(2-ethylhexyl) phthalate, dibutyl phthalate, chlorpyrifos, bisphenol A, and enrofenox, with IC50 values ranging from 1.80 to 3.88×10-6 M. Then their PXR-agonistic activities were assessed by PXR-mediated CYP3A4 reporter gene assays. Subsequently, the regulation of gene expressions of PXR and its target CYP3A4, UGT1A1, and ABCB1 by these compounds was further investigated. Intriguingly, all the tested compounds interfered with these gene expressions, confirming their endocrine disrupting effects via PXR-mediated signaling. The compound PXR-ligand docking and molecular dynamics simulations revealed that these compounds primarily bound between the interested helix 3 of the PXR binding capacities. The weak electrostatic interactions are key players in stabilizing these compound-PXR-LBD complexes. During the simulation process, 2,2′,4,4′,5,5′-hexachlorobiphenyl remained stable within the other 5 compounds underwent relatively severe disturbances. In conclusion, these food contaminants might exhibit endocrine disrupting effects via PXR.	Food Chem Toxicol. 2023 May;175:113711.	10.1016/j.fct.2023.113711	36893891	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1863	X. Liang, N. Yin, S. Liang, R. Yang, S. Liu, Y. Lu, L. Jiang, Q. Zhou, G. Jiang and F. Faiola	2020	Bisphenol A and several derivatives exert neural toxicity in human neuron-like cells by decreasing neurite length	Bisphenol A (BPA) and its derivatives, including bisphenols S (BPS), F (BPF), B (BPB), E (BPE), and AF (BPAF), are widely used in consumer products. Moreover, they are typically detected in the environment, food, and human samples. Studies have associated BPA exposure with several health risks, but it is still unclear whether BPA substitutes are safe. In this study, we used human neuron-like cells (SH-SY5Y cells) differentiated with retinoic acid (RA) to evaluate the potential neural toxicity of these compounds. We observed that bisphenols affected the viability of RA/SH-SY5Y cells after 48 h of treatment (stem cells: 100–200 μM; mature cells: 50–100 μM). Bisphenol A and BPAF (the strongest cytotoxic compound) At human relevant concentrations, the bisphenols did not significantly interfere with gene expression and protein levels during RA/SH-SY5Y differentiation into the neural subtype, as well as during specification of neuron-like cells from NSCs. Nevertheless, monitoring of cell morphology changes indicated that exposure to BPA and its derivatives impaired neurite length in neuron-like cells. Thus, our findings provide insights into the molecular mechanisms of bisphenol-dependent neurotoxicity at low nanomolar levels and support the view that BPA substitutes may not be sufficiently safe for widespread use as industrial chemicals.	Food Chem Toxicol. 2020 Jan:135:111015.	10.1016/j.fct.2019.111015	31812737	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1864	X. Liang, R. Yang, N. Yin and F. Faiola	2021	Evaluation of the effects of low nanomolar bisphenol A-like compounds' levels on early human embryonic development and lipid metabolism with human embryonic stem cell in vitro differentiation models	The widely used chemical bisphenol A (BPA) has been associated with several health effects. In recent years, many derivatives were developed to replace BPA although without thorough toxicological evaluation. Here, we employed a human embryoid body (EB) based in vitro global differentiation and hepatic specification models, followed by RNA-seq analyses, to comprehensively study the potential developmental toxicity of six BPA replacements: BPS, BPF, BPZ, BPB, BPE, and BPAF, as compared to BPA. We found that these bisphenols may disrupt lineage commitment and lipid metabolism during early embryonic development. These effects may be manifested via the dysregulation of HOX and KPCI family genes. Moreover, among the seven bisphenols analyzed, BPE seemed to have the mildest effects.	J Hazard Mater. 2021 Apr 5:407:124387.	10.1016/j.jhazmat.2020.124387	33172680	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1865	N. Liang, W. Song and J. Li	2024	BPA promotes lung fibrosis in mice by regulating autophagy-dependent ferroptosis in alveolar epithelial cells	BACKGROUND: Bisphenol A (BPA) is an industrial chemical that is commonly found in daily consumer products. BPA is reportedly associated with lung diseases. However, the impact of BPA on pulmonary fibrosis (PF) and its possible mechanisms of action both remain unclear. METHODS: A PF mouse model was induced by bleomycin (BLM). Mouse lung fibroblasts (MLF-2808) and mouse alveolar epithelial cells (MLE-12) were treated with BPA and BLM. Cell viability was detected by CCK-8 assay. Ferroptosis was detected by Fe2+ assay, GSH/GSSG assay, and MDA assay. RESULTS: BPA exposure aggravated BLM-induced PF in mice, as indicated by increased oxidative stress and reduced ferroptosis, leading to PF. The ferroptosis inhibitor Fer-1 partly attenuated the effect of BPA. In addition, among the two main cell types associated with PF in the lung, BPA was cytotoxic to MLE-12 cells, but not to MLF-2808 cells, and BPA induces ferroptosis in MLE-12 cells. Furthermore, BPA promoted autophagy-mediated ferroptosis by activating the AMPK/mTOR signaling pathway, thereby exacerbating the progression of PF. The autophagy inhibitor 3-MA partly attenuated the effect of BPA. CONCLUSIONS: BPA promotes the progression of PF by promoting autophagy-dependent ferroptosis in alveolar epithelial cells, which provides a new theoretical basis for understanding BPA-induced PF.	Ecotoxicol Environ Saf Vol.278 Pages 116412	10.1016/j.ecoenv.2024.116412	38691879	in vitro	-	-	-	-	-	-	-	-	-	-	-	0	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1866	B. Liang, J. Chen, L. Wang, L. Zhang, S. Huang, Y. Zhou, M. Ni, L. Zhang, X. Lv and X. Li	2024	Mode of action exploration for prostate epithelial cell injury caused by bisphenol A	Bisphenol A (BPA) is a typical food chemical contaminant with various detrimental effects, especially on reproductive system. Male prostate damage is also one of its major adverse health effects, of which mode of action (MOA) remains unclear. This study aims to explore the MOA for prostate toxicity of BPA using human normal prostate epithelial cell RWPE-1 for 28-day human relevant-level exposure. A physiological-based pharmacokinetic model was used to determine the concentration of BPA based on the actual oral exposure in China. The possible key events were identified by high-throughput transcriptome sequencing and validated by in vitro and in vivo experiments. Transcriptomic results revealed that BPA exposure could induce cell cycle arrest, DNA damage, and cell apoptosis. Cell cycle arrest was further confirmed by pathology, TEM increased BPA concentrations, the increased mRNA and/or protein expressions of MAPK/PI3K-1, ATR and γ-H2a.X in the MAPK signaling pathway, the increased mRNA expressions of CCND1 and CDK4, the decreased mRNA expression of CCDC2BC, the increased proportion of G0/G1 phase and S phase, as well as the decreased proportion of G2/M phase, were observed. The lowest value of benchmark concentration lower confidence limit (BMCL) was estimated from G2/M phase ratio, with 12.5 ng/kg bw/day (95% CI: 11.2, 13.8) and 8.96 (6.62, 13) ng/kg bw/day, much higher than the male prostate exposure concentration of 0.159 ng/kg bw/day at the current exposure level of adult Chinese males. In conclusion, the MOA of BPA-induced male prostatic toxicity at human-relevant levels may include: key event (KE) 1: MAPK signaling pathway activation; KE2: cell cycle arrest; KE3: DNA damage; KE4: cell apoptosis; KE5: prostatic epithelial cell injury. Adverse outcome pathway (AOP) network construction of CCDC2BC1, and KE3-4 disturbance of cell cycle (increased proportion of G1/G1 and S phases, decreased proportion of G2/M phases). However, more studies are needed to validate and complete the MOA.	Ecotoxicol Environ Saf. 2024 Nov 1:286:117228.	10.1016/j.ecoenv.2024.117228	39442252	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1867	Z. Li, H. Yin, Y. Shen, M. Ren and X. Xu	2021	The influence of phenolic environmental estrogen on the transcriptome of uterine leiomyoma cells: A whole transcriptome profiling-based analysis	OBJECTIVE: The study aimed to recognize potential molecular targets and signal pathways whereby phenolic environmental estrogen promotes the proliferation of uterine leiomyoma cells. METHODS: Primary cultured cells from of uterine leiomyoma were treated with 0.1% DMSO, 10(-5) mol/L Bisphenol A (BPA), and 10(-5) mol/L Nonylphenol (NP) for 48 h before RNA-seq was performed. These genes affected by BPA and NP were identified by Venn diagram. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed. Then, the protein-protein interaction (PPI) and ceRNA (competing endogenous RNA) networks were constructed to identify the differentially expressed genes and mRNAs. RESULTS: Compared to cells the control group, 728 differentially expressed genes were identified in both the BPA group and the NP group. GO enrichment analysis showed that the most enriched GO terms were connective tissue development and ECM-receptor interaction. The results of KEGG pathway enrichment analysis revealed that the most significantly enriched pathways were ECM-receptor interaction, focal adhesion, and PI3K-Akt signaling pathway. The results of GSEA showed that the gene sets of ECM-receptor interaction, focal adhesion, and PI3K-Akt signaling pathway were significantly enriched. Then, PCR and western blot verified the cell cycle-associated genes and proteins were upregulated in both BPA- and NP-treated cells. Moreover, the PI3K-AKT signaling pathway, CCND1-CDK6 Phenolic environmental estrogens may promote the proliferation and cell cycle progression of uterine leiomyoma cells through vascular genome. ER-signaling, which leads to disordered cell cycle regulation and accelerates the transition of the cell cycle from G0/G1 phase to S phase. In addition, as an external stimulant, phenolic estrogen promotes the upregulation of inflammatory factors in uterine leiomyoma.	Ecotoxicol Environ Saf Vol.211 Pages 111945	10.1016/j.ecoenv.2021.111945	33516137	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10.0 μmol/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1868	Z. Li, T. Xu, X. Fan, K. Chen, C. Wan, X. Li, H. Yin and S. Li	2023	Bisphenol A aggravate selenium deficiency-induced apoptosis via miR-215-3p/Dio1 to activate ROS/PI3K/AKT pathway in chicken arterial	Both bisphenol A (BPA) and selenium (Se) deficiency can affect the expression of microRNAs (miRNAs), which can specifically regulate its target mRNA and induce apoptosis, and play a significant role in cardiovascular injury diseases. To explore the mechanism of apoptosis induced by BPA and Se deficiency in chicken arterial endothelial tissue and the role of miRNAs in this process, the model of BPA exposure/Se deficiency in chicken and PACC cells have been employed. The targeting relationship between miR-215-3p and iodothyronine deiodinase 1 (Dio1) mRNA was verified by double luciferase gene report. The level of miR-215-3p was detected by qRT-PCR. The ultrastructural stress level of arterial endothelial cells was detected by oxidative stress kit and JC2Y4 DA probe method. The PI3K/AKT pathway, mitochondrial dynamics, and apoptosis-related genes were detected by Western blot. The results showed that BPA exposure and Se deficiency led to a compromise of miR-215-3p, aggravated oxidative stress, inhibited activation of PI3K/AKT pathway, promoted mitochondrial division, increased expression of apoptosis-related genes, and finally led to apoptosis of chicken arterial endothelial cells. We also established knockdown/overexpression models of miR-215-3p and Dio1 in vivo and found that overexpression of miR-215-3p and knockout of Dio1 can induce apoptosis. Interestingly, miR-215-3p inhibitor and Si-mRNA + Lysotracker DND2 partially prevented apoptosis caused by BPA exposure and Se deficiency, and, CONCLUSIONS: Bisphenol A aggravates selenium deficiency-induced apoptosis via miR-215-3p/Dio1. The miR-215-3p/Dio1 axis provides a new way to understand the toxic mechanism of BPA exposure and Se deficiency, and reveals a new regulatory model of apoptosis damage in vascular diseases.	J Cell Physiol. 2023 Jun;238(6):1256-1274.	10.1002/jcp.31007	37012668	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

通格性評価（動物）1：該当、0：該当しない

通格性評価（疫学）1：該当、0：該当しない

通格性評価（in vitro）1：該当、0：該当しない

通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階で除外。当該性評価段階で原著に基づき精査。

引用評価機関
● ：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	通格性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1869	Z. Li, Y. Ren, X. Li and W. Wang	2023	KDM2A interacts with estrogen receptor α to promote bisphenol A and S-induced breast cancer cell proliferation by repressing TET2 expression	As a recognized endocrine disruptor in the environment targeting estrogen receptors (ERs), Bisphenol A (BPA) and its bisphenol S (BPS) analogs are involved in the development of breast cancer. Epigenetic modifications are crucial in many biological processes, and DNA hydroxymethylation (5hmC) coupled with histone methylation is involved in epigenetic machinery covering cancer occurrence. Our previous study indicated that BPA/BPS induces breast cancer cell (BCC) proliferation with enhanced estrogenic transcriptional activity and causes the change of 5hmC depending on ten-eleven translocation 2 (TET2) disagreement. Herein, we found that BPA/BPS-induced BCC proliferation was dependent on lysine demethylase 2A (KDM2A) and ERα. Mechanistically, KDM2A was highly expressed in BCCs induced by BPA/BPS. We found that BPA/BPS-treated BCCs presented increased KDM2A mRNA and protein levels but reduced TET2 and genomic 5hMethe. Furthermore, KDM2A overexpression BCCs mimicked 5hmC and suppressed TET2-dependent 5hMethe by inducing its chromatin binding during BPA/BPS-induced cell proliferation. Results of Co-IP & ChIP assays suggested the direct interplay of KDM2A with ERα. In multiple manners, KDM2A reduced the lysine methylation of ERα, proving to increase its phosphorylation function. On the other hand, ERα also affected KDM2A expression, while KDM2A protein levels decreased after ERα deletion, indicating that ERα binding might maintain KDM2A protein stability. In conclusion, a potential feedback circuit of KDM2A/ERα→TET2 5hMethe was identified among ERs/BCCs, which significantly affects on regulating BPA/BPS-induced cell proliferation. These insights advanced the understanding of the relationship between histone methylation, 5hMethe, and cancer cell proliferation with ER attributed to BPA/BPS exposure in the environment.	Ecotoxicol Environ Saf. 2023 Jun 12:262:115132.	10.1016/j.ecoenv.2023.115132	37315367	in vitro	-	-	-	-	-	-	-	-	1	0	100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1870	Z. Li, C. Lyu, Y. Ren and H. Wang	2020	Role of TET Dioxygenases and DNA Hydroxymethylation in Bisphenols-Stimulated Proliferation of Breast Cancer Cells	BACKGROUND: Bisphenol A (BPA), a ubiquitous environmental endocrine disruptor targeting estrogen receptors (ERs), has been implicated in the promotion of breast cancer. Perinatal exposure of BPA could induce longitudinal alteration of DNA hydroxymethylation in imprinted loci of mouse blood cells. To date, no data has been reported on the effects of BPA on DNA hydroxymethylation in breast cells. Therefore, we asked whether BPA could induce DNA hydroxymethylation in breast cells, and if so, whether the induction was dependent on ERs. Moreover, we asked whether BPA-induced DNA hydroxymethylation was involved in cancer development, and specifically, whether and how BPA and its analogs promote breast cancer development via DNA hydroxymethylation. OBJECTIVES: We aimed to explore the interplay of the estrogenic activity of bisphenols at environmental exposure dose levels with TET dioxygenase-catalyzed DNA hydroxymethylation and to elucidate their roles in the proliferation of ER+ breast cancer cells as stimulated by environmentally relevant BPA analogs. METHODS: MCF-7 and T47D cells, two ER+ breast cancer cell lines, were used as the models. Cell proliferation was measured by cell counting and EdU incorporation assays. These cells were treated with BPA or bisphenol S (BPS) to examine BPA/BPS-induced proliferation. Ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) and enzyme-linked immunosorbent assays (ELISAs) were used to detect DNA hydroxymethylation. Co-IP, ChIP-seq and RNA interference technologies, quantitative polymerase chain reaction (qPCR), and Western blot analyses were used to evaluate the expression and function of genes. Co-immunoprecipitation (Co-IP), bisulfite sequencing PCR (BSP), and chromatin immunoprecipitation-qPCR (ChIP-qPCR) were used to identify the interactions of target proteins. RESULTS: We measured higher proliferation in ER+ breast cancer cells treated with BPA or its replacement, BPS, accompanied by an ERα- dependent decrease in genomic DNA hydroxymethylation. The results from Co-IP and ChIP assays suggested the direct interplay of TET1 with ERα. Moreover, TET1 was highly expressed in BPA/BPS-induced BCCs, and TET1 knockdown mimicked BPA/BPS-induced cell proliferation. We observed that TET1 was negatively regulated by the activation of ERα. Ethinylestradiol(methylated), which was also induced by BPA/BPS binding. Instead of a direct transaction between TET1 and ERα, data of co-IP, BSP, and ChIP-qPCR experiments indicated that the activated ERα increased the DNA methyltransferase 3(DNMT) mediated promoter methylation of TET1, leading to an inhibition of the TET1 expression and DNA hydroxymethylation. CONCLUSIONS: We identified a new feedback circuit of ERα activation-DNMT-TET1 DNA hydroxymethylation in ER+ breast cancer cells and uncovered a pivotal role of TET1-mediated DNA hydroxymethylation in modulating BPA/BPS -stimulated proliferation. Moreover, to our knowledge, we for the first time established a linkage among chemical exposure, DNA hydroxymethylation, and tumor-associated proliferation. These findings further clarify the estrogenic activity of BPA/BPS and its profound implications for the regulation of epigenetic DNA hydroxymethylation and cell proliferation. https://doi.org/10.1289/EHP5862	Environ Health Perspect. 2020 Feb;128(2):27008.	10.1289/ehp5862	32105160	in vitro	-	-	-	-	-	-	-	-	1	0	10–1,000 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1871	Z. Li, C. Chen, P. Ying, G. Ji-Ju, D. Lian-Jia, H. Dan, Z. Xuan-Min, G. Tian-Yue, Z. Chao and H. Jia-Hu	2023	Bisphenol A and its analogue bisphenol S exposure reduce estradiol synthesis via the ROS-mediated PERK/ATF4 signaling pathway	As a kind of endocrine-disrupting chemicals, BPA may affect the human placenta. Due to consumers' anxious about BPA, many manufacturers are using alternatives to BPA, such as BPS. However, some reports suggest that BPS may produce similar results to BPA. To understand how BPA/BPS leads to reduced synthesis of placental steroids (E2), we conducted studies using a human choriocarcinoma cell (JEG-3) model for research. Our results showed that BPA/BPS exposure significantly reduced the E2 synthesis in JEG-3 cells. Moreover, BPA/BPS exposure significantly increased the ROS levels in JEG-3 cells. Then, we found that BPA/BPS exposure significantly reduced the E2 synthesis in JEG-3 cells. In addition, Western blot assays revealed that BPA/BPS induced ER stress PERK/ATF4. ATF4 signaling pathway expression was increased. The inhibition of ROS or ATF4 alleviated BPA/BPS-induced decreased the E2 synthesis in JEG-3 cells. In addition, Western blot assays revealed that BPA/BPS induced ER stress PERK/ATF4. ATF4 signaling pathway expression was increased. The inhibition of ROS or ATF4 alleviated BPA/BPS-induced decreased the E2 synthesis in JEG-3 cells. Second, BPA/BPS exposure may reduce E2 synthesis in JEG-3 cells. Third, BPA/BPS exposure may reduce E2 synthesis in JEG-3 cells by increasing ROS levels and thus activating endoplasmic reticulum stress.	Food Chem Toxicol Vol.182 Pages 114179	10.1016/j.fct.2023.114179	37944787	in vitro	-	-	-	-	-	-	-	-	1	0	50 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1872	Y. Li, H. Xu, Z. Ma, Q. Li, Y. Xiong, X. Xiong, J. Li, D. Lan and W. Fu	2024	Comprehensive cognition of yak (Bos grunniens) AIFM2 gene and its anti-ferroptosis role in bisphenol A-induced fetal fibroblast model	Apoptosis-inducing factor mitochondrion-associated 2 (AIFM2) has been identified as a gene with anti-ferroptosis properties. To explore whether AIFM2 exerts anti-ferroptosis role in yaks (Bos grunniens), we cloned yak AIFM2 gene and found that AIFM2 was highly expressed in the heart, liver, and kidney tissues of yaks. Bisphenol A (BPA) is a widely distributed environmental endocrine disruptor, and the expression of AIFM2 in yak tissues. Furthermore, we isolated yak skin fibroblasts (YSFs) and established a bisphenol A (BPA)-induced ferroptosis model to further investigate the role of AIFM2. BPA stimulated endocrine disruption organic synthesis, ROS and lipid peroxidation (malondialdehyde, MDA, and GSH/GPX), and reduced cell viability and antioxidant capacity (glutathione, GSH), with the severity depending on the dosage. Of note, a supplement of Ferrostatin-1 (Fer), an inhibitor of ferroptosis, restored the antioxidant imbalance. Subsequently, we constructed an AIFM2-overexpression cell model and AIFM2-specific interfering mRNAs (which were transfected into YSFs. The results showed that overexpressing AIFM2 alleviated ferroptosis, characterizing by significant changes of cell viability, ROS, MDA/GPX, MDA and GSH. Meanwhile, interfering AIFM2 aggravated ferroptosis, demonstrating the critical anti-ferroptosis role of the yak AIFM2 gene. This study sheed light on further exploring the molecular mechanism of AIFM2 in plateau adaptability.	Anim Biotechnol Vol.35 Issue 1 Pages 2377209	10.1080/10495398.2024.2377209	39037081	in vitro	-	-	-	-	-	-	-	-	1	0	100, 150, 200, and 250 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1873	Y. Li, S. Liu, F. Gao, Z. Peng, J. Zhang, S. Li, D. Lu and X. Pan	2023	BPA interferes with granulosa cell development and oocyte meiosis in mouse preantral follicles	Bisphenol A (BPA) is an established environmental endocrine disruptor and can interfere with the development of female germ cells. However, the underlying mechanisms are still unclear. We investigated the effects of BPA on granulosa cell development and meiosis of oocytes using in vitro culture system of mouse preantral follicles. Preantral follicles from ICR mouse ovary were treated with 10 μg/mL BPA in vitro for 12 days. The adherent area of follicles was measured. On D12, cumulus cell expansion was observed. The meiosis resumption rate was calculated. Western blot detected PR2, proliferating cell nuclear antigen (PCNA), estrogen receptor α (ERα), and insulin receptor substrate 2 (IRS2) that mediated estrogen and progesterone levels. Immunofluorescence detected Cx37 on oocyte membrane. Gap junction communication was assessed. We found that BPA significantly decreased the adherent area of follicles, the proliferation of granulosa cells, and the meiosis resumption rate of oocytes. Moreover, BPA reduced the levels of estradiol(E2) in the follicular fluid. However, it reduced the expression of cumulus cells, Cx37 expression and the gap junction communication between cumulus cells and oocytes on D12. BPA promoted the recovery of oocytes from meiosis. Interestingly, BPA increased the expression of cyclin B1 protein in arrested germinal vesicle breakdown (GVBD) oocytes, and reduced this in vitro maturation rate of oocytes. These GVBD oocytes come from follicular apoptosis or death. Conclusively, BPA disturbs the development of granulosa cells and the meiosis progression of oocytes by decreasing gap junction communication between oocytes and the granulosa cells, as well as regulating cyclin B1 expression in GVBD oocytes.	Exp Biol Med (Maywood) Vol.248 Issue 13 Pages 1145-1158	10.1177/15353702231179940	37452689	in vitro	-	-	-	-	-	-	-	-	1	0	10 μg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1874	Y. Li, Z. Dong, S. Liu, F. Gao, J. Zhang, Z. Peng, L. Wang and X. Pan	2022	Astaxanthin improves the development of the follicles and oocytes through alleviating oxidative stress induced by BPA in cultured follicles	This study is to investigate whether astaxanthin could alleviate the oxidative stress damages of follicles induced by BPA and improve the development of the cultured follicles and oocytes. Compared with BPA group, the survival rate, antrum formation rate, oocyte maturation rate and adherence area of the GE and GLE follicles of the BPA+Asta group were significantly higher. The estrogen and progesterone in the culture medium of the BPA+Asta group were significantly higher than BPA group. The ROS level in the oocytes of the BPA+Asta group was significantly lower than BPA group. The levels of malondialdehyde in the follicular culture medium, levels of ROS in the oocytes, the expression levels of caspase 3 and caspase 9 in the oocytes of the BPA+Asta group were significantly lower. However, the mitochondrial membrane potential, and the expression levels of antioxidant genes (CAT, SOD1 and SOD2) and anti-apoptotic gene Bcl-2 in the oocytes in the BPA+Asta group were significantly higher. Astaxanthin improves the development of follicles and oocytes through increasing the antioxidant capacity of follicles and oocytes, and relieving the BPA-induced oxidative stress during follicular development and oocyte maturation.	Sci Rep. 2022 May 12;12(1):7853.	10.1038/s41598-022-11566-1	35551214	in vitro	-	-	-	-	-	-	-	-	1	0	25 μmol/L or 2.5 mmol/L	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1875	X. Li, M. Ni, W. Xiong, L. Tian, Z. Yang, L. Zhang and J. Chen	2022	Transcriptomics analysis and benchmark concentration estimating-based in vitro test with IOSE80 cells to unveil the mode of action for female reproductive toxicity of bisphenol A at human-relevant levels	Bisphenol A (BPA) is of great concern in public health, of which female reproductive toxicity is one major adverse health effect with the ovarian mode of action (MOA) yet. Based on the principle of Toxicity Testing in the 21st Century, the purpose of this study is to explore the MOA for female reproductive toxicity using human normal ovarian epithelial cells IOSE80 at 28 day human-relevant-level exposure. A physiologically-based pharmacokinetic model was used to select the administration concentrations according to the BPA levels in female groups at human actual exposure scenario. Enrichment GO and pathways, benchmark dose (BMD) estimation, and RNA transport, ribosome biogenesis in eukaryotes, cell cycle, cellular senescence, progesterone-mediated oocyte maturation, and oocyte meiosis. Increased relative mRNA and protein expressions of ERK and CDK1/2, decreased expressions of cyclin B1 and cyclin E1, and increased expressions of p21 and p27 were observed in the BPA-exposed IOSE80 cells. Moreover, BPA exposure at human-relevant concentration (corr-confidence limits, mRNA expression of SGPP2 served as the lowest. In conclusion, the MOA of BPA-induced female reproductive toxicity at human-relevant levels may include (via exert ERK1/ERK activation, KIF2 increased expression of CDK1/2, and KIF2 cell cycle arrest. However, more in vivo studies may be needed to complete the MOA.	Ecotoxicol Environ Saf. 2022 Jun 1:237:113523.	10.1016/j.ecoenv.2022.113523	35429799	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1876	Q. Li and Z. Zhao	2019	Influence of N-acetyl-L-cysteine against bisphenol a on the maturation of mouse oocytes and embryo development: in vitro study	BACKGROUND: Bisphenol A (BPA), an endocrine disruptor, is a widely used chemical that has adverse effects on animal development and reproduction. The current research aimed to evaluate the effect of BPA on the in vitro maturation (IVM) and subsequent embryo development of mouse oocytes following in vitro fertilization (IVF). METHODS: IVM was performed in the presence of different concentrations (0, 25, 50, or 100 μg/mL) of BPA. Nuclear maturation, IVF efficiency and embryonic development were determined. The levels of reactive oxygen species (ROS) and glutathione (GSH) in the BPA-exposed oocytes were evaluated. We explored the ability of N-acetyl-L-cysteine (NAC) in the IVM medium to rescue the BPA-induced damage by examining changes in nuclear maturation, IVF rate, blastocyst formation, ROS levels and GSH content. RESULTS: Compared with the control group, exposure to BPA significantly decreased the rates of germinal vesicle breakdown (GVBD), metaphase II (MII) and blastocyst formation, increased ROS levels, and decreased GSH content in oocytes. The addition of NAC ameliorated the BPA-induced suppression of nuclear maturation, relieved the BPA-induced decrease/rise of the fertilization and blastocyst formation rates, and mitigated the increased ROS levels and decreased GSH content. CONCLUSION: BPA affects mouse oocyte maturation and subsequent early embryonic developmental competence following IVF by increasing intracytoplasmic oxidative stress in mature oocytes. NAC can reduce these harmful effects to a certain extent.	BMC Pharmacol Toxicol Vol.20 Issue 1 Pages 43	10.1186/s40360-019-0323-9	31331389	in vitro	-	-	-	-	-	-	-	-	1	0	25、50、および 100 μg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1877	M. Li, J. Gong, L. Ge, H. Gao, J. Yang, C. Yang, J. Kang, Y. Fang and H. Xu	2022	Development of human retinal organoid models for bisphenol toxicity assessment	Bisphenols, including Bisphenol A (BPA), Tetramethylbisphenol A (TMBPA), and Tetramethylbisphenol S (TMBPS), have been widely applied in the production of polycarbonate plastics and epoxy resins, and have been detected in various environmental media and human tissues. Bisphenol A (BPA) is a well-known endocrine disruptor (ED) that has been reported to cause developmental toxicity in the retina, the most sensitive tissue of the central nervous system. However, the effects of bisphenols on human retinal development is still unknown. In this study, to evaluate the toxicity of bisphenols on early retinal development, human embryonic stem cells were induced to differentiate into retinal organoids that responded to BPA, TMBPA, and TMBPS, at human exposure relevant concentrations. The global gene expression of retinal organoids was analyzed by RNA sequencing (RNA-seq). A set of retinal development related biological processes, including neuron differentiation, photoreceptors, eye development, and retina layer formation, were identified in retinal organoids corresponding to different developmental stages. The RNA-seq data also showed that BPA, TMBPA, and TMBPS influenced retinal development by interfering with the Cytokine-cytokine receptor interaction pathway. Moreover, BPA, TMBPA, and TMBPS significantly disrupted the expression of CNTFR, IL6ST, and LIFR, which are the receptor complex components of the Cytokine-cytokine receptor interaction pathway, appearing to exert more toxicity than BPA and TMBPS. Furthermore, these bisphenols exhibited different effects at different ranges of neural retina development. The sensitivity of retinal development to bisphenols depends on their developmental stages. This study provides new insights into the deep dissection of retinotoxicity after prenatal bisphenol exposure.	Ecotoxicol Environ Saf. 2022 Oct 15:245:114094.	10.1016/j.ecoenv.2022.114094	36126549	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1878	J. Li, Z. Yin, L. Hua, X. Wang, F. Ren and Y. Ge	2022	Evaluation of BPA effects on autophagy in Neuro-2a cells	Bisphenol A (BPA), which is used for the industrial production of polycarbonate plastics and epoxy resins, is found in many commercially available products. Plasticizer BPA produces chemical substances worldwide, and knowledge of its effects on humans and animals is increasing. In the present work, the morphology of cells was observed by optical microscopy and phalloidin staining of nuclei was observed by optical microscopy and phalloidin staining of nuclei. Autophagy has an important role in the regulation of cell metabolism. To study the effect of BPA on the autophagy in Neuro-2a cells, the expression distribution of LC3 was detected by immunofluorescence, and the autophagosomes and autolysosomes were observed by transmission electron microscopy. The results showed that BPA could induce the formation of autophagosomes in Neuro-2a cells in a dose-dependent manner. The cell viability was detected by CCK-8 assay, and the results showed that the density of cells in the BPA-treated group was lower than that in the control group, and that the density of cells in the BPA-treated group was lower than that in the control group. Immunofluorescence analysis demonstrated that the expression of LC3 fluorescence intensity increased as increasing BPA concentration. Western blot results showed that the relative expression of protein p62 increased significantly and that the relative expression levels of the Beclin1 and the LC3 proteins significantly decreased with increasing BPA concentration. qRT-PCR results showed that the relative expression level of autophagy-related p62 mRNA increased significantly and that the relative expression level of Beclin1 mRNA decreased significantly with increasing BPA concentration. The above results indicated that BPA treatment exerted dose-dependent toxic effects on Neuro-2a cells, and BPA inhibited the autophagy level of Neuro-2a cells, thereby providing a new perspective in studying the toxic effects of BPA on Neuro-2a cells.	Toxicol Ind Health. 2022 Mar;38(3):151-161.	10.1177/07482337221076587	35261310	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1879	M. M. Li, Y. W. Dai, J. Y. Yu, P. Duan, X. L. Ma, W. W. Dong, N. Li and H. G. Li	2019	Comprehensive circRNA/miRNA/mRNA analysis reveals circRNAs protect against toxicity induced by BPA in GC-2 cells	Aim: To identify the circRNAs expression pattern and roles in bisphenol A (BPA)-induced germ cell apoptosis. Materials & methods: We performed circRNA/miRNA/mRNA-Seq in C57 a/J BPA-treated and nontreated GC-2 cells. Bioinformatics analysis, qRT-PCR, apoptosis assays, luciferase report assay were done in the function analysis. Results: A large number of apoptosis related circRNAs/miRNAs/mRNAs were differentially expressed with competing endogenous RNA network constructed. Interestingly, most investigated upregulated circRNAs, including circ-Dcaf13, circ-Nsd1, circ-Rps19 and circ-Tra2a820 showed protective effects in antagonizing BPA toxicity, with the effects individually and synergistically observed. Conclusion: circRNAs can play protective role via sponging miRNAs in toxicity. Some circRNAs may serve as novel targets for BPA toxicity intervention or as biomarkers.	Epigenomics. 2019 Jun;11(8):935-949.	10.2217/epi-2018-0217	31020848	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1880	H. Li, Y. Zhao, Q. Shen and H. Li	2022	Multiple circRNAs regulated by QKI5 conjointly spongemiR-214-3p to antagonize bisphenol A-inducedspermatocyte toxicity	Although circular RNAs (circRNAs) are found to play important roles in many pathophysiological processes, the canonical theory that they act as microRNA sponges is too recent and more challenged, given that most circRNAs are not highly abundant. Bisphenol A (BPA) is a widely distributed environmental endocrine disruptor (EDC) that has been reported to cause male reproductive toxicity. Here, we found that circRNA expression profiles in the testis of mice exposed to BPA were altered, especially circ_0001347 and circ_0001359, which were downregulated by BPA. Moreover, circ_0001347 and circ_0001359 were enriched mainly in spermatocytes and in the cytoplasm and were conserved between species. Overexpression of circ_0001347 and circ_0001359 significantly inhibited BPA-induced reproductive toxicity. They share binding sites with miR-214-3p and collectively reinforce the sponging effects. In addition, the upstream regulation mechanism, proven by bioinformatics analysis and in vitro gain- and loss-of-function study, shows that down-regulation of RNA binding protein QKI5 after BPA exposure can increase the expression of these protective circRNAs, which activate the cell protection process. The QKI5-circ0001347/circ0001359-miR-214-3p-ATF4 axis ameliorates the toxic effect of BPA on GC-2 cells. Many other circRNAs are regulated upon BPA treatment and QKI5-driven regulation also has binding sites with miR-214-3p. Thus the above axis may also be extrapolated to other circRNAs. Our results enrich the content of circRNA sponge mode and may provide new ideas to future medical studies and therapy.	Acta Biochim Biophys Sin (Shanghai) Vol.54 Issue 8 Pages 1090-1099	10.3724/abbs.2022101	35959880	in vitro	-	-	-	-	-	-	-	-	1	0	40、80、160 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1881	C. H. Li, D. H. Zhang, L. D. Jiang, Y. Qi and L. H. Xiao	2021	Binding and activity of bisphenol analogues to human peroxisome proliferator-activated receptor β / δ	Several studies have indicated metabolic function disruption effects of bisphenol analogues through peroxisome proliferator-activated receptor (PPAR) alpha and gamma pathways. In the present study, we found for the first time that PPARβ / δ might be a novel cellular target of bisphenol analogues. By using the fluorescence competition binding assay, we found seven bisphenol analogues could bind to PPARβ / δ directly, among which tetrabromobisphenol A (TBBPA, TA) bi(4-hydroxyphenyl) sulfone (TGSD), and tetramethylbisphenol A (TCTBP-A, 12-26-fold) exhibited stronger binding affinity than bisphenol A (BPA). In PPARβ / δ -mediated luciferase reporter gene assay, the seven bisphenol analogues showed stronger agonistic activities than BPA. Moreover, in human liver HL-7702 cells, the bisphenol analogues promoted the expression of the PPARβ / δ target genes PDK4 and ANGPTL4. Molecular docking simulation indicated the binding patterns of bisphenol analogues to PPARβ / δ might depend on halogenation and hydrophobicity and the transcriptional activity might depend on their binding affinity and hydrogen bond interactions. Overall, the PPARβ / δ pathway may provide a new mechanism for the metabolic function disruption of bisphenol analogues, and TBBPA and TCTBP-A might exert higher metabolic disruption effects than BPA via PPARβ / δ pathway.	Ecotoxicol Environ Saf. 2021 Dec 15:226:112849.	10.1016/j.ecoenv.2021.112849	34627044	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通帳性評価（動物）1：該当、0：該当しない　通帳性評価（疫学）1：該当、0：該当しない　通帳性評価（in vitro）1：該当、0：該当しない　通帳性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通帳性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通帳性評価基準適合（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1882	C. Li, Z. Cui, Z. Liu, H. Fan, Y. Lan, J. Luo, F. Ruan, Y. Huang, K. Chu, Y. Wu, D. Xia and J. Zhou	2024	MIR-204 regulates autophagy and cell viability by targeting BDNF and inhibiting the NTRK2-dependent PI3K/Akt/mTOR pathway in a human granulosa cell line exposed to bisphenol A	Bisphenol A (BPA) is a widespread endocrine disruptor that mimics estrogen. The accumulation of BPA within the human body has been shown to be detrimental to ovarian function. However, few studies have focused on the specific mechanisms by which it causes harm to granulosa cells (GCs). ovarian carcinoma cells that are responsible for the growth and function of oocytes. In vitro research was conducted using human GC line (KGN cells). The results indicated that exposure to BPA significantly reduced the viability of KGN cells, induced autophagy, and altered the expression of microRNA-204 (miR-204). Through inhibiting the PI3K/Akt/mTOR pathway. Interestingly, these effects could be partly reversed by miR-204 mimics. Using the human ovarian granulosa tumor cell line COV434 as a model, we investigated and compared the transcriptomic changes induced by BPA with 2D6 was predicted to target BDNF. Additionally, our findings confirmed that miR-204 has the ability to directly target BDNF through a luciferase assay. Downregulation of miR-204 abrogated the BPA-exposure-mediated effects on proliferation and autophagy. Furthermore, the inhibition of miR-204 significantly reversed the downregulation of PI3K/Akt/mTOR pathway-related molecules. Similarly, co-cultivated with 2D as a result, mRNA2 involved in BPA-mediated damage to GC proliferation and autophagy, and our data provide the first in vivo evidence that increasing miR-204 expression and inhibiting the BDNF/NTRK2-mediated PI3K/Akt/mTOR signaling pathway are involved in the BPA-induced toxic effects. In KGN cells.	Ecotoxicol Environ Saf Vol.287 Pages 117304	10.1016/j.ecoenv.2024.117304	39520743	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1883	C. T. Leung, Y. Yang, T. F. Chan, X. Lin, A. S. T. Wong, W. Y. Lui, K. W. Y. Yuet, R. Y. C. Kong, K. P. Lai and R. S. S. Wu	2023	Chromatin modifiers: A new class of pollutants with potential epigenetic effects revealed by in vitro assays and transcriptomic analyses	A great variety of endocrine-disrupting chemicals (EDCs) have been used extensively and become widespread in the environment nowadays. Limited mammalian studies have shown that certain EDCs may target chromatin modifiers and induce epigenetic changes. However, the mechanisms underlying these changes remain unclear. Here, we used a panel of 12 EDCs to investigate their potential to induce chromatin changes. Induced by these pollutants remain unanswered. Using the human ovarian granulosa tumor cell line COV434 as a model, we investigated and compared the transcriptomic changes induced by the 12 EDCs with diverse chemical structures (i.e. BDE-47, BPA, BP-3, DEHP, DHP, EE2, TCS, TDCPP and TPT), to inquire if there is any common epigenetic modification associated with reproductive functions induced by these EDCs. Our results showed that COV434 cells were more responsive to BP-3, MP, DEHP and EE2, and more importantly, these four EDCs altered the expression of gene clusters related to DNA damage response, cell cycle, proliferation, and chromatin remodeling, which can potentially lead to epigenetic modifications and transgenerational inheritance. Furthermore, dysregulation of similar gene clusters was common in DEHP and MP exposure. Our findings suggested that chromatin modifiers could be a novel class of pollutants that induce epigenetic changes and transgenerational reproductive impairments. Our study highlighted chromatin modifications caused by a class of chemicals which that may potentially lead to epigenetic changes and transgenerational reproductive impairments. Overall, this study highlighted chromatin modifications caused by a class of chemicals which that may potentially lead to epigenetic changes and transgenerational reproductive impairments.	Toxicology. 2023 Jan 15:484:153413.	10.1016/j.tox.2022.153413	36581016	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1884	D. Lei, T. Hong, L. Li, L. Chen, X. Luo, Q. Wu and Z. Liu	2021	Isobaric tags for relative and absolute quantitation-based proteomics analysis of the effect of ginger oil on bisphenol A-induced breast cancer cell proliferation	Several chemicals in the environment, particularly those with estrogenic activity and small amounts (micromolar or lower) of environmental estrogen can cause changes in cell function and interfere with endocrine functions of animals and humans. These compounds enter the human body and increase the load of estrogen in the body, leading to an increasing incidence of estrogen-related tumors, breast cancer, ovarian cancer and endometrial cancer. Previous studies have demonstrated that ginger can inhibit the expression of estrogen receptors, while the bioactive ingredients of ginger rig will barely inhibit proliferation and promote the apoptosis of breast cancer cells. However, the molecular mechanisms underlying the anti-breast cancer effects of ginger oil remain unclear. Therefore, in this study, we investigated the effects of BPA, ginger oil, and combined treatment on the proteomic characteristics of MCF-7 cells. In total, 5,586 proteins were identified, and 1,000 proteins were differentially expressed. Overall, 538 differentially expressed proteins were identified. Compared with the control group, MCF-7 cells treated with BPA and GEO BPA resulted in 69 DE up- and 33 downregulated, 681 DE up- and 382 downregulated and 31 up- and 31 downregulated differentially co-pressed proteins, respectively. Compared with the BPA group, MCF-7 cells treated with GEO BPA resulted in 250 DE up- and 154 downregulated differentially expressed proteins, among the 216 differentially expressed proteins in the GEO BPA group, 10 proteins were associated with oxidative phosphorylation pathways, while succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial (SDHA) was significantly downregulated. Moreover, SDHA was significantly downregulated in MCF-7 cells treated with BPA compared with those treated with GEO BPA combined treatment. Through the analysis of Gene Ontology and Kyoto Encyclopedia of Genes and Genomes, the cellular localization, functional annotation and biological pathways of differentially expressed proteins were co-annoted. The results indicated that GEO BPA may act through the oxidative phosphory lation pathway, decreased the expression of SDHA and SDHC, affected the structure of c ell cycle and increased the reactive oxygen species (ROS). This may have led to oxidative stress and the death of breast cancer cells, and the SDH signaling pathway may be an important mediator of the inhibitory effects of GEO. In MCF-7 breast cancer cells. GEO can inhibit the proliferation of breast cancer MCF-7 cells induced by BPA, and the underlying mechanism may be associated with oxidative phosphorylation. These results may aid the development of future treatment strategies for breast cancer caused by environmental estrogen exposure.	Oncol Lett. 2021 Feb;21(2):101.	10.3892/ol.2020.12362	33376534	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10 h, 10 d, 15 ?, 10 d and 10 d each	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1885	S. G. Lee, G. E. Song, J. Seok, J. Kim, M. W. Kim, J. Rhee, S. Park, K. S. Jeong, S. Lee, Y. H. Lee, Y. Jeong, H. M. Chung and C. Y. Kim	2024	Evaluation of the cardiotoxicity potential of bisphenol analogues in human induced pluripotent stem cells derived cardiomyocytes	The importance of evaluating the cardiotoxicity potential of common chemicals as well as new drugs is increasing as a result of the development of animal alternative test methods using human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM). Bisphenol A (BPA), which is used as a main material in plastics, is known as an endocrine-disrupting chemical, and recently reported to cause cardiotoxicity through inhibition of hERG channels. Although BPA analogues are used as substitutes for BPA in various products, including BPS, BPF, and BPAF, their safety has not been sufficiently verified. Therefore, cardiotoxicity data for analogues of BPA are still lacking. In this study, in order to evaluate the cardiotoxicity potential of bisphenols, including BPA as a substitute, in hiPSC-CMs, we used a multielectrode array-based cardiotoxicity evaluation method that was previously established. Acute exposure to all bisphenol analogues did not affect cardiac rate, but spike amplitude, beat period, and field potential duration were decreased in a dose-dependent manner in most of the bisphenols except bisphenol S. In addition, bisphenols, except for bisphenol S, reduced the contractile force of hiPSC-CMs and resulted in beating arrest at high doses. Taken together, it can be suggested that the developed bisphenol analogues could cause cardiotoxicity even with acute exposure, and it is considered that the application of the MEA-based dual cardiotoxicity evaluation method can be an effective help in the development of safe alternatives.	Ecotoxicol Environ Saf Vol.272 Pages 116108	10.1016/j.ecoenv.2024.116108	38364764	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1, 10, 30, 100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1886	J. K. Lee, W. S. Choi, J. Y. Song, O. S. Kwon, Y. J. Lee, J. S. Lee, S. Lee, S. R. Choi, C. H. Lee and J. Y. Lee	2023	Anti-inflammatory effects of Athyrium yokoscense extract via inhibition of the Erk1/2 and NF-κB pathways in bisphenol A-stimulated A549 cells	Bisphenol A is an environmental endocrine disruptor that has similar functions to estrogen in humans. However, few studies have investigated pulmonary inflammation induced by BPA, and the effect of Athyrium yokoscense extract on this inflammatory response is unknown. In this study, we investigated the effect of BPA on A549 human alveolar epithelial cells. BPA at concentrations higher than 100 μM was cytotoxic to A549 cells, and 30 μM BPA was selected as a non-cytotoxic dose. BPA at 30 μM induced the production of inflammatory cytokines and chemokines, including IL-6 and IL-8, and BPA also increased the production of reactive oxygen species (ROS). Furthermore, BPA activated nuclear factor-κB (NF-κB) and IκB-α and IκB-β were phosphorylated by BPA. However, the mRNA level of the calcium channel gene Orai3, contraction-related genes Rho-associated coiled-coil kinase (Rock) 1 and Rock2, and cadherin development and morphogenesis genes Fibin, Lefty, and Sox2 were significantly decreased in the PD-, DP-, and BPA-treated groups. Interestingly, treatment with Rb188 rescued the altered calcium channel gene, contraction-related genes, and cardiac development and morphogenesis genes. PD, DP, and BPA treatments reduced the intracellular calcium level. Taken together, these results indicate that EDCs (DP and BPA) has a structure similar to that of endogenous steroid hormones such as progesterone and estrogen, and DP and BPA act like progesterone to inhibit and disrupt cardiomyocyte differentiation of mESCs.	Toxicol Res. 2022 Nov 7;39(1):135-146.	10.1007/s43188-022-00154-0	36726827	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1～100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1887	J. H. Lee, Y. M. Yoo, E. M. Jung, C. H. Ahn and E. B. Jeung	2019	Inhibitory effect of octyl-phenol and bisphenol A on calcium signaling in cardiomyocyte differentiation of mouse embryonic stem cells	Endocrine-disrupting chemicals (EDCs) have structures similar to steroid hormones and can interfere with hormone synthesis and normal physiological functions of reproductive organs. For example, sex steroid hormones influence cardiac signaling of the cardiac muscle to early embryo development. To confirm the effect of environmental EDCs, octyl-phenol (OP) and bisphenol A (BPA) on early differentiation of mouse embryonic stem cells (mESCs) into cardiomyocytes, mESCs were treated with PD, OP, and BPA two days after attachment and media were replaced every two days. In addition, cells were treated with ethylene (RUBB), a synthetic steroid hormone, and tamoxifen (TAM), a synthetic estrogen receptor (ER) antagonist, to confirm the effect of OP and BPA on the ER. The differentiation ratio of mESCs into cardiomyocytes was not affected by treatment groups. However, the mRNA level of the calcium channel gene Orai3, contraction-related genes Rho-associated coiled-coil kinase (Rock) 1 and Rock2, and cadherin development and morphogenesis genes Fibin, Lefty, and Sox2 were significantly decreased in the PD-, OP-, and BPA-treated groups. Interestingly, treatment with Rb188 rescued the altered calcium channel gene, contraction-related genes, and cardiac development and morphogenesis genes. PD, OP, and BPA treatments reduced the intracellular calcium level. Taken together, these results indicate that EDCs (OP and BPA) has a structure similar to that of endogenous steroid hormones such as progesterone and estrogen, and OP and BPA act like progesterone to inhibit and disrupt cardiomyocyte differentiation of mESCs.	J Physiol Pharmacol. 2019 Jun;70(3).	10.26402/jpp.2019.3.10	31566189	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1888	H. Lee, I. Park and K. Park	2023	Mixture Effects of Bisphenol A and Its Structural Analogs on Estrogen Receptor Transcriptional Activation	Bisphenol A (BPA) exposure has been widely linked to endocrine-disrupting effects. Recently, many substitutes for BPA have been developed as safe structural analogs. However, they have still been reported to have similar adverse effects. The current study evaluated the effects of bisphenol A and eight structural analogs on the transcriptional activity of estrogen receptor alpha (ERα). The effects of binary and ternary mixtures prepared for different combinations of BPA analogs were also evaluated for transcription activity. The measured data of the mixtures were compared to the predicted data obtained by the full logistic model, and the model deviation ratio (MDR) was calculated to determine whether the effects were synergistic, antagonistic, or additive. Overall, the results suggest that the effect of bisphenol compounds on additive in binary and ternary mixtures.	Toxics. 2023 Dec 4;11(12):986.	10.3390/toxics11120986	38133387	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10－11~10－3 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1889	C. T. Lee, C. F. Hsieh and J. Y. Wang	2021	Bisphenol a Induces Autophagy Defects and AIF-Dependent Apoptosis via HO-1 and AMPK to Degenerate N2a Neurons	Bisphenol A (BPA) is an environmental contaminant widely suspected to be a neurological toxicant. Epidemiological studies have demonstrated close links between BPA exposure, pathogenetic brain degeneration and altered neurobehaviors, considering BPA a risk factor for cognitive dysfunction. However, the mechanisms of BPA resulting in neurodegeneration remain unclear. Herein, cultured N2a neurons were subjected to BPA treatment, and neurotoxicity was assessed using neuronal viability and differentiation capacity. Signaling events were also investigated to define cell degeneration were also evaluated. Results revealed that BPA induced cell viability and axon outgrowth (e.g., by down-regulating GAP43 and CaMKII), thus confirming its role as a neurotoxicant. BPA-induced neurotoxicity by down-regulating Bcl-2 and initiating apoptosis and autophagy. Pan-inhibitor (Ivacaftor) by nuclear translocation of apoptosis-inducing factor (AIF). Moreover, BPA-induced autophagy was characterized by the formation of autophagosomes and the accumulation of LC3-II and p62 proteins, mediated the molecular signaling involved in apoptosis and autophagy. HO-1 inhibition or AIF silencing effectively reduced BPA-induced neuronal death. Although BPA-elicited intracellular oxygen free radical production, ROS scavenger NAC exerted no effect against BPA insults. These results suggest that BPA induces N2a neurotoxicity characterized by AIF-dependent apoptosis and p62-related autophagy defects via HO-1 up-regulation and AMPK activation, thereby resulting in neuronal degeneration.	Int J Mol Sci. 2021 Oct 11;22(20):10948.	10.3390/ijms222010948	34681608	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.01～100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1890	C. K. Lee, F. T. Wang, C. H. Huang, H. J. Liu and W. H. Chan	2025	Effects and regulatory mechanisms of bisphenol a on the increases apoptosis and decreases differentiation potential in mouse embryonic stem cells	Bisphenol A has deleterious effects on reproductive, developmental, cell biological, and physiological functions. Here, we investigated the dosage effects of bisphenol A on the differentiation potential and apoptosis of mouse embryonic stem cells, and assessed some relevant regulatory mechanisms. The results showed that bisphenol A at doses of 1.2 μmol/L triggers apoptotic processes, without necrotic cell death in the ES1 36 mouse embryonic stem cell line. To death effect was seen at treatment dosages of 0.6 μmol/L or less. Mechanistically, the application of 1.2 μmol/L bisphenol A directly increased the intracellular oxidative stress levels, significantly increased the cytoplasmic calcium and nitric oxide contents, decreased the mitochondrial membrane potential, activated caspases 8 and 3, and triggered apoptotic cell death. Interestingly, embryoid body formation assays showed that 0.3 μmol/L bisphenol A decreased the differentiation potential of ES1 40 cells without inducing apoptotic processes. Together, our results indicate that treatment with 1.2 μmol/L bisphenol A induces apoptosis in mouse embryonic stem cells via oxidative stress-mediated mitochondrial dysfunction and activation of caspase cascades. In this. These results provide important evidence that bisphenol A should be considered a potent cytotoxin that has dose-dependent impacts on differentiation and apoptosis in a mouse embryonic stem cell line.	Toxicol Res (Camb) Vol.14 Issue 2 Pages tfaf043	10.1093/toxres/tfaf043	40161257	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.5 μmol/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1891	D. Lavoglina, N. Vinzer, K. Samuel, E. Davey, R. D. Björnerg, J. Hassan, J. Kuopnen, P. Rantakokko, H. Kiviranta, A. Rinken, M. Divossin, A. Salumets and P. Damdimopoulou	2022	Endocrine disrupting chemicals interfere with decidualization of human primary endometrial stromal cells in vitro	Multiple studies have shown associations between exposure to endocrine disrupting chemicals (EDCs) and reduced fertility in women. However, little is known about the target organs of chemical disruption of female fertility. Here, we investigated the hypothesis that exposure to EDCs impairs the decidualization of human endometrial stromal cells (hESCs), a process essential for successful establishment of endometrial receptivity, which is crucial for successful implantation, placentation, and pregnancy. We investigated the effect of nine selected EDCs on primary human endometrial stromal cell decidualization in vitro. The cells were exposed to a decidualization inducing mixture in the presence or absence of 1 μM of nine different EDCs. For nine days. Extent of decidualization was assessed by measuring the activity of cAMP dependent protein kinase, Rho-associated coiled-coil containing protein kinase, and prolactin (PRL) secretion. Cytotoxicity, mitochondrial membrane potential, and secretion of prolactin into the media by using ELISA. Decidualization inducing mixture upregulated activity of protein kinases and prolactin secretion in cells derived from all women. Of the tested chemicals, diethylstilbestrol (DES), hexachlorobenzene (HCB) and mono-(2-ethylhexyl) phthalate (MEHP) significantly impaired decidualization in a dose-dependent manner. Bisphenol A (BPA) and tetrabromobisphenol A (TBBPA) significantly affected activity of the kinases. None of the EDCs was cytotoxic, based on the assessment of total protein content or activity of the viability marker secret kinase 2 in lysates. These results indicate that EDCs commonly present in the blood circulation of reproductive aged women can reduce decidualization of human endometrial stromal cells in vitro. Future studies should focus on detailed hazard assessment to define possible risks of EDC exposure to endometrial dysfunction and implantation failure in women.	Front Endocrinol (Lausanne). 2022 Aug 19:13:903505.	10.3389/fendo.2022.903505	36060944	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1892	F. Lamberto, B. Shashaadze, R. Ekholuenetale, S. O. Lumbuenii, A. A. Hoskraday, A. Balogh, K. Kiviranta, M. Zara, J. Mencha, T. Frühlich and A. Dimyati	2023	Low-dose Bisphenol A exposure alters the functionality and cellular environment in a human cardiomyocyte model	Early embryonic development represents a sensitive time window during which the foetus might be vulnerable to the exposure of environmental contaminants, potentially leading to heart diseases also later in life. Bisphenol A (BPA), a synthetic chemical widely used in plastics manufacturing, has been associated to different developmental defects, even in low concentrations. This study aims to investigate the effects of environmentally relevant doses of BPA on developing cardiomyocytes using a human induced pluripotent stem cell (hiPSC)-derived model. Firstly, a 3D in vitro differentiation system to obtain cardiomyocytes from hiPSCs was established. Cardiomyocytes were exposed to BPA doses ranging from 0.01 nM to 10 μM for 30 days, starting from the beginning of the differentiation process. Cell viability was assessed throughout the differentiation process, were evaluated. The chemical significantly decreased the beat rate of hiPSC-CMs, extending the contraction and relaxation time in a dose-dependent manner. Quantitative proteomic analysis revealed a high abundance of basement membrane (BM) components (e.g., COL1A1, COL1A2, LAMC1, NID2) and a significant increase in TGFBC1 and DDR1 proteins in hiPSC-CMs treated with 10 μM BPA. Moreover, BPA exposure altered the expression of proteins involved in cell-matrix adhesion, cytoskeleton organization, and cell-cell communication, thus compromising cardiac integrity. Finally, BPA-induced changes in the cellular environment were also associated with a functional impairment, with hiPSC-CMs showing altered contractility. Taken together, our results revealed that a long-term treatment, even with low doses of BPA, can interfere with hiPSC-CMs functionality and alters the surrounding cellular environment, providing new insights about diseases that might arise upon the foetal exposure. Our study contributes to the current understanding of BPA effects on developing human foetal cardiomyocytes, in accordance with human clinical observations and animal studies, and it provides a suitable model for New Approach Methodologies (NAMs) for environmental chemical hazard and risk assessment.	Environ Pollut. 2023 Oct 15:335:122359.	10.1016/j.envpol.2023.122359	37567409	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.01-100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1893	S. S. Yi, Lam, Z. Shi, C. K. M. Ip, C. K. C. Wong and A. S. T. Wong	2023	Environmental-relevant bisphenol A exposure promotes ovarian cancer stemness by regulating microRNA biogenesis	Bisphenol A (BPA) is a ubiquitous environmental xenobiotic impacting millions of people worldwide. BPA has long been proposed to promote ovarian carcinogenesis, but the detrimental mechanistic target remains unclear. Cancer stem cells (CSCs) are considered as the trigger of tumor initiation and progression. Here, we chose the first line therapeutic resistance/environmentally relevant concentration of BPA can markedly increase the formation and expansion of ovarian CSCs concomitant. This effect is observed in both estrogen receptor (ER)-positive and ER-defective ovarian cancer cells, suggesting that is independent of the classical ERα. Rather, BPA induces ovarian CSC enrichment by activating the ERβ/GPER1-mediated c-Src/EGFR/STAT3 signaling pathway. Moreover, BPA exposure significantly suppressed the biogenesis of microRNA (miRNA) let-7 family, which is a direct downstream target of STAT3. Treatment in ALL-when administered before or together with the drug. We found that these three pollutants at nanomolar concentrations, lower than those established by current regulations, can reduce the cytotoxic effects of vincristine on ALL cells. Interestingly, we found that this is only achieved when exposure to pollutants occurs prior to administration of the chemotherapeutic drug. Moreover, we found that this effect could be mediated by activation of the PI3K/AKT pathway and stabilization of microtubules. This work strengthens the idea of exerting to take into account exposure to pollutants to improve the efficacy of chemotherapy treatments.	J Cell Mol Med. 2023 Sep;27(18):2792-2803.	10.1111/jcmm.17920	37610061	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10, 50 and 100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1894	F. A. Lagunas-Rangel, W. Liu and H. B. Schiöth	2023	Interaction between environmental pollutants and cancer drug efficacy: Bisphenol A, Bisphenol A diglycidyl ether and Perfluorooctanoic acid reduce vincristine cytotoxicity in acute lymphoblastic leukemia cells	Every day, we are exposed to many environmental pollutants that can enter our body through different routes and cause adverse effects on our health. Epidemiological studies suggest that these pollutants are responsible for approximately nine million deaths per year. Acute lymphoblastic leukemia (ALL) represents one of the major cancers affecting children, and although substantial progress has been made in its treatment, relapses are frequent after initial treatment and are now one of the leading causes of cancer-related death in pediatric patients. Currently, relatively little attention is paid to pollutant exposure during drug treatment and this is not taken into consideration in the clinical setting. Here, we investigated the effects of three pollutants, Bisphenol A (BPA), Bisphenol A diglycidyl ether (BADGE), and Perfluorooctanoic acid (PFOA), on the cytotoxicity of vincristine in ALL cells when administered before or together with the drug. We found that these three pollutants at nanomolar concentrations, lower than those established by current regulations, can reduce the cytotoxic effects of vincristine on ALL cells. Interestingly, we found that this is only achieved when exposure to pollutants occurs prior to administration of the chemotherapeutic drug. Moreover, we found that this effect could be mediated by activation of the PI3K/AKT pathway and stabilization of microtubules. This work strengthens the idea of exerting to take into account exposure to pollutants to improve the efficacy of chemotherapy treatments.	J Appl Toxicol. 2023 Mar;43(3):458-469.	10.1002/jat.4398	36181250	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該時点評価段階で原則として除外。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1908	H. Kim, H. S. Kim, Y. J. Piao and W. K. Moon	2019	Bisphenol A Promotes the Invasive and Metastatic Potential of Ductal Carcinoma In Situ and Protumorigenic Polarization of Macrophages	Increased cancer risk and immune disorders linked with exposure to environmental endocrine disruptors like bisphenol A (BPA) have been steadily reported. Nevertheless, the impacts of BPA on the breast ductal carcinoma in situ (DCIS) progression and macrophage polarization remain to be elucidated. Here, we analyzed the differentially expressed genes (DEPs) exposed DCIS cells and explored BPA effects on DCIS progression and macrophage polarization. BPA exposure to DCIS cells induced DEPs enriched in cell cycle, cell adhesion, and immune response pathways. BPA exposure to DCIS cells activated extracellular signal-regulated kinase (ERK) signaling and subsequent epithelial-to-mesenchymal transition-like changes, including extracellular matrix degradation of cell sheet, cell adhesion, and immune response were up-regulated. Q1 N-BPA promoted the proliferation and migration of U937 cells and the expression levels of M2 marker genes (Fig. 1 and C). BPA exposure to DCIS cells induced the expression of IL6 (M2) in M0 markers (Fig 1 and CD206) in macrophages. In coculture system, the migratory capacity of both cells and the expression levels of M2(IL-6 by 1, and CD206 in macrophages were significantly enhanced upon Q1 N-BPA. In a DCIS xenograft model, and exposure to an environmentally human-relevant low dose of 2.5 μg/l BPA for 7 days via drinking water led to an approximately 2-fold promotion in the primary tumor growth rate and a significant enhancement of lymph node metastasis, along with increased pulmonary(p< CD206 + M2 polarization of macrophages. These results demonstrate that BPA acts as an accelerator to promote DCIS progression to invasive breast cancer by affecting DCIS cell proliferation and migration as well macrophage polarization toward a protumorigenic phenotype.	Toxicol Sci. 2019 Aug 1;170(2):283-295.	10.1093/toxsci/kfz119	31143956	動物、in vitro	-	1	1	1	DCIS異種移植モデル	0	2.5 μg/l BPA	-	-	-	1	0	10-8 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1909	H. Kim, H. S. Kim and W. K. Moon	2019	Comparison of transcriptome expression alterations by chronic exposure to low-dose bisphenol A in different subtypes of breast cancer cells	The impacts of chronic bisphenol A (BPA) exposure suspected to be a potential risk factor for breast cancer progression are not thoroughly understood in different subtypes of breast cancer cells (BCCs). This study aimed to compare the differentially expressed genes (DEGs) and biological functions in MCF-7 (luminal A), SK-BR3 (HER2-enriched), and MDA-MB-231 (triple-negative) cells exposed to BPA at environmentally human-relevant low dose (10 -8 M) for 30 days, by using the approach of RNA sequencing and online informatics tools. BPA exposure resulted in 172, 137, and 134 DEGs in MCF-7 (98% 5th BRS/BPA, and MDA-MB-231 (69% respectively. The significantly enriched gene ontology terms of DEGs in each cell were different: cellular response to granulocyte-colony stimulating factor stimulus, regulation of fibrinolysis, sterile metabolism, glutamate receptor signaling pathway, and cellular response to cAMP in MCF-7, SK-BR3, and MDA-MB-231 cells, respectively. Moreover, BPA exposure altered the expression of genes involved in different cancer signaling pathways in MDA-MB-231/BPA cells. The immune-related analysis of DEGs across the breast cancer cells indicated MCF_M6 and T cell activation and dendritic cell migration by regulating the expression of immunostimulatory genes. High expression of IL1R, CAR and EPHB1 identified in MCF-7/BPA, SK-BR3/BPA, and MDA-MB-231/BPA are detrimental gene signatures to predict poor overall survival in luminal A, HER2-enriched and triple-negative breast cancer patients, respectively. These findings indicate chronic BPA exposure has dissimilar impacts on the regulation of gene expression and diverse biological functions, including immune modulation, in different subtypes of BCCs.	Toxicol Appl Pharmacol. 2019 Dec 15:385:114814.	10.1016/j.taap.2019.114814	31715268	in vitro	-	-	-	-	-	-	1	0	10 (-8) M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1910	C. H. Kim, M. J. Kim, J. Park, J. Kim, J. Y. Kim, M. J. An, G. S. Shin, N. M. Lee and J. W. Kim	2021	Bisphenol A Exposure Changes the Transcriptomic and Proteomic Dynamics of Human Retinoblastoma Y79 Cells	Bisphenol A (BPA) is a xenoestrogen chemical commonly used to manufacture polycarbonate plastics and epoxy resin and might affect various human organs. However, the cellular effects of BPA on the eyes have not been totally investigated. This study aimed to investigate the cellular variations by BPA exposure on human retinoblastoma cells. BPA did not show cytotoxic effects, such as apoptosis, alterations in cell viability and cell cycle regulation. Comparative analysis of the transcriptome and proteome profiles, even investigated after long-term exposure of 178 cells to low doses of BPA. Transcriptome analysis using RNA-seq revealed that mRNA expression of the post-transcriptional regulation-associated gene sets was significantly upregulated in the BPA-treated group. Cell cycle regulation-associated genes were also significantly more upregulated by exposure to BPA. Interestingly, RNA-seq analysis at the transcript level indicated that alternative splicing events, particularly retained introns, were noticeably altered by low-dose BPA treatment. Additionally, proteome profiling using SWATH-TOF-MS identified a total of nine differentially expressed proteins. These results suggest that alternative splicing events and altered gene/protein expression patterns are critical phenomena affected by long-term low-dose BPA exposure. This represents a novel marker for the detection of various diseases associated with environmental pollutants such as BPA.	Genes (Basel) Vol.12 Issue 2	10.3390/genes12020264	33670352	in vitro	-	-	-	-	-	-	1	0	20, 40, 80, 160, 500, and 1000 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1911	L. Khosnandi, A. Heidari-Moghadam, E. Yousefi, M. Javad Khodapar and Y. Asadi-Fard	2023	Naringenin ameliorates cytotoxic effects of bisphenol A on mouse Sertoli cells by suppressing oxidative stress and modulating mitophagy: An experimental study	BACKGROUND: Bisphenol A (BPA), an endocrine-disrupting agent, is widely used as polycarbonate plastics for producing food containers. BPA exposure at environmentally relevant concentrations can cause reproductive disorders. OBJECTIVE: The effect of Naringenin (NG) on BPA-induced Sertoli cell toxicity and its mechanism was examined in the present study. MATERIALS AND METHODS: In this experimental laboratory study, the Sertoli cells were treated with BPA (100 μM), NG (50 and 100 μM), and BPA + NG for 24 h. Cell viability, apoptosis, oxidative stress, and mitophagy were evaluated. Also, the mitochondrial membrane potential (MMP) was examined. The expression of mitophagy-related genes, including Parkin and PTEN-induced putative kinase 1 (Pink1), was also evaluated. RESULTS: BPA significantly lowered the viability of the Sertoli cells (p< 0.001). Pink1 and Parkin levels of the BPA group were significantly increased (p < 0.001), while the MMP was considerably decreased (p < 0.001). BPA-raised ROS and MDA levels (p < 0.001) and reduced antioxidant biomarkers (p< 0.001). NG at the 50 and 100 μg/ml concentrations could significantly improve the viability and MMP of TM4 cells (p< 0.05). NG depending on concentration, could decrease Pink1 and Parkin in mRNA and protein levels compared to the BPA group (p < 0.01). NG enhanced antioxidant factors, while ROS and MDA levels were decreased in the BPA-exposed cells. CONCLUSION: The beneficial impacts of NG on BPA-exposed Sertoli cells are related to the suppression of mitophagy and the reduction of oxidative stress.	Int J Reprod Biomed Vol.22 Issue 3 Pages 219-228	10.18502/ijrm.v22i3.16166	33868445	in vitro	-	-	-	-	-	-	1	0	0.8 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1912	L. Khiari, M. Staddari, L. Martin-s, M. Gorokwasz and L. Puberti	2025	Tetrabromobisphenol A, but not bisphenol A, disrupts plasma membrane homeostasis in myeloid cell models - A novel threat from an established persistent organic pollutant	Bisphenol A (BPA, a plastic polymer component and tetrabromobisphenol A (TBBPA, a brominated flame retardant) are industrial compounds and representative persistent organic pollutants (POPs) with similar chemical structures. Both are found in human blood and environmental samples, but their toxicological profiles differ significantly. BPA is a well-known endocrine disruptor, while TBBPA has not. As BPA, leads to disruption of the lipid bilayer homeostasis of the plasma membrane in myeloid cell models (HL-60, THP-1 and Raw 264.7). Applied methods include: Laurdan fluorescence spectroscopy, subcellular/cell-wide sub-resolution (using di-4-ANEPPDHQ), ARGOS and Laurdan) and fluorescence recovery after photobleaching. TBBPA increased rotational and lateral mobility and decreased general polarity (as confirmed in plasma membranes of myeloid cells, but decreased mobility and increased rigidity in internal membranes of the same cells. Strikingly, BPA had no significant membrane effects in these cells, suggesting a specific molecular interaction mechanism of TBBPA action which may potentially lead to disruption of immune function. Identification of this novel threat from an established pollutant with documented exposure pathways highlights the possibility that hematotoxicity of POPs may contribute to their environmental toxicity burden.	Sci Total Environ Vol.961 Pages 178284	10.1016/j.scitotenv.2024.178284	39798458	in vitro	-	-	-	-	-	-	1	0	5～200μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1913	N. G. Khan, D. Adiga, P. S. Rai and S. P. Kabekkodu	2024	Integrated In-Silico and In Vitro analysis to Decipher the contribution of bisphenol-A in cervical cancer	Bisphenol A (BPA) is a synthetic chemical widely used as a monomer for producing polycarbonate plastics. The present investigation employed an in-silico approach to identify BPA-responsive genes and comprehend the biological functions affected owing to this exposure. A Comparative Toxicogenomics Database search identified 29 BPA-responsive genes in cervical cancer (CC). Twenty-nine genes were screened using published datasets, and thirteen of those showed differential expression between normal and CC samples. Protein-Protein Interaction Networks (PPIN) analysis identified BIRC5, CHEK1, CCNB1, ESPL1, FOXM1, NPTX2, VEGFA, and TOP2A as hub genes. The hub genes were validated in the TCGA-CESC cohort, and BIRC5, CHEK1, and FOXM1 were significantly overexpressed in CC tissues. Survival analysis revealed that increased expression of these genes was correlated to poor survival outcomes. Changes in cell morphology, remodeling of the actin cytoskeleton, increased number and length of filopodia, elevated intracellular reactive oxygen species and calcium, and lipid droplet accumulation were noted upon BPA exposure. BPA treatment upregulated the expression of epithelial to mesenchymal transition pathway members and enhanced the nuclear translocation of CTNNB1. We showed that the enhanced migration and nuclear translocation of CTNNB1 upon BPA exposure is a calcium dependent process. The present study identified potential BPA-responsive genes and provided novel insights into the biological effects and mechanisms affected by BPA in CC. Our study raises concern over the use of BPA.	Toxicology. 2024 May:504:153791.	10.1016/j.tox.2024.153791	38555994	in vitro	-	-	-	-	-	-	1	0	1 nM, 1 μM, 1 mM, and 1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1914	V. M. Katata, M. D. Maximin-s, C. Y. Silva and P. Alessio	2022	The Role of Cholesterol in the Interaction of the Lipid Monolayer with the Endocrine Disruptor Bisphenol-A	Among pollutants of emerging concern, endocrine disruptors (EDs) have been shown to cause side effects in humans and animals. Bisphenol-A (BPA) is an ED by-product of the plastic industry and one of the chemicals with the highest volume produced yearly. Here, we studied the role of cholesterol in the BPA exposure effects over membrane models. We used Langmuir films of both neat lipid DPPC (1,2-dipalmitoyl-sn-glycero-3-phosphocholine) and DPPC/cholesterol (molar ratio 7:3) monolayers at the air/water interface. Surface pressure-area isotherms, surface potential measurements, and infrared reflection-absorption spectroscopy (IRRAS) measures induced changes in the DPPC and Chol-neat monolayers, namely, more molecular area expansion and ordering effects. However, at high surface pressure, the BPA was expelled from the air-water interface. For the DPPC:Chol mixture, BPA-induced expansion throughout the whole compression, indicating that BPA is present at the monolayer interface. The PM-IRRAS analysis showed that BPA interacted with the phosphate group of DPPC through hydrogen bonding, which caused the ionic expansion. Such evidence might be biologically relevant to better understand the mechanism of action of BPA in cell membranes since phospholipid/cholesterol and Chol are found in mammalian membranes.	Membranes (Basel) Vol.12 Issue 8	10.3390/membranes12080729	35893447	in vitro	-	-	-	-	-	-	1	0	1 × 10 − 5 mol/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1915	A. A. Kaicongo, M. Lemu-i, I. Amrouche-Mekkioui, M. Belhadj-Gomezy and C. Aguer	2022	BPA exposure in L6 myotubes increased basal glucose metabolism in an estrogen receptor-dependent manner but induced insulin resistance	Exposure to bisphenol A (BPA) is associated with insulin resistance and type 2 diabetes (T2D). Since muscle insulin resistance is the primary defect in T2D, we aimed to determine whether BPA alters glucose metabolism in skeletal muscle. L6 (L6-GLUT4) myotubes were exposed to 10 nM BPA for 48 h. Glucose uptake, GLUT4 translocation, and insulin signaling were assessed in the absence or presence of 1 μM insulin. Vehicle-treated cells were used as controls. Exposure to BPA increased basal glucose uptake and insulin-stimulated GLUT4 translocation to the plasma membrane. Insulin-induced phosphorylation of Akt and ERK1/2 was also increased. Co-exposure to BPA and insulin significantly decreased insulin-stimulated glucose uptake and GLUT4 translocation to the plasma membrane. Insulin-induced phosphorylation of Akt and ERK1/2 was also decre

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1921	G. Jocsak, E. Ujla, D. S. Kiss, I. Toth, Z. Banoy, T. Bartha, L. V. Frenyo and A. Zsarnovszky	2019	Endocrine Disruptors Induced Distinct Expression of Thyroid and Estrogen Receptors in Rat versus Mouse Primary Cerebellar Cell Cultures	The endocrine system of animals consists of fine-tuned cell-regulating mechanisms that maintain the hormonal and neuronal milieu during tissue development. This complex system can be influenced by endocrine disruptors (EDs), which are exogenous chemicals that can interfere with hormone action. Here we compared the effects of bisphenol A (BPA), a well-known ED, on cerebellar cell cultures prepared from neonatal rat and mouse pups. Their identification and sensitivity has been a hard to solve problem.Recent indications that the ED effects may be species-specific just further complicate the determination of biological ED effects. Here we compare the effects of bisphenol A, oxadiazon, and arsenic (well-known EDs) exerted on mouse and rat neural cell cultures by measuring the differences of the ED-affected neural estrogen- and thyroid-receptors. EDs alters the receptor expression in a species-like manner. Remarkable differences were detected in the magnitude as well as in the nature of biological responses. It is concluded that the interspecies differences (or species-specificity) in ED effects should be considered in the future testing of ED effects.	Brain Sci. 2019 Dec 5;9(12):359.	10.3390/brainsci9120359	31817561	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10－10 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1922	H. J. Jin, Z. D. Qiu, C. Qian, C. Y. Zhang and Y. Zhang	2025	Identification of the metabolomic alterations associated with the formation of bisphenol-A sulfate metabolite in HepG2 cells	The elucidation of the causal relationship between bisphenol A (BPA) exposure and hepatotoxic outcomes is challenging because of the complexity in both the BPA-derived metabolites formed in the liver and the associated endogenous molecular responses. We performed parallel metabolic experiments with BPA to characterize the BPA sulfate formation and the associated alterations in the metabolomic level in HepG2 cells using mass spectrometry-based metabolomic wide-association study. Briefly, HepG2 cells were exposed to 0 or 26 h to 2 or 10 μM BPA or DMSO or DMSO alone. The levels of BPA sulfate in the cell culture media were quantified by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). Metabolomic profiling was performed using UPLC-Q-TOF-MS/MS. Following the decreasing of amino sulfate, estrogen metabolism was observed as the top 3 enriched pathways in response to BPA exposure. MANOVA suggests that BPA sulfate formation in HepG2 cells involved in cluster B6 deficiency and dysregulated cluster B6-dependent processes, for example, the kynurenine pathway in tryptophan metabolism. These findings collectively provide insights into the linkage between exogenous and endogenous metabolism and the potential initial events in BPA exposure-induced hepatotoxicity.	Food Chem Toxicol Vol.200 Pages 115382	10.1016/j.fct.2025.115382	40058625	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1, 10 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1923	C. Jiménez-Torres, L. C. Hernández-Kelly, M. Najimi and A. Ortega	2020	Bisphenol A exposure disrupts aspartate transport in HepG2 cells	The liver is the organ responsible for bisphenol A (BPA) metabolism, an environmental chemical agent. Exposure to this toxin is associated with liver abnormalities and dysfunction. An important role played by excitatory amino acid transporters (EAATs) of the rat's gene family has been reported in liver injuries. To gain insights into a plausible effect of BPA exposure in the liver glutamate/aspartate transport, using the human hepatoblastoma cell line HepG2, our report a BPA-dependent dynamic regulation of SLC1A3 and SLC1A2. Through the use of radioactive [3 H]-D-aspartate uptake assessment and immunofluorescence approaches, we characterized time and dose-dependent regulation of the protein levels and function of these transporters after acute exposure to BPA. An increase in nuclear Yin Yang 1 was found. These results, suggest an important involvement of the EAATs in liver physiology and its disruption after acute BPA exposure.	J Biochem Mol Toxicol. 2020 Aug;34(8):e22516.	10.1002/jbt.22516	32363662	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1924	X. Jiang, S. Sun, C. Shi, K. Liu, Y. Yang, J. Cao, J. Gu and J. Liu	2024	Rsad2 mediates Bisphenol A-induced actin cytoskeletal disruption in mouse spermatocytes	Bisphenol A (BPA) is widely exposed in populations worldwide and has negative effects on spermatogenesis both in animals and humans. The homeostasis of the actin cytoskeleton in the spermatogenic epithelium is crucial for spermatogenesis. Actin cytoskeleton destruction in the seminiferous epithelium is one of the important reasons for BPA-induced spermatogenetic disorder. However, the underlying molecular mechanisms remain unclear. Here, we found that BPA exposure induced actin cytoskeleton disruption in mouse spermatocytes. Mechanistically, BPA exposure induced the expression of Rsad2 in spermatocytes, which interacted with cytoskeleton was dramatically disrupted and the cell morphology was markedly altered accompanied by significant increase in Rsad2 expression both in vitro and in vivo. Furthermore, the phalloidin intensities, and cell morphology were restored obviously when interfering with the expression of Rsad2 in BPA-treated GC-2 cells. In addition, we observed a significant decrease in intracellular ATP levels after BPA treatment, while the ATP level was obviously upregulated when knocking down the expression of Rsad2 in BPA-treated cells compared to cells treated with BPA alone. Moreover, Rsad2 elicited by mitochondria after BPA exposure in GC-2 cells. BPA promoted Rsad2 expression by activating type I IFN signaling in GC-2 cells. In summary, Rsad2-mediated BPA-induced actin cytoskeletal disruption in GC-2 cells, which provided clues to reveal the mechanism of BPA-induced male reproductive toxicity.	J Appl Toxicol. 2024 Oct;44(10):1478-1488.	10.1002/jat.4649	38828519	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1925	S. Ila, C. Li, M. Fang, M. Marques Dos Santos and S. A. Snyder	2022	Non-targeted metabolomics revealing the effects of bisphenol analogues on human liver cancer cells	Bisphenol analogues (BPs) are widely used in plastics, food packaging and other commercial products as non-safe alternative of BPA. As emerging environmental contaminants, BPs have received considerable attention in recent years. However, the toxicity of BPs is controversial and the mechanism of toxicity is unclear. In this study, non-targeted metabolomics based on UPLC-Q-TOF-MS/MS technology was applied to characterize the cellular metabolome alterations with treat the specific biomarkers of the metabolic disorders associated with BPs' toxicity. Eight structural BPF (BPF) analogs were applied to characterize the cellular metabolome alterations with treat the specific biomarkers of the metabolic disorders associated with BPs' toxicity. BPF, BPS and BPAF were selected using widefield embryos and human vascular endothelial cells (HUVECs). BP exposure at a sublethal concentration of 1/10 IC50 to mediate bilial concentration (96 h LC50) significantly hindered intersegmental vessel (ISV) growth, delayed common cardinal vein (CCV) remodeling and decreased subintestinal vessels (SIVs) in Tg (fli1:EGFP) zebrafish embryos. Meanwhile, the results of the endothelial tube formation assay showed that in vitro angiogenesis was inhibited by BP exposure. Mechanistically, BP exposure increased oxidative stress characterized by a significant decrease in superoxide dismutase (SOD) and catalase (CAT) activities and an increase in malondialdehyde (MDA) content. Moreover, BP exposure induced cell cycle arrest in the G0/G1 phase and apoptosis in HUVECs. Finally, BPF, BPS and BPAF were compared and evaluated, ranking as follows: BPAF > BPF > BPS > BPA. To the best of our knowledge, the present work, for the first time, systematically provides direct evidence for BPA and its alternatives on developmental vascular toxicity in vitro and in vivo. Therefore, these findings will provide insight into the rational and safe application of BPA substitutes.	Chemosphere. 2022 Jun;297:134088.	10.1016/j.chemosphere.2022.134088	35216976	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1926	G. Ji, J. Gu, M. Guo, L. Zhou, Z. Wang, L. Shi and A. Gu	2022	A systematic comparison of the developmental vascular toxicity of bisphenol A and its alternatives in vivo and in vitro	Due to the potential toxicity of bisphenol A (BPA), several bisphenols (BPs), including bisphenol F (BPF), bisphenol S (BPS) and bisphenol AF (BPAF), have been gradually used as its main substitutes, and the levels of BPs in the environment have increased significantly in recent years. However, the toxicity of BPs is controversial, and the mechanism of toxicity is unclear. In this study, we systematically compared BPA, BPF, BPS and BPAF's developmental vascular toxicity in vivo and in vitro. Comparative studies on the cardiovascular toxicity of BPs have not been evaluated. In this study, the developmental vascular toxicity of BPA and three predominant substitutes (BPF, BPS and BPAF) were evaluated using zebrafish embryos and human vascular endothelial cells (HUVECs). BP exposure at a sublethal concentration of 1/10 96 h median bilial concentration (96 h LC50)) significantly hindered intersegmental vessel (ISV) growth, delayed common cardinal vein (CCV) remodeling and decreased subintestinal vessels (SIVs) in Tg (fli1:EGFP) zebrafish embryos. Meanwhile, the results of the endothelial tube formation assay showed that in vitro angiogenesis was inhibited by BP exposure. Mechanistically, BP exposure increased oxidative stress characterized by a significant decrease in superoxide dismutase (SOD) and catalase (CAT) activities and an increase in malondialdehyde (MDA) content. Moreover, BP exposure induced cell cycle arrest in the G0/G1 phase and apoptosis in HUVECs. Finally, BPF, BPS and BPAF were compared and evaluated, ranking as follows: BPAF > BPF > BPS > BPA. To the best of our knowledge, the present work, for the first time, systematically provides direct evidence for BPA and its alternatives on developmental vascular toxicity in vitro and in vivo. Therefore, these findings will provide insight into the rational and safe application of BPA substitutes.	Chemosphere. 2022 Mar;291(Pt 2):132936.	10.1016/j.chemosphere.2021.132936	34798105	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1927	D. H. Jeong, D. W. Jung, J. W. Kim and H. S. Lee	2024	Beauvericin, produced by Fusarium oxysporum inhibits bisphenol A-induced proliferation of human breast cancer cell line by regulating ERα/p38 pathway	Research in BEA is a cyclic depsipeptide secondary metabolite of Fusarium species. It causes chemical hazards in food products and exists in an environment containing soil and various host types. On the other hand, bisphenol A (BPA) is a well-known endocrine disruptor. It is widely used in the production of polycarbonate plastics and epoxy resins. Although BPA has been reported to induce proliferation in breast cancer cells by regulating the estrogen receptor alpha (ERα) or p38 pathway, 17-α and 28-isoacyl, verified that BEA is a competitive ER antagonist. Additionally, BEA suppressed cell proliferation in the anti-proliferative assay involving ER-positive human breast cancer cells co-treated with BPA and BEA. In respect to an anti-proliferative activity, the BPA-induced phosphorylation of p38 protein was inhibited in the presence of BEA. These results suggested that BEA exerts inhibitory potentials on endocrine-disrupting effects and possibly acts as a natural therapeutic material for human estrogen-hormonal health.	J Steroid Biochem Mol Biol. 2024 May;239:106483.	10.1016/j.jsbmb.2024.106483	38369033	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1928	N. Jangid, A. Sharma and N. Srivastava	2024	Potential involvement of ferroptosis in BPA-induced neurotoxicity: An in vitro study	BACKGROUND: Ferroptosis is a newly recognized cell death pathway having distinct characteristics compared to traditional cell death pathways such as apoptosis, necroptosis, or autophagy. However, the potential involvement of ferroptosis in bisphenol A (BPA)-induced neurotoxicity has not been well explored so far. In present study, our analysed the relationship between ferroptosis and BPA-induced neurotoxicity. METHODS: In this study, a human neuroblastoma cell line, SH-SY5Y, was treated with BPA, ferrostatin-1 (FST-1, ferroptosis inhibitor) and RSL-3 (ferroptosis inducer). The cell viability was measured using MTT assay. Additionally, the levels of lipid peroxidation, total iron content, reactive oxygen species (ROS) generation, and nitric oxide content were measured to evaluate the key markers of ferroptosis. To further test the involvement of ferroptosis in BPA-induced neurotoxicity, other ferroptosis markers such as glutathione peroxidase (GPx) activity, total glutathione contents and antioxidant parameters were also evaluated. RESULTS: The cell viability of SH-SY5Y cells was significantly decreased in a concentration-dependent manner when treated with BPA for 24 h. BPA treatment also induced ferroptosis in SH-SY5Y cells, as indicated by increased ROS, lipid peroxidation (LPO), and GSSG/GSH ratio. Also the antioxidant parameters including catalase and superoxide dismutase activity of neuronal cells were dose-dependently upregulated upon BPA exposure. However, the levels of lipid peroxidation, total iron, reactive oxygen species, and nitric oxide contents were increased in a concentration-dependent manner which could be rescued by FST-1 and exacerbated by RSL-3. The total iron in SH-SY5Y cells at 12 μM concentration was found to be 2.3 fold (p < 0.05) of control and at highest BPA concentration total iron was about 4.15 fold (p < 0.001) of control. CONCLUSIONS: The present study indicated that, ferroptosis plays an important role in the progression of BPA-induced neurotoxicity, and ferroptosis may become a novel target in the treatment of various neurological disorders.	Environ Toxicol Pharmacol. 2024 Mar;106:104355.	10.1016/j.etap.2023.104355	38154758	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1～10μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1929	J. W. Jang, J. W. Lee, Y. D. Yoon, J. S. Kang and S. Y. Moon	2020	Bisphenol A and its substitutes regulate human B cell survival via Nrf2 expression	B cells contribute to produce inflammatory cytokines and antibodies, to present autoantigens, and to interact with T cells, which lead to body defense and disease control. Nuclear factor (erythroid-derived 2)-like 2(Nrf2) is responsible for gene expression of antioxidant enzymes to protect cells from oxidative stress by reactive oxygen species(ROS) production. Bisphenol A(BPA) may not be safe due to the effect on body's physiological function. This study investigated the effect of BPA and its substitutes on human B cell survival via Nrf2 expression. Bisphenol A(BPA), bisphenol S(BPS), 4-hydroxyphenyl 4-isoprooxyphenylsulfone(D-70), and 2,2,6,6-tetramethyl-1,1-oxidedesmol(TMDO) were treated to human B cells. Intracellular ROS was also measured by using various substitutes for BPA. TMDO and D70-7 were not investigated whether N-Acetyl-L-cysteine(NAC) or ROS scavenger could inhibit BPA-treatment enhanced gene expression of antioxidant enzymes, heme oxygenase(HO)-1, catalase, superoxide dismutase(SOD) 1 and 2. As HO1(2) treatment induced cell death and ROS amount in WIL2-NS cells, BPA treatment significantly increased ROS amount in human B lymphoblastoid cells. When cytotoxicity was measured by using various substitutes for BPA, TMDO and D70-7 showed significantly lower cytotoxicity. Cell viability was reduced by Nrf2 overexpression compared to control cells. Taken together, these results implicate that B cell cytotoxicity by substitutes should be lower than BPA and Nrf2 can prevent B cells from BPA- or BPA substitutes- induced cytotoxicity via ROS production. Data suggest that the comprehensive studies on evaluation could be necessary to replace BPA in manufacture by other substitutes.	Environ Pollut. 2020 Apr;259:113907.	10.1016/j.envpol.2019.113907	32023790	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1930	T. Jambor, E. Kovacikova, H. Greifova, A. Kovacik, L. Libova and N. Lukac	2019	Assessment of the effective impact of bisphenols on mitochondrial activity and steroidogenesis in a dose-dependency in mice TM3 Leydig cells	The increasing worldwide production of bisphenols has been associated to several human diseases, such as chronic respiratory and kidney diseases, diabetes, breast cancer, prostate cancer, behavioral troubles and reproductive disorders in both sexes. The aim of the present in vitro study was to evaluate the potential impact bisphenols A, B, S and F on the cell viability and testosterone release in TM3 Leydig cell line. Mice Leydig cells were exposed to bisphenols A, B, S and F in concentrations 0.04–50 μg/ml for 24 h. Cell viability was examined using the metabolic activity assay, while the level of testosterone in cell culture media was determined by enzyme linked immunosorbent assay. Within the panel of substances under investigation, the highest cytotoxic effect was demonstrated by BPA. BPA and BPF in concentrations 10, 25 and 50 μg/ml (P<0.001) decreased Leydig cells viability, while the same doses of BPA and BPB also reduced testosterone production significantly (P<0.001). Taken together, the results of our study reported herein is a consistent with the conclusion that higher experimental doses of bisphenols have a cytotoxic effect and could have a dose-dependent impact on testosterone production.	Physiol Res Vol.68 Issue 4 Pages 689-693	10.33549/physiolres.934200	31342755	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.04－50 μg/ml	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1931	T. Jambor, N. Kolcatova, H. Greifova, A. Kovacik and N. Lukac	2023	Toxicity of bisphenol A and its replacements in the mice Leydig cells in vitro	The aim of the study was to examine the potential impacts of bisphenol A (BPA) and its analogues BPB, BPF, and BPS on mice TM3 Leydig cells, with respect to basal cell viability parameters such as metabolic activity, mitochondrial membrane potential, and cell membrane integrity. Cell viability was examined using the metabolic activity assay, while the level of testosterone was determined by enzyme linked immunosorbent assay. Obtained results revealed significant cell viability and testosterone production inhibition and cytotoxic effect of BPA in concentrations 10, 25 and 50 mcg/ml. Cell membrane integrity was significantly decreased at 5 mcg/ml of BPA and BPF and 10, 25, and 50 mcg/ml of BPA and BPS. The lysosomal activity was significantly affected at 10, 25, and 50 mcg/ml of applied bisphenols. A significant overproduction of ROS was recorded mainly at 5 and 10 mcg/ml of tested compounds. In addition, significant inhibition of GJIC was observed at 5 mcg/ml of BPA followed by a progressive decline at higher applied doses. In the case of testosterone production, a significant decline was confirmed at 10, 25 and 50 mcg/ml.	Physiol Res Vol.72 Issue 1 Pages 71-86	10.33549/physiolres.934989	36545881	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10 μg/ml	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1932	L. Q. Icmad, Y. Y. Kaong, H. Bahai, C. A. Lan and K. B. Yin	2024	Bombesin-like receptor 3 expression induced by bisphenol A is likely associated with reduced cell proliferation by inhibiting DNA synthesis and inducing inflammation in liver cells	BACKGROUND: Bisphenol A (BPA) is an exogenous endocrine disruptor mimicking hormones closely associated with health complications, such as cancer progression. BPA is also related to an increase in the prevalence of obesity, diabetes, and cardiovascular diseases. Bombesin-like receptor 3 (BRS-3) is an orphan G protein-coupled receptor (GPCR) that regulates energy homeostasis. However, its role in BPA-induced liver damage is unclear. METHODS: Therefore, the present study aimed to investigate the messenger ribonucleic acid (mRNA) expression of BRS3 in human liver THLE-2 cells upon BPA treatment by real-time polymerase chain reaction. The effects of BPA on the levels of pro-inflammatory proteins, interleukin-6 (IL6) and C-C motif chemokine ligand 2 (CCL2), in conditioned media of BPA-treated THLE-2 cells and deoxyribonucleic acid (DNA) synthesis in BPA-treated THLE-2 cells were also investigated by enzyme-linked immunosorbent assay (ELISA) and 5-bromo-2'-deoxyuridine (BrdU) incorporation assay, respectively. RESULTS: BPA treatment for 24 h significantly increased BRS3 mRNA levels in THLE-2 cells. Increased BRS3 mRNA levels were also observed from the transcriptome analysis of IL6- and CCL2-mediated signal transduction pathways in BPA-treated THLE-2 cells after IL6 or BPA treatment. Subsequently, the DNA synthesis analysis showed that bromodeoxyuridine-positive (BrdU-P) stained positive cells were decreased in BPA-treated THLE-2 cells at 72 h of treatment. CONCLUSION: The study demonstrates that BRS3 expression induced by BPA is likely associated with reduced cell proliferation by inhibiting DNA synthesis and inducing cellular inflammation in liver cells.	Mol Biol Rep. 2024 Feb 1;51(1):271.	10.1007/s11033-023-09080-2	38302795	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1933	L. Q. Icmad, A. R. Abdulhameed, Y. Y. Kaong, M. N. H. Abdullah, H. Bahai, T. J. Jarand, K. B. Yin	2022	Bisphenol A is a carcinogen that induces lipid accumulation, peroxisome proliferator-activated receptor-γ expression and liver disease	Bisphenol (BP) A is an exogenous endocrine disruptor that mimics hormones closely associated with health complications, e.g., obesity and cancers. The present study aimed to evaluate the effects of BPA on human liver cell proliferation and lipid accumulation in human liver THLE-2 cells. The cytotoxicity of BPA was evaluated using an MTT assay. Cytotoxic BPA levels (0.1% and 0.2% of the 50% cytotoxic concentration (CC50) of BPA) were used to treat THLE-2 cells. The cell proliferation was evaluated by a 5-bromo-2'-deoxyuridine (BrdU) incorporation assay. The cell viability was evaluated using an MTT assay. Clusters PPARα and PPARγ gene expression in BPA-treated THLE-2 cells was assessed using RT-PCR. Lipid accumulation and sterol/fatty acid synthesis were evaluated using Oil Red O staining, and liver tissue was examined using haematoxylin and eosin staining. Finally, cytochrome P450 (CYP) gene expression was assessed in BPA-treated THLE-2 cells using real-time PCR. PPARγ is likely the primary nuclear receptor protein involved in lipid accumulation in THLE-2 cells following BPA treatment and is associated with liver disease. THLE-2 cells exposed to BPA showed a decrease in viability and lipid accumulation after 48 h treatment. Higher PPARγ gene expression was observed in BPA-treated THLE-2 cells than in untreated cells. Liver tissue from BPA-treated mice showed hepatocyte ballooning and lipid droplet accumulation. Cytochrome P450 gene expression was also increased in BPA. Downregulated CYP1A1 and CYP2B1 gene expression implied that BPA-treated THLE-2 cells decreased capacity for carcinogen metabolism, while upregulated CYP2E1 gene expression exceeded normal cytotoxicity. The present study revealed that BPA served as a carcinogen, enhanced tumorigenesis susceptibility and may induce other types of liver disease.	Exp Ther Med Vol.24 Issue 6 Pages 735	10.3892/etm.2022.11671	36466761	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	[illegible]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通過性評価（動物）1：該当、0：該当しない

通過性評価（疫学）1：該当、0：該当しない

通過性評価（in vitro）1：該当、0：該当しない

通過性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通過性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	通過性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1934	L. Iskandaroni, S. Romaniello, B. F. Hales and B. Robaire	2025	The effects of bisphenol A and its analogs on steroidogenesis in MA-10 Leydig cells and KGN granulosa cells	Bisphenols are a family of chemicals used in the manufacture of consumer products containing polycarbonate plastics and epoxy resins. Studies have shown that exposure to bisphenol A (BPA) may disrupt steroidogenesis and induce adverse effects on male and female reproduction, but little is known about BPA replacements. We determined the effects of six bisphenols on the steroidogenic function of MA-10 Leydig cells and KGN granulosa cells. Cells were treated with bisphenol A (BPA), bisphenol AF (BPAF), bisphenol S (BPS), bisphenol F (BPF), bisphenol AF (BPAF), or bisphenol TMC (0.1 nM–100 μM) for 24 h. Cells were exposed for 30 min or 4 h to bisphenols (0.01 M–100 M) with BPA, bisphenol F, bisphenol S, bisphenol AF, or bisphenol TMC, were tested and efficacy) cAMP (Gs/cAMP) stimulated conditions. In MA-10 cells, most bisphenols increased the Gs/cAMP-stimulated production of progesterone. In KGN cells, there was a general decrease in progesterone production, while estradiol levels were increased following exposure to many bisphenols. Quantitative real-time polymerase chain reaction analyses revealed that all six bisphenols (≥1 μM) upregulated the expression of STAR, a cholesterol transporter, in both cell lines after stimulation. Numerous lipids directly involved in steroid and cholesterol biosynthesis were significantly altered in a cell line, chemical, and concentration-dependent manner. Thus, BPA and five of its analogs can disrupt steroid production in two steroidogenic cell lines and alter the levels of transcripts involved in this process. Importantly, BPA replacements do not appear to have fewer effects than BPA.	Biol Reprod. 2025 Feb 14;112(2):399-414.	10.1093/biolre/ioae165	39520287	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1935	L. Iskandaroni, T. McHattie, B. Robaire and B. F. Hales	2022	Effects of Bisphenols A, AF, and S on Endochondral Ossification and the Transcriptome of Murine Limb Buds	Bisphenols are a family of chemicals commonly used to produce polycarbonate plastics and epoxy resins. Exposure to bisphenol A (BPA) is associated with a variety of adverse effects; thus, many alternatives to BPA, such as bisphenol AF (BPAF) and bisphenol S (BPS), are now emerging in consumer products. We have determined the effects of 3 bisphenols on endochondral ossification and the transcriptome in a murine limb bud culture system. Embryonic mandibles were cultured in the presence of vehicle, BPA, BPAF, or BPS (0.1 nM–100 μM). BPAF (≥1 μM) and BPS (≥10 nM) reduced the area of hypertrophic chondrocytes and osteoblasts. Chondrogenesis was suppressed by exposure to ≥10 μM BPA, ≥1 μM BPAF, or ≥10 μM BPS and osteogenesis was almost completely arrested at 100 μM BPA or 10 μM BPAF. RNA sequencing analysis revealed that BPA, BPAF, and BPS altered the expression of 1,000, 1,500, and 1,200 genes, respectively. Pathway analysis revealed that BPA, BPAF, and BPS altered the expression of genes involved in lipid metabolism, cell cycle, and cell death. Of these genes, 200 were differentially expressed and altered in the same direction by all 3 bisphenols, suggesting that they have a common chemical-specific mechanism. Although the genes that were differentially expressed and altered by each bisphenol also had distinct chemical-specific alterations in gene expression. BPA- and BPAF-treated limbs exhibited a downregulation of fibroblast growth factor receptor 2 and cholesterol biosynthesis. Exposure to BPA and BPS resulted in the upregulation of key genes involved in cholesterol biosynthesis, whereas exposure to BPAF induced an upregulation of genes involved in bone formation and in the p53 signaling pathway. These data suggest that BPAF may be more detrimental to endochondral ossification than BPA, whereas BPS is of comparable toxicity to BPA.	Toxicol Sci Vol.187 Issue 2 Pages 234-253	10.1093/toxsci/kfab145	34850234	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1936	S. A. Hyun, C. Y. Lee, M. Y. Ko, S. H. Choi, Y. J. Kim, J. W. Seo, K. K. Kim and M. Ka	2021	Cardiac toxicity from bisphenol A exposure in human-induced pluripotent stem cell-derived cardiomyocytes	Bisphenol A (BPA) is a well-known endocrine-disrupting chemical that is widely used in a variety of products, including plastics, medical equipment and receipts. Hence, most people are exposed to BPA through the skin, inhalation and via the digestive system, and such exposure has been linked to cardiovascular diseases including coronary artery disease, hypertension, atherosclerosis, and myocardial infarction. However, the cardiotoxicity mechanism of xenobiotics, including BPA, remains poorly understood. In this study, we investigated the BPA exposure dose-dependent cardiac toxicities in human-induced pluripotent stem cell (hiPSC)-CMs. Acute BPA exposure in hiPSC-CMs resulted in reduced field potential, as measured by multi-electrode array (MEA). Furthermore, we observed that BPA dose dependently inhibited hERG tail current (IKr) in HEK293 cells. In addition, BPA exposure dose dependently inhibited calcium transients and contraction in hiPSC-CMs. Our findings suggest that BPA exposure leads to cardiac dysfunction and cardiac risk factors, such as arrhythmia.	Toxicol Appl Pharmacol. 2021 Oct 1:428:115696.	10.1016/j.taap.2021.115696	34419494	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1937	Y. S. Huang, A. A. Chang, Z. J. Yang, J. A. Chen, C. K. Lin and H. C. Lan	2024	Long-term subculture induces syncytialization and influent the response to bisphenol A (BPA) of placental JEG-3 cells	The placenta is a temporary organ that exists only during pregnancy, responsible for connecting the mother and the fetus. During placental development, the cytotrophoblast cells differentiate into multinucleated, syncytialized cells that overlap the chorionic villi, a process known as syncytialization. These syncytiotrophoblast cells serve as a barrier between maternal circulation and the fetus and secrete important hormones such as human chorionic gonadotropin (hCG) and progesterone, which are crucial for maintaining pregnancy. Abnormal syncytialization can lead to various pregnancy complications, including miscarriage, preeclampsia, and fetal growth restriction. Previous studies showed that Bisphenol A (BPA), an endocrine-disrupting chemical (EDC), exposure, especially during pregnancy, it affects placental development, hormone synthesis, and can probably increase the risk of pregnancy complications. Furthermore, some compounds like hCG and forskolin induce the cell differentiation and affecting hormone secretion in trophoblast. In this study, we found that long-term subculture of JEG-3 cells to cultivate an increase in cell differentiation, alterations in physiological properties, and changes in hormone secretion profiles. Our results also demonstrate distinct responses in JEG-3 cells to BPA stimulation in later passages, suggesting that long-term subculture alters cell characteristics and elicits varied responses to stimuli. This implies potential harm from BPA exposure at different stages of pregnancy, albeit through different mechanisms.	Reprod Toxicol. 2024 Dec:130:108738.	10.1016/j.reprotox.2024.108738	39477191	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1938	Y. Huang, W. Zhang, C. Zhang, N. Cui, Z. Xiao, R. Wang and X. Su	2022	Rapid and reagent-free bioassay using autobioluminescent yeasts to detect agonistic and antagonistic activities of bisphenols against rat androgen receptor and progesterone receptor	Bisphenol A (BPA) and its analogues have been classified as endocrine disruptors (ECDIs) owing to nuclear receptors. Two novel bioassays, BLYAR1 and BLYAP2, were developed for rapid detection of agonistic and antagonistic activities of BPA and five of its analogues binding rat androgen receptor (rAR) and rat progesterone receptor (rPR). The reporter bioassays were based on two autonomously bioluminescent strains of the yeast Saccharomyces cerevisiae, recombinant with a bacterial luciferase reporter gene cassette but their own endogenous androgen and progesterone receptors, regulated by the corresponding hormone receptor antagonist, the exogenous promoter. The bioluminescent signal is autonomous and continuous without cell lysis or addition of exogenous reagents. The AR agonist R1881 could be detected at 3 h with a half-maximal effective concentration (EC50) of 0.1 nM. The AR antagonist hydroxyflutamide (OHF) could be detected at 3 h with a half-maximal inhibitory concentration (IC50) of 0.1 nM. The PR agonist progesterone (P4) and PR antagonist mifepristone (MIF) could be detected at 3 h with EC50 and IC50 values of 0.1 nM and 0.01 nM, respectively. The AR antagonistic and anti-rat AR activities of BPA and five analogues were 80% acted as PR antagonistics with different potency. The BLYAR1 and BLYAP2 bioassay characterized by autonomous bioluminescent signal acquisition without additional manipulations is cost-saving and applied for simple and rapid detection of agonistic and antagonistic activities of BPs and other compounds acting as agonists or antagonists of rAR and rPR. Based on data derived by use of this bioassay endocrine-disrupting activities of some BPA analogues are more potent than BPA.	Reprod Toxicol. 2024 Dec:130:108738.	10.1016/j.jsbmb.2022.106151	35787454	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1939	X. Huang, X. Cang and J. Liu	2019	Molecular mechanism of Bisphenol A on androgen receptor antagonism	Bisphenol A (BPA), one of the highest production volume chemicals, is a typical endocrine-disrupting chemical (EDC) that exhibits antiandrogenic activity. However, how BPA antagonizes androgen effects remains ambiguous. In this study, the in silico and in vitro assay were carried out to explore the molecular mechanism(s) of BPA as an androgen receptor (AR) antagonist. In reporter gene assay, BPA caused a significant concentration-dependent (0.1–100 μM) inhibition of transactivation induced by 0.1 nM R1881 in MDA-kb2 cells. Molecular docking revealed that BPA could bind to the ligand-binding domain of AR. BPA treatment prevented the inhibition of receptor degradation caused by DHT binding to AR. BPA exposure also abolished DHT-dependent dissociation of AR from its co-chaperone, 90-kDa heat-shock protein (hsp90), and resulted in the blockage of DHT-induced AR nuclear translocation. This is the first report to show that BPA inhibited the DHT- induced stabilization of AR and the DHT- induced dissociation of AR-hsp90 complex. This study provided new evidence for further understanding the precise mechanisms of antagonism of BPA on AR.	Toxicol In Vitro. 2019 Dec:61:104621.	10.1016/j.tiv.2019.104621	31415812	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1940	M. Huang, G. Xu, M. Li and M. Yang	2024	Bisphenol A and bisphenol AF co-exposure induced apoptosis of human ovarian granulosa cells via mitochondrial dysfunction	Bisphenol A (BPA) is a synthetic chemical primarily utilized in the manufacturing of polycarbonate plastics and epoxy resins that are present in various consumer products. While the BPA impacts on female reproductive toxicity have been widely investigated, very little is currently identified about the mixed toxicity of BPA and bisphenol AF (BPAF), another common BPA derivative that is used in many industrial applications. In this study, human ovarian granulosa cells (KGN cells) were exposed to BPA, BPAF, and their combination for 24 h. Cell viability, mitochondrial membrane potential, mitochondrial ROS production, and mitochondrial calcium levels were individual or their mixtures exposure of KGN cells induced significant mitochondrial dysfunction by reducing mitochondrial mass, reducing ATP production, and damaging the mitochondrial ultrastructure. In addition, we found that the combination of BPA and BPAF significantly induced mitochondrial stress by increasing calcium levels and the production of ROS in mitochondria. Mitochondrial stress induced by BPA and BPAF was determined to be a mechanism that promoted cell apoptosis after pretreating the cells with the mitochondrial-targeted antioxidant and the calcium chelator. Our results provide novel evidence of the cytotoxicity of mixtures of different bisphenol compounds.	Food Chem Toxicol Vol.191 Pages 114894	10.1016/j.fct.2024.114894	39074574	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1941	M. Huang, S. Liu, L. Fu, X. Jiang and M. Yang	2020	Bisphenol A and its analogues bisphenol S, bisphenol F and bisphenol AF induce oxidative stress and biomacromolecular damage in human granulosa KGN cells	Bisphenol A (BPA) is gradually being replaced by presumably safer analogues such as bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF), due to its toxic, endocrine-disrupting and possible carcinogenic effects. Although these bisphenols are widely used to produce a variety of everyday household items, the effects of BPA and its analogues, on oxidative stress, and cellular energy metabolism of the female reproductive system are still poorly understood. The aim of this study was to evaluate the oxidative stress, biomacromolecular damages and changes in calcium ion (Ca^{2+}) levels induced by subcytotoxic doses of BPA, BPS, BPF, and BPAF, which are moderate physiological characteristics of ovarian granulosa cells. We have observed that BPA and BPAF significantly reduced the viability of KGN cells, while BPS and BPF exhibited a slight toxic effect on the cells. Moreover, BPA, BPAF, and BPF significantly increased the production of reactive oxygen species (ROS) and induced oxidative damage to DNA, proteins, and lipids. In addition, we found that the damage to biomacromolecules, which are the main targets of oxidative stress was significantly increased after treatment with BPA, BPF, BPS, and BPAF. The increased Ca^{2+} levels in KGN cells were significantly increased after exposure to high concentrations of BPA and BPAF, respectively. These results suggest that BPA and its analogues may play different roles in regulating the biologic functions of granulosa cells and the process of ovarian follicular development.	Chemosphere. 2020 Aug:253:126707.	10.1016/j.chemosphere.2020.126707	32289607	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1942	M. Huang, Y. Li, K. Wu, S. Hao, Q. Cai, Z. J. Zhou and H. F. Yang	2019	Effects of environmental chemicals on the proliferation and differentiation of neural stem cells	The objective of the present study was to explore the effects of environmental chemicals, such as methylmercury, paraquat, and bisphenol A, on cell proliferation and apoptosis, as well as the expression levels of neural differentiation related genes in neural stem cells (NSCs). NSCs, originated from human umbilical cord blood (HUCB-NSCs), were used as cell models in the current study. CCK-8 and flow cytometry were performed to assay the effects of methyl mercury, paraquat, and bisphenol A on the proliferation and apoptosis of HUCB-NSCs at different processes, including proliferation and differentiation stages. The expressions of neuronal differentiation related genes were determined by reverse transcription-polymerase chain reaction and enzyme-linked analysis. The results showed that methyl mercury, paraquat, and bisphenol A treatments significantly inhibited cell proliferation and induced cell apoptosis in HUCB-NSCs, as well as decreased the expressions of Ox6, GAP3, and Ox2, whereas increased Pax6 and Nes2 expressions at both mRNA and protein levels. In conclusion, this study demonstrates that environmental chemicals can impair the proliferation and differentiation of NSCs, which may cause abnormal development of the nervous system.	Environ Toxicol. 2019 Dec;34(12):1285-1291.	10.1002/tox.22829	31400064	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1943	M. Huang, M. Huang, X. Li, S. Liu, L. Fu, X. Jiang and M. Yang	2021	Bisphenol A induces apoptosis through GPER-dependent activation of the ROS/Ca(2+)-ASK1-JNK pathway in human granulosa cell line KGN	Bisphenol A (BPA) is widely distributed in the environment and human surroundings and is closely related to the occurrence of many chronic diseases including female infertility. Although BPA-induced granulosa cell apoptosis has been widely reported, the underlying mechanisms remain unknown. In this study, we evaluated the induction effect of BPA exposure on apoptosis and mechanisms of regulation in KGN cells (a human granulosa-like tumor cell line). Our results indicated that BPA induced apoptosis of KGN cells in a dose- and time-dependent manner. BPA exposure significantly promoted the expression of pro-apoptotic proteins and inhibited the expression of anti-apoptotic proteins. Moreover, BPA induced apoptosis through the activation of G protein-coupled estrogen receptor (GPER). Additionally, BPA induced the involvement of ROS and Ca^{2+} in BPA-induced ROS cell apoptosis was confirmed by pretreatment with ROS- the antioxidant and BAPTA-AM (a calcium chelator). Other inhibitors selectively block the corresponding signaling pathways. It was found that BPA induced phosphorylation of ASK and ASK1 proteins, and apoptosis of KGN cells were significantly inhibited. We pretreated with GSK (a GPER inhibitor) and found that BPA-induced ROS generation and Ca^{2+} accumulation and apoptosis were significantly inhibited. These results suggest that BPA exposure induces KGN cell apoptosis through GPER-dependent activation of the ROS/Ca^{2+}-ASK1-JNK signaling pathway. Our study provides mechanisms by which BPA induced apoptosis of granulosa cells and ovarian dysfunction.	Ecotoxicol Environ Saf. 2021 Jan 15:208:111429.	10.1016/j.ecoenv.2020.111429	33039870	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1944	C. Y. Huang, R. H. Xie, P. H. Li, C. Y. Chen, B. H. You, Y. C. Sun, C. K. Chou, Y. H. Chang, W. C. Lin and G. Y. Chen	2025	Environmental Exposure to Bisphenol A Enhances Invasiveness in Papillary Thyroid Cancer	Bisphenol A (BPA) is a prevalent environmental contaminant found in plastics and known for its endocrine-disrupting properties, posing risks to both human health and the environment. Despite its widespread presence, the impact of BPA on papillary thyroid cancer (PTC) progression, especially under realistic environmental conditions, is not well understood. This study examined the effects of BPA on PTC using a 3D thyroid papillary tumor spheroid model, which better mimics tumor interactions within the human tumor, compared to traditional 2D models. Our findings demonstrated that BPA, at environmentally relevant concentrations, could induce significant changes in PTC cells, including a decrease in E-cadherin expression, an increase in vimentin expression, and reduced thyroglobulin (Tg) secretion. These changes suggest that BPA exposure may promote epithelial-mesenchymal transition (EMT), a critical process in cancer metastasis, and impair the differentiation of thyroid cells, which is crucial for effective thyroid cancer therapy. The research highlights BPA's hazardous nature as an environmental contaminant and emphasizes the need for enhanced in vivo models, like 3D tumor spheroids, to better assess the risks posed by such chemicals. It provides valuable insights into the environmental implications of BPA and its role in thyroid cancer progression, enhancing our understanding of endocrine-disrupting chemicals.	Int J Mol Sci. 2025 Jan 19;26(2):814.	10.3390/ijms26020814	39859529	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1945	C. C. Huang, C. Y. Yang, C. C. Su, K. M. Fang, C. C. Yen, C. T. Lin, J. M. Liu, K. I. Lee, Y. W. Chen, G. H. Liu and C. F. Huang	2021	4-Methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene, a Major Active Metabolite of Bisphenol A, Triggers Pancreatic β-Cell Death via a JNK/AMPK/α Activation-Regulated Endoplasmic Reticulum Stress-Mediated Apoptotic Pathway	4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene (MBP), a major active metabolite of bisphenol A (BPA), is generated in the mammalian liver. Some studies have suggested that MBP exerts greater toxicity than BPA. However, the effects of MBP on pancreatic β-cell dysfunction remain unclear. Here, we found that MBP induced pancreatic β-cell apoptosis in a concentration-dependent manner. Moreover, MBP-induced β-cell death was involved in MBP-induced β-cell death. Our results showed that MBP exposure significantly increased β-cell death, caused insulin secretion dysfunction, and induced apoptotic events including increased caspase-3 activity and the expression of active forms of caspase-12 (17 kDa) and PARP protein. In addition, MBP triggered endoplasmic reticulum (ER) stress, as indicated by the upregulation of GRP 78, CHOP, and cleaved caspase-12 (37 kDa) protein expression. Furthermore, MBP induced the phosphorylation of JNK and AMPKα proteins. Pretreatment of β-cells with pharmacological inhibitors for JNK (SP600125) and AMPK (compound C) significantly attenuated the MBP-induced apoptosis-related signals. Both JNK and AMPK inhibitors also suppressed the MBP- induced activation of JNK and AMPK α at each other. In conclusion, these findings suggest that MBP exposure exerts cytotoxicity on β-cells via the interdependent activation of JNK and AMPKα, which regulates the downstream apoptotic signaling pathway.	Int J Mol Sci Vol.22 Issue 9	10.3390/ijms22094379	33922211	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1946	C. Huang, X. Chen, Z. Ouyang, L. Meng, J. Liu, Q. Pang and R. Fan	2024	Bisphenol a accelerates the glucolipotoxicity-induced dysfunction of rat insulinoma cell lines: An implication for a potential risk of environmental bisphenol a exposure for individuals susceptible to type 2 diabetes	Epidemiological studies have suggested a correlation between bisphenol A (BPA) and type 2 diabetes (T2DM). The effects of BPA on β-cell dysfunction may reveal the risks from an in vivo perspective. We used the rat insulinoma (INS-1) cell line (a type of β cells) to set up normal or damaged models (GNG), which were exposed to various concentrations of BPA (0.001, 0.01, 0.1, 1, 10 and 100 μM). An increase in reactive oxygen species (ROS) and apoptosis, and a decrease in cell viability were observed in INS-1 cells exposed to high doses of BPA for 24 h. Interestingly, exposure to lower doses of BPA for 24 h resulted in increased ROS levels and apoptosis rates in INS-1 in the GNA group, along with decreased cell viability, suggesting that BPA exerts toxicity to INS-1 cells, particularly in the GNA group. Insulin levels and GLUT expression, glucose consumption, intracellular Ca^{2+}) and insulin secretion were increased in INS-1 cells after 24 h exposure to high doses of BPA. Stronger effects were observed in the GNA group, even those exposed to low doses of BPA for 24 h. Moreover, BPA exposure induced β-cell dysfunction in these cells. Our research suggests that low doses of BPA exacerbate the dysfunction caused by glucolipotoxicity, implying environmental BPA exposure poses a risk for individuals with prediabetes or T2DM.	Toxicol In Vitro. 2024 Aug:99:105866.	10.1016/j.tiv.2024.105866	38844119	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1947	Q. Hu , K. Q. Guan, L. L. Sang, H. N. Wang, Y. Xiong, J. L. Liu, H. Yin, Y. F. Cao, J. Hou, L. Yang and G. B. Ge	2020	Inhibition of pancreatic lipase by environmental xenoestrogens	Environmental xenoestrogens are the most accessible endocrine-disrupting chemicals that have been reported with harmful effects on human health. Although the influences of xenoestrogens on the endocrine system have been widely studied, little is known about their effects on digestive enzymes. In this study, we investigated the inhibitory effects of 3 environmental xenoestrogens and 2 xenoestrogen synthetic estrogens (including hexestrol, diethylstilbestrol, dienestrol, bisphenol S, bisphenol AF and bisphenol Z) on pancreatic lipase (PL), a key digestive enzyme responsible for lipid digestion and absorption in mammals. The results clearly demonstrated that hexestrol, diethylstilbestrol and dienestrol exhibited strong inhibition on PL, with the IC50 values of less than 1.0 μM. Further investigations elucidated that these three synthetic estrogens functioned as mixed inhibitors of PL, with the Ki/Ki' values of less than 1 μM. Moreover, molecular dynamics simulations showed that diethylstilbestrol and its analogues might block the entry of substrate at PL via occupying the portal to the active site of PL and thereby inhibit the hydrolytic activity of this key enzyme. Collectively, these results suggested that diethylstilbestrol and its analogues were potent PL inhibitors, which might play a profound role in lipid absorption and weight gain in mammals.	Ecotoxicol Environ Saf Vol.192 Pages 110305	10.1016/j.ecoenv.2020.110305	32070782	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1.0 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1948	J. Hu, J. Liu, X. Lv, L. Ye, S. Lan, Y. Li and Y. Yang	2021	Assessment of epigenotoxic profiles of Dongjiang River: A comprehensive of chemical analysis, in vitro bioassay and in silico approach	This research explored the occurrence, epigenetic toxic profiling and main toxic pollutants of PDPs in surface water of Dongjiang River, southern China. The concentrations of selected PDPs including polycyclic aromatic hydrocarbons (PAHs), endocrine disrupting chemicals (EDCs), pharmaceuticals and personal care products (PPCPs) were investigated. Environmental risk assessment of PDPs in water was also evaluated. Results showed that 3 PAHs and 3 EDCs had low pollution levels. PAHs, EDCs, and PPCPs showed higher concentrations. In dry season than those in wet season, and the loading of selected PDPs in estuaries was higher than those in upstream and midstream. Epigenotoxicity was investigated by using in vitro cell transformation assay (CTA). Results showed that PDPs in water samples had significant indications for epigenetic toxicity. The DNMT1-mediated epigenetic expressions toxicity of organic extracts in Dongjiang River were most serious than those of HDAC1 and HDAC8. Correlation analysis showed binding affinity between PDPs and DNMT1, HDAC1 and HDAC8 could be regarded as toxic explanatory factors. Risk assessment suggested that 3 nonylphenol and bisphenol A were the largest contributors to epigenetic risk. This study is the first attempt to quantify epigenetic toxicity and epigenetic risk evaluation of river water.	Environ Pollut. 2021 Aug 1:282:116961.	10.1016/j.envpol.2021.116961	33823309	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1949	Y. Hong, J. Li, Z. Du, N. Xu, Q. Yang, J. X. Zhou and W. Shi	2025	Genomic evidence based on eQTL data implicates endocrine disruptors as environmental risk factors for estrogen receptor-positive breast cancer	BACKGROUND: Estrogen receptor-positive (ER+) breast cancer is the most common molecular subtype of breast cancer and is strongly influenced by hormonal and environmental factors. Endocrine-disrupting chemicals (EDCs) can mimic estrogen and may contribute to ER+ breast cancer development. METHODS: We integrated 1,156 ER+ breast cancer genomes from The Cancer Genome Atlas (TCGA) and 1,715 individuals with large-scale genetic datasets to investigate the relationship between EDC-regulated gene expression and ER+ breast cancer. A total of 1,939 EDC-related genes were identified and filtered using six expression quantitative trait loci (eQTL) data from eQTLGen. Mendelian randomization (MR) and colocalization analyses were performed using ER+ breast cancer GWAS summary statistics to assess causal associations and shared genetic signals. Interacting EDCs were identified using a gene co-expression network. RESULTS: Among 1,921 genes with available cis-eQTLs, 50 showed significantly protective associations (FDR < 0.05) with ER+ breast cancer. Of these, 23 genes, including CHRF, RASSF2, and TET2, demonstrated strong evidence of colocalization. Key EDCs, such as bisphenol A and phthalates, were identified to interact with multiple high-risk genes, suggesting potential environmental drivers of ER+ breast cancer. CONCLUSION: This study provides genetic evidence supporting the causal role of EDC-regulated gene expression in ER+ breast cancer. The integration of MR, colocalization, and chemical-gene networks offers a novel framework for identifying environmentally relevant risk factors and contributes to understanding the gene-environment interactions underlying hormone-dependent cancers.	Int J Surg Vol.111 Issue 8 Pages 5664-5674	10.1097/js9.0000000000002642	40576180	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1950	X. Hong, S. Wang, Q. Zhang, L. Li, H. Liu, H. Yang, D. Wu, X. Liu and T. Shen	2025	Bisphenol A exacerbates colorectal cancer progression through enhancing ceramide synthesis	Bisphenol A (BPA) is a typical environmental endocrine disruptor which have been broadly confirmed to be associated with malignant tumors, including colorectal cancer (CRC). Lipid metabolism reprogramming performed as a hallmark of cancer progression. However, the role of BPA in CRC lipid metabolism remains unclear. In this study, we found that BPA exposure significantly promoted CRC cell proliferation, migration, and invasion, along with upregulated ceramide synthase in high-BPA tumor tissue of CRC patients. Simultaneously, in vivo experiments demonstrated that BPA exposure exacerbated tumor biological behavior and epithelial-mesenchymal transition (EMT), concurrent with elevated EMT expression of CRC tissue in high-BPA group. Subsequently, the inhibition of ceramide synthase and pharmacological stimulation experiments revealed that ceramide accumulation activated EMT and exacerbated CRC progression, including Fer-1(0.5 μM) and Cer (0.05-0.2 μM). Collectively our findings elucidated the pathogenesis of ceramide accumulation escalating tumor-progressive under environmental BPA exposure, providing a strong basis for further investigation of dysregulated ceramide metabolism to boost tumor development and assist metastatic release.	Toxicology. 2025 Feb:511:154054.	10.1016/j.tox.2025.154054	39809339	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1951	Q. He, A. Ma, Z. Yang, X. Pang, C. Li, J. Dao, Y. Liu, Q. Liu, Q. Zhang, Z. Dang and D. Zhang	2025	Bisphenol A promotes OSCC progression via GABBR1-mediated MAPK signaling and macrophage polarization: A network toxicology based study	BACKGROUND: Bisphenol A (BPA), an environmental pollutant, has been implicated in oral squamous cell carcinoma (OSCC) progression, yet its molecular mechanisms remain unclear. This study explores the role of GABBR1 in BPA-induced OSCC progression, focusing on its impact on tumor cell behavior and immune microenvironment. METHODS: Network toxicology and bioinformatics identified BPA-related OSCC conditions. Molecular docking and dynamics simulations further elucidated the binding interactions between BPA and GABBR1. Functional assays, including cytotoxicity, transwell, CCK-8, EdU, and western blot, evaluated the effects of BPA exposure and GABBR1 knockdown on OSCC cell function. Transwell co-culture, RT-PCR and ELISA assays examined monocyte-mediated interactions between OSCC cells and macrophage M2/M1 BPA exposure enhanced OSCC proliferation, migration, and invasion while promoting stemness through the GABBR1/MEK/ERK signaling pathway. Additionally, it induced M2 macrophage polarization via paracrine communication, contributing to an immunosuppressive microenvironment. CONCLUSION: This study uncovers a novel mechanism by which BPA promotes OSCC progression via GABBR1-mediated signaling and immune-driven immunomodulation, highlighting GABBR1 as a potential therapeutic target in BPA-associated OSCC.	Ecotoxicol Environ Saf Vol.303 Pages 118835	10.1016/j.ecoenv.2025.118835	40779845	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1952	V. Hautanen, T. Toimela, M. Paparella and T. Heinonen	2023	A Human Cell-based Assay to Assess the Induction of Vasculature Formation for Non-genotoxic Carcinogenicity Testing Purposes: A Pilot Study	The induction of vasculature formation is proposed to be a significant mechanism behind the non-genotoxic carcinogenicity of a chemical. The vasculature formation model used in this study is based on the co-culture of human primary HUVECs and MSCs. The model was used to develop an assay to assess the induction of vasculature formation. Three assay protocols, based on different conditions, were developed and compared in order to identify the optimal conditions required. Some serum supplements and growth factors were observed to be essential for initiating vasculature formation. Of the studied positive reference chemicals, aspartame, sodium nitrite, bisphenol S and nicotine treatment led to a clear induction of vasculature formation, but arsenic and cadmium treatment only led to a slight increase. This human cell-based assay has the potential to be used as one new within a non-genotoxic testing battery, to assess the non-genotoxic carcinogenicity of a chemical through the mechanism of vasculature formation induction.	Altern Lab Anim. 2023 May;51(3):188-203.	10.1177/02611929231171165	37125451	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1953	K. G. Harnett, A. Chin and S. M. Schuh	2021	BPA and BPA alternatives BPS, BPAF, and TMBPF, induce cytotoxicity and apoptosis in rat and human stem cells	Bisphenol A (BPA) is a ubiquitous industrial chemical found in everyday plastic products and materials. Due to scientific findings on the reproductive, developmental, and cellular defects caused by BPA and heightened public awareness, manufacturers have begun to use new chemicals in place of BPA in "BPA-free" products. These alternatives are chemical analogs of BPA and include dozens of new compounds that have undergone relatively little testing and oversight, including bisphenol S (BPS), bisphenol AF (BPAF), and the recently developed trimethylol bisphenol F (TMBPF). We exposed rat uniPSC-TSC, their rat uniPSC-derived neural stem cells (rNSCs) and human neuroectoderm stem cells (hNSCs) to compare the toxic dose and potencies of these BPA alternatives in vitro. Rat and human stem cells were exposed to BPS (0.10 μM), 17,17-bis(4-hydroxyphenyl)-4-methylpentanoic acid (BPAF) (0.10 μM), TMBPF (0.10 μM), or control media alone (with 0.01% ethanol) for varying time intervals from 30 min to 5 hrs. Using universal assays to measure cell viability and caspase activity, we treated rNSCs with each BPA analog, as well as 10 min of exposure, and at later, physiologically relevant doses. BPAF showed consistently to be a dose-dependent inverted U-CRD: <0.01 μM (rNSCs) and 0.001 μM (hNSCs), whereas TMBPF showed a bimodal response, with low and high concentrations being the most toxic (LOAEL: <0.01 μM (rNSCs) and 0.01 μM (hNSCs)). Estimated caspase-3/7 levels increased in nearly all cells treated with the BPA analogs indicating the majority of cell death was due to caspase-3/7 mediated apoptosis. These results illustrate rat and human stem cells undercore the toxicity and potency of these BPA analogs, and establish a rank order of potency of BPAF>TMBPF>BPS>BPA. Further, these and other recent findings indicate that these newer BPA analogs may be triggering cell death through similar mechanisms as BPA, but with greater potency. Taken together, these findings highlight the need for further toxicological characterization, better regulation, greater public awareness, and the development of safer, more sustainable chemicals and non-plastic products.	Ecotoxicol Environ Saf Vol.216 Pages 112210	10.1016/j.ecoenv.2021.112210	33866271	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1～10 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1954	K. G. Harnett, A. Chin and S. M. Schuh	2021	Cytotoxic and apoptotic data of BPA and BPA alternatives TMBPF, BPAF, and BPS in female adult rat and human stem cells	Here, we used female adult rat adipose-derived stem cells (rASCs) and human adipose-derived stem cells (hASCs) to compare the toxicities and potencies of several widespread environmental toxins that may be endocrine-disrupting chemicals, including bisphenol A (BPA), and the seven BPA alternatives bisphenol S (BPS), bisphenol AF (BPAF), and bis(4-hydroxyphenyl)-2,2,2-trifluoromethylphenylethane (BPAF), and tetramethyl bisphenol F (TMBPF). rASCs and hASCs were cultured in BSS-conditioning in vivo and then exposed to BPS (1.nM–10 μM), 17,β -estradiol (E2; 10 μM), BPAF (1 × 10−10 M–10 μM), TMBPF (1 × 10−10 M–10 μM), TMBPF (0.10 μM), or control media alone (with 0.01% ethanol) for varying time intervals from 30 min to 5 hrs. Using universal assays to measure cell viability, the levels of cell death, apoptosis, caspase-3/7 activation, and proliferation were compared across chemical treatments and time points. These data significantly decreased cell viability and increased apoptosis in rat and human stem cells treated with each BPA analog, as early as 30 min of exposure, and at low doses. With higher magnification, higher resolution fluorescence microscopy, we found that BPA and BPA analogs induced dose-dependent changes in cell morphology indicative of apoptosis, including cell shrinkage, membrane blebbing, and the formation of late-stage apoptotic and necrotic nuclei. Quantification of late-stage apoptosis and necrosis was localized to the nuclei of cells. Notably, BPAF and TMBPF showed apotency to a dose-dependent manner (BPAF: LOAEL: 0.001 μM (rASC) and 0.01 μM (hASC); TMBPF: LOAEL: 0.001 μM (rASC) and 0.01 μM (hASC)). Estimated caspase-3/7 levels increased in nearly all cells treated with the BPA analogs indicating the majority of cell death was due to caspase-3/7 mediated apoptosis. These results illustrate rat and human stem cells undercore the toxicity and potency of these BPA analogs, and establish a rank order of potency of BPAF>TMBPF>BPS>BPA. Further, these and other recent findings indicate that these newer BPA analogs may be triggering cell death through similar mechanisms as BPA, but with greater potency. Taken together, these findings highlight the need for further toxicological characterization, better regulation, greater public awareness, and the development of safer, more sustainable chemicals and non-plastic products.	Data Brief Vol.37 Pages 107183	10.1016/j.dib.2021.107183	34141841	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1μMおよび10μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1955	A. Hale, A. Dhoonmoon, I. Straka, C. M. Nicolae and G. L. Moldovan	2023	Multi-step processing of replication stress-derived nascent strand DNA gaps by MRE11 and EXO1 nucleases	Accumulation of single-stranded DNA (ssDNA) gaps in the nascent strand during DNA replication has been associated with cytotoxicity and hypersensitivity to genotoxic stress, particularly upon inactivation of the BRCA tumor suppressor pathway. However, how ssDNA gaps contribute to genotoxicity is not well understood. Here, we describe a multi-step nucleolytic processing of replication stress-induced ssDNA gaps which converts them into cytotoxic double-stranded DNA breaks (DSBs). We show that ssDNA gaps are extended bidirectionally by MRE11 in the 5′ direction and by EXO1 in the 3′ direction, in a process which is suppressed by the RAD51 paralogs. Extensive ssDNA gaps are converted into DSBs in BRCA-deficient cells, leading to chromosome instability and cell death. We identify the Fanconi anemia (FA) protein FANCD2 and SLX4/FANCP (SLX4/BTBD12) nuclease scaffold protein as novel factors that counteract MRE11 activity, which uses unprotected nascent strand ssDNA gaps during replication. These gaps are processed through the same mechanism described above to generate DSBs. Our work sheds light on both the relevance of ssDNA gaps as major determinants of genomic instability, as well as the mechanisms through which they are processed to generate genomic instability and cytotoxicity.	Nat Commun. 2023 Oct 7;14(1):6265.	10.1038/s41467-023-42011-0	37805499	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	1	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1956	K. G. U. Gözel, M. Nazıroğlu and O. Geyhan	2026	Bisphenol A-Induced Cell Proliferation and Mitochondrial Oxidative Stress Are Diminished via Modulation of TRPV1 Channel in Estrogen Positive Breast Cancer Cell by Selenium Treatment	Cancer cell proliferation and apoptosis are induced by overload Ca2+ entry. Transient receptor potential vanilloid 1 (TRPV1) as a Ca2+ permeable cation channel is activated by capsaicin and reactive oxygen species (ROS), although it is blocked by capsazepine and sodium selenite (Na-Se). Bisphenol A (BPA) induces estrogenic action and tumor stimulation, the proliferation of estrogen-receptor positive MCF-7 cell through increased production ROS and Ca2+ influx. However, whether or not Na-Se can influence BPA-induced oxidative stress and apoptosis through modulation of TRPV1 in breast cancer cells has not drawn much attention. The MCF-7 cells were treated with BPA (100 μM), capsazepine (CPZ, 10 μM), Na-Se (2 μM), and BPA + CPZ, BPA + Na-Se for 24 h. Cell viability, proliferation, apoptosis, mitochondrial oxidative stress, and TRPV1 channel activity modulation of MCF-7 cells, which was proved by the suppression of cell viability, excessive ROS production, mitochondrial membrane disturbances, lipid peroxidation, early apoptosis (Annexin-V), late apoptosis (propidium iodide) and upregulation of reduced glutathione, glutathione peroxidase, and cell death (propidium iodide/Hoechst rate). The similar effects of Na-Se were observed in the MCF-7 cells by capsazepine treatment. However, the effects of BPA were not observed in the MDA-MB-231 breast cancer cells. In conclusion, cell proliferation and oxidative effects of BPA were increased by activation of TRPV1, but its action on the values was decreased by the Na-Se treatment. The results may be a good set of preliminary data for designing animal studies on estrogenic effect of bisphenol A and anticarcinogenic of selenium.	Biol Trace Elem Res Vol.198 Issue 1 Pages 118-130	10.1007/s12011-020-02057-3	32040846	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1mM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1957	Y. Guo, Y. Wang, Q. Li, Q. Liu, X. Zhang, J. Ren and C. Wang	2024	Bisphenol A disrupts the neuronal F-actin cytoskeleton by activating the RhoA/ROCK/LIMK pathway in Neuro-2a cells	Bisphenol A (BPA) is an environmental endocrine disruptor that is widely present in the environment and has been reported to affect neuronal cytoskeleton and neural function. However, the exact molecular mechanisms remain unclear. In the present study, the effects of BPA on cytoskeleton rearrangement were examined, and the associated signaling pathways, which were influenced by the RhoA/ROCK/LIMK pathway in Neuro-2a cells, in vitro, were identified. Specifically, Neuro-2a cells were exposed to BPA, and the effects of BPA exposure on the cytoskeleton of neuronal cells and on the activation or reestablishment of the RhoA/ROCK signaling pathway were evaluated using Cell Counting Kit-8 (CCK8), phalloidin staining, western blot, and real-time PCR. A RhoA inhibitor (Rhosin hydrochloride) and ROCK inhibitor (Y-27632) were then used to elucidate the interior function of the pathway. The results demonstrated that 50–100 μ M BPA exposure inhibited Neuro-2a cell viability and caused the formation of abnormally polymerized F-actin and stress fibers. In addition, the RhoA/ROCK/LIMK signaling pathway was activated by BPA exposure. Rhosin hydrochloride and Y-27632 reversed the BPA-induced cytoskeleton damage. Moreover, the inhibition of ROCK by Y-27632 resulted in a decrease in F-actin polymerization in the Neuro-2a cells, the disassembly of stress fibers, and a noteworthy drop in the levels of molecules involved in the RhoA/ROCK pathway affected by BPA. Together, these new findings indicated that BPA exposure thus activated the RhoA/ROCK signaling pathway and caused an abnormal accumulation of F-actin in the Neuro-2a cells, in turn altering the microfilament cytoskeleton. F-actin was restored when the RhoA/ROCK pathway was inhibited, suggesting that the process of BPA-induced neuronal cytoskeletal degradation is linked to the RhoA/ROCK signaling cascade.	Toxicology. 2024 Dec:509:153994.	10.1016/j.tox.2024.153994	39527977	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1958	Y. Guo, B. Li, X. Yan, X. Shen, J. Ma, S. Liu and Z. Zhang	2020	Bisphenol A and polychlorinated biphenyls enhance the cancer stem cell properties of human ovarian cancer cells by activating the WNT signaling pathway	Cancer stem cells (CSCs) are a very small subpopulation that have stem cell qualities, such as exhibiting self-renewal, immortality, and pluripotency, and the capability to differentiate into different tumor cell subtypes, thus leading to tumorigenesis, metastasis, and chemoresistance. Bisphenol A (BPA) and polychlorinated biphenyls (PCBs) are two typical environmental endocrine disruptors (EEDs). Exposure to BPA and polychlorinated biphenyls (PCBs), are two chemicals that are usually ingested via dietary exposure and other exposure routes and can accumulate through the food chain. Many reports and studies increase the risk of ovarian cancer depending on their estrogenic effects. Nonetheless, most previous studies have focused on the toxic effects of these pollutants on the proliferation, metastasis and development of ovarian cancer cells. However, the effects of these pollutants on ovarian CSCs remain unclear. In this study, we found that BPA, PCB126 and PCB153 promoted the formation of ovarian cancer spheres. Moreover, BPA, PCB126 and PCB153 greatly increased the expression of CSC markers in ovarian cancer cells. The stemness of OVCAR-3 cells, ovarian cancer cells, under low-dose exposure, for 3 months (OVCAR3-LDE) cell subpopulation was increased in nude mice and was correlated with increased expression of cancer stem cell markers, including ALDH1A1, CD133, SOX2, NANOG and OCT4, was demonstrated in treated cells compared to untreated cells. In summary, these data demonstrate that the oncogenic effects of pollutants can be evaluated according to changes in cancer stem cell properties.	Chemosphere. 2020 May:246:125775.	10.1016/j.chemosphere.2019.125775	31918092	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1959	S. Guo, Q. Zhao, Y. Li, S. Chi, F. He, K. Li, N. Sun, W. Zong and R. Liu	2023	Potential toxicity of bisphenol A to α -chymotrypsin and the corresponding mechanisms of their binding	Bisphenol A (BPA) is an endocrine disruptor widely existing in plastics and resins, which can accumulate in animals and human bodies, posing a potential threat to the physiological and biochemical reactions of human enzymes. α-chymotrypsin (α-CT) is a digestive enzyme that plays a crucial role in the digestion and absorption of food. However, there is little information about the toxicity of BPA as an endocrine disruptor affecting α-chymotrypsin activity. In this study, the interaction between BPA and α-chymotrypsin was proved via multiple spectroscopic approaches, enzyme activity change, isothermal titration calorimetry and molecular docking. Results showed that α-chymotrypsin's polypeptide chains were unfolded, and protein skeletons were loosened with the exposure to BPA. α-Helix content increased and β -sheet content was decreased. The particle size of the BPA- α-chymotrypsin complex became smaller. Fluorescence combination may also be explained by a perturbation of the chromophore Try 152. The thermodynamic parameters of the binding reaction were measured by isothermal titration calorimetry (ITC), which showed that there was hydrophobic interaction between BPA and α-chymotrypsin, which was consistent with the results of molecular docking. The activity of α-chymotrypsin was inhibited by BPA, and the inhibition rate increased with the increase in BPA concentration. The inhibition rate of α-chymotrypsin increased to 1.28% when exposed to high-dose BPA (50 μM). Taken together, the effects of BPA on the structure and function of α -chymotrypsin were clarified at the molecular level, which made up the gaps in the mechanism of BPA on the proteolytic enzyme, and provided a reliable basis for disease avoidance and prevention.	Spectrochim Acta A Mol Biomol Spectrosc Vol.285 Pages 121910	10.1016/j.saa.2022.121910	36167003	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	40 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を依頼性評価へ進め、当該性評価段階で原則として除外。

利用評価機関
●：該当

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1960	Y. Gui, C. Li, W. Wang, Y. Hu and X. Guo	2025	Bisphenol A induces cellular senescence in SW1353 chondrocytes via miRNA-449a-mediated downregulation of SIRT1	Bisphenol A (BPA) is maternally linked to multiple human diseases. Recent studies have tried to elucidate cartilage development and homeostasis. However, the exact molecular mechanisms are mostly unknown. This study aimed to elucidate how BPA impacts chondrocyte senescence and the regulatory molecular mechanism involved. After exposing SW1353 cells to 25, 5 or 10 μ M BPA for 72h, we found that 5 and 10 μ M BPA notably increased the percentage of senescence-associated β-galactosidase-positive cells by 53.7% and 85.1%, respectively. The expression of senescence-associated proteins p53, p21 and p16 were notably upregulated. Moreover, BPA exposure significantly increased the mRNA expression of matrix metalloproteinase-13 (MMP-13) and a disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5), while notably decreased those in the ECM (decay by 5.6%). Additionally, BPA strongly downregulated the expression of cell cycle markers cyclin D1, cyclin-dependent protein kinases 4 (CDK4) and CDK6. BPA also induced dependently upregulated senescence-associated secretory phenotype factors interleukin-1 alpha, interleukin-1 beta, transforming growth factor beta and matrix metalloproteinase-13. Notably, BPA-downregulated sirtuin-1 (SIRT1) expression. Resveratrol, an activator of SIRT1, effectively reversed the effects of BPA on senescence-associated proteins and reduced cell cycle arrest. We further identified that SIRT1 was a direct target of microRNA-449a by a luciferase reporter assay. Importantly, inhibition of miR-449a greatly reduced the percentage of SA-β-gal-positive cells by 21.1% and reversed the expression of senescence-associated factors induced by BPA. Taken together, our results indicated that BPA induces chondrocyte senescence via miR-449a-mediated downregulation of SIRT1, revealing a novel molecular mechanism of BPA-induced chondrocyte senescence.	Ecotoxicol Environ Saf Vol.303 Pages 118906	10.1016/j.ecoenv.2025.118906	40848421	in vitro	-	-	-	-	-	-	-	-	-	1	0	10 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1961	Y. X. Gu, X. X. Liang, N. Y. Yin, Y. Yang, B. Wan, L. h. Guo and F. Faiola	2019	New insights into mechanism of bisphenol analogue neurotoxicity: implications of inhibition of O-GlcNAcase activity in PC12 cells	Bisphenol analogues including bisphenol A and its derivatives are ubiquitous environmental contaminants and have been linked to adverse neurodevelopment effects in animals and humans. Most toxicological research has focused on bisphenol A (BPA), and little information is available regarding the neurotoxicity of BPA analogues. Here, we used a high-throughput in vitro screening approach with rat pheochromocytoma (PC12) cells to identify toxicity hazards for nine bisphenol analogues. In this study, we intend to investigate the underlying molecular mechanisms for the neurotoxicity of bisphenol analogues by identifying potential cellular targets and the associated effects. The inhibitory actions of seven bisphenol analogues on the OGA activity at molecular level were investigated by our developed electrochemical biosensor. We found that their potency varied with substituent groups, in which tetrabromo bisphenol A (TBBPA) was the strongest. The seven bisphenol analogues (5–100 μM) also significantly inhibited OGA activity and up-regulated protein O-GlcNAcylation level in PC12 cells. Inhibition of OGA by bisphenol analogues further induced intracellular calcium, ROS, inflammation, increased acetylation, inserted cells cell cycle, induced apoptosis. And especially, 10 μ M tetrabromo bisphenol A (TBBPA) significantly increased the percentage of cells in the G0/G1 phase and decreased the percentage of cells in the S phase. Molecular docking of bisphenol analogue complexes revealed the hydrophobicity dominated inhibition potency. OGA, as a new cellular target of bisphenol analogues, would illuminate the molecular mechanism of bisphenol analogues neurotoxicity.	Arch Toxicol Vol.93 Issue 9 Pages 2661-2671	10.1007/s00204-019-02525-3	31332466	in vitro	-	-	-	-	-	-	-	-	-	1	0	0—100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1962	M. F. Grasso, E. Řeháková, I. Virmani, E. Sychrová, I. Soukhovec and P. Babica	2025	Impact of endocrine disruptors on key events of hepatic steatosis in HepG2 cells	Endocrine-disrupting chemicals (EDCs) may contribute to the rising incidence of metabolic dysfunction-associated steatotic liver disease (MASLD). We investigated the potential of 10 environmentally relevant EDCs to affect key events of hepatic steatosis in HepG2 human hepatoblastoma cells. Increased lipid droplet formation, a key marker of steatosis, was induced by PFOA, bisphenol F, DEP, butylparaben, and DEHP, within the non-cytotoxic concentration range (1.46–25 μM). Cadmium also induced this effect, but at concentrations impairing cell viability (>1 μM). At non-cytotoxic concentrations, these compounds, along with bisphenol S, dysregulated major genes controlling lipid homeostasis. Cadmium, PFOA, DEP, and DEHP significantly upregulated the CYP7A1 gene, involved in triglyceride synthesis, while bisphenol F and butylparaben increased the expression of the FATP2 SLC27A2 gene responsible for fatty acid uptake. Bisphenol A downregulated the CPT1A gene involved in fatty acid oxidation. No significant effects on lipid droplet accumulation or lipid metabolism-related genes were observed for PFOS, bisphenol S, and ethyl phthalate. Among the tested EDCs, lipid accumulation positively correlated with the expression of PPARG, CIDEC, and CPT1A. These findings provide additional evidence that EDCs—at/when MASLD-overlapping the utility of in vitro methods in the screening of EDCs with hazardous steatogenic and metabolism-disrupting properties.	Food Chem Toxicol Vol.197 Pages 115241	10.1016/j.fct.2025.115241	39778647	in vitro	-	-	-	-	-	-	-	-	-	1	0	1 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1963	M. I. Gión-Pérez, G. H. Ventura-Ramón, C. E. Cruz-tas-Rosales, A. B. Benítez-Trinidad, F. F. Rasura-Carmona, L. G. Marmolejo-Murillo, C. E. Pérez-Arevalao, J. Morales-Montor and K. J. G. Díaz-Resendiz	2025	Effect of bisphenol-A and bisphenol-S on functional parameters of human leukocytes	BACKGROUND: Bisphenol A (BPA) and bisphenol S (BPS) are commonly used in the food industry to manufacture epoxy resins in food packaging. Both compounds are characterized as potent carcinogenic and immunotoxic endocrine disruptors. Nevertheless, the immunotoxic effects of BPS are poorly understood. METHODS: Cell viability was evaluated by the MTT assay. Peripheral blood mononuclear cells (PBMCs) were isolated from healthy donors by density gradient centrifugation. Leukocytes isolated from human peripheral blood were exposed in vitro to 0.1 ng/mL (0.4 nM) of BPA and 0.1 ng/mL (0.2 nM) of BPS for 6, 12, and 24 hours. Neutrophil chemotaxis, mitochondrial membrane potential (ΔΨm), mitochondrial mass, reactive oxygen species (ROS), and intracellular Ca2+ flux were subsequently assessed through flow cytometry. RESULTS: Data suggest that in vitro exposure to BPA or BPS does not cause leukocyte death; however, it induces loss of mitochondrial membrane potential (-1.5 mV), senescence, as well as ROS production and intracellular Ca2+ flux (CONCLUSION: These findings demonstrate that even low concentrations (0.1 ng/mL) of BPA or BPS, levels that have been reported in human blood, can cause alterations in leukocyte function.	Immunopharmacol Immunotoxicol. 2025 Oct;47(5):621-630.	10.1080/08923973.2025.2542133	40739598	in vitro	-	-	-	-	-	-	-	-	-	1	0	0.1 ng/mL	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1964	S. Gill and V. M. R. Kumara	2021	Comparative Neurodevelopment Effects of Bisphenol A and Bisphenol F on Rat Fetal Neural Stem Cell Models	Bisphenol A (BPA) is considered as one of the most extensively synthesized and used chemicals for industrial and consumer products. Previous investigations have established that exposure to BPA has been linked to developmental, reproductive, cardiovascular, immune, and metabolic effects. Several jurisdictions have imposed restrictions and to have banned the use of BPA in packaging material and other consumer goods. Hence, bisphenol F (BPF) is considered as one of the most widely used substitutes for BPA. However, the toxicity of BPF is not well studied. In the present investigation, we compared the neurodevelopmental effects of BPA and its most replacement Bisphenol F (BPF) on rat fetal neural stem cells (NSCs) in vitro. Accordingly, cytotoxicity, neural differentiation media were used to cytotoxic doses of BPA or BPF at the range of 0.01 M to 100 M concentrations and measured the degree of cell proliferation, differentiation, and neurotoxicity parameters. Both of these compounds increased cell proliferation and impaired the differentiation potency of oligodendrocytes and neurons, in a concentration dependent manner. Further, there were concentration dependent decreases in the generation of oligodendrocytes and neurons, with a concomitant increase in immature oligodendrocytes and neurons. In contrast, neither BPA nor BPF had any overall effect on cellular proliferation or the cytotoxicity of astrocytes. However, there was a concentration dependent increase in the generation of astrocytes and astrocytic lineage cells. Morphometric analysis for the neurons, oligodendrocytes, and neurons, showed a reduction in the arborization. These data show that both NSCs exposed to either BPA or BPF lead to comparable changes in the cellular differentiation, proliferation, and arborization processes.	Cells. 2021 Apr 2;10(4):793.	10.3390/cells10040793	33918242	in vitro	-	-	-	-	-	-	-	-	-	1	0	0.01 μM, 0.05 μM, 0.1 μM, 0.5 μM, 1.0 μM, 5.0 μM, 10.0 μM, 50.0 μM, 100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1965	C. Garoche, A. Boulahtouf, M. Grimaldi, B. Chiavarina, L. - Tsiperova, M. - J. den Broeder, J. Legler, W. Bourguet and P. Balaguer	2021	Interspecies Differences in Activation of Peroxisome Proliferator-Activated Receptor γ by Pharmaceutical and Environmental Chemicals	Endocrine-disrupting chemicals (EDCs) are able to deregulate the hormone system, notably through interactions with nuclear receptors (NRs). The mechanisms of action and biological effects of many EDCs have mainly been tested on human and mouse but other species such as zebrafish and xenopus are increasingly used as models to study the effects of EDCs. Among NRs, peroxisome proliferator-activated receptor γ (PPARγ) is a main target of EDCs, for which most experimental data have been obtained from human and mouse models. To assess interspecies differences, we tested eleven human PPARγ ligands on reporter cell lines expressing PPARγ from human, mouse, rat, pig, cow, dog, rabbit, turtle, xenopus, and zebrafish. Most of these compounds behaved as full agonists on human PPARγ, but showed lower efficacy (e.g. as partial agonists) on PPARγ from a similar manner, while pPPARγ1 was less responsive and pPPARγ2 was not modulated at all by these compounds. On the contrary, human Exn-1 mutant (hL185L) ligands (GW 1929 and GW 0072) were only active on pPPARγ1. Among environmental compounds, several molecules activated the PPARγ of the four species similarly, e.g., phthalates (MEHP), perfluorinated compounds (PFOA, PFOS), and halogenated derivatives of BPA (TBBPA, TCBPA), but some of them like di-n-butyltin and the organophosphorus compounds tri-n-butyl phosphate and tributoxyl phosphate were more active on pPPARγ1. This study confirms or shows for the first time that hNRs, pNRs, and pPNRs' activities of several chemicals and demonstrates the importance of the use of species-specific models to study endocrine and metabolism disruptors by environmental chemicals.	Environ Sci Technol. 2021 Dec 21;55(24):16489-16501.	10.1021/acs.est.1c04318	34843233	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1966	E. García-Recio, A. González-Acedo, F. J. Manzano-Moreno, E. De Luna-Bertos and C. Ruiz	2024	Gene Expression Modulation of Markers Involved in Bone Formation and Resorption by Bisphenol A, Bisphenol F, Bisphenol S, and Bisphenol AF	BACKGROUND: Bisphenol A (BPA) and its analogs (BPF, BPS, and BPAF) are recognized for inducing detrimental effects on various tissues, including bone. OBJECTIVE: The aim of this study is to investigate their impact on the expression of osteoblastic markers of differentiation, such as ALP, RUNX2, OCN, OPN, BSP, and OSX, as well as the receptors TGFβ1, TGFβ2, TGFβR1, TGFβR2, and TGFβR3. METHODS: Human osteoblastic isolated through primary culture from bone samples of healthy volunteers were subjected to cultivation in the presence of various dosage levels (10-12, 10-11, 10-10, 10-9, 10-8, 10-7, 10-6, 10-5 M) of BPA, BPF, BPS, or BPAF for 21 h. Gene expressions of RANKL, OPG, TGF-β1, TGFRI, TGFR2, TGFR3, and VEGF were analyzed by real-time polymerase chain reaction (RT-PCR). All experiments included untreated cells as controls. RESULTS: Expressions of RANKL and OPG were dose-dependently downregulated by the presence of all tested bisphenols. BPS showed a lower effect on RANKL expression compared with BPA, BPF, and BPAF. Gene expressions of RANKL, OPG, TGF-β1, TGFRI, TGFR2, TGFR3, and VEGF were analyzed by real-time polymerase chain reaction (RT-PCR). All experiments included untreated cells as controls. RESULTS: Expressions of RANKL and OPG were dose-dependently downregulated by the presence of all tested bisphenols. BPS showed a lower effect on RANKL expression compared with BPA, BPF, and BPAF. BPS expression was downregulated by all BP treatments, and TGF-β1 receptor expression was also downregulated as a function of the BP and dose. VEGF expression was upregulated by BPA, BPF, and BPAF, but BPS did not show significant differences with respect to the control. CONCLUSIONS: BPA, BPF, BPS, and BPAF can alter bone remodeling (2024 The Author(s). Published by S. Karger AG, Basel). The inhibition of both RANKL and OPG by the BPs, with a higher forbiddance of RANKL than of OPG, appears to reduce BP-induced activation of osteoclastogenesis via RANKL/RANK/OPG. Nevertheless, the effect of the BPs on the expression by osteoblasts of TGF-β1, TGF-βR receptors, and VEGF indicates that these compounds can be responsible for major molecular changes in this cell population, contributing to their adverse effects on bone tissue.	Genes (Basel). 2024 Nov 11;15(11):1453.	10.3390/genes15111453	39596653	in vitro	-	-	-	-	-	-	-	-	-	1	0	10E-12, 10E-11, 10E-10, 10E-9, 10E-8, 10E-7, 10E-6, 10E-5 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1967	E. García-Recio, V. J. Cortés-Ruiz, L. Melguizo-Rodríguez, J. Remor-Torrecillas, O. García-Martínez, C. Ruiz and E. de Luna-Bertos	2022	Repercussions of Bisphenol A on the Physiology of Human Osteoblasts	(1) Background: Bisphenol A (BPA) is an endocrine disruptor that is widely present in the environment and exerts adverse effects on various body tissues. The objective of this study was to determine its repercussions on bone tissue by examining its impact on selected functional parameters of human osteoblasts. (2) Methods: Cells from human osteoblast line were treated with BPA at doses of 10E-12 M, 10E-11 M, 10E-10 M, 10E-9 M, 10E-8 M, 10E-7 M, 10E-6 M, and 10E-5 M for 24 h. Cell viability was assessed by the MTT assay, cell proliferation by the BrdU assay, cell differentiation by measuring ALP activity, and cell mineralization by Alizarin Red staining. (3) Results: The expression of COL1 and COL3 was determined by RT-PCR. (4) Results: The expression of COL1 and COL3 and integrins was increased at doses of 10E-12 and 10E-11 M, while the expression of integrins was decreased at doses of 10E-10 M and higher. According to these findings, BPA exerts adverse effects on osteoblasts by altering their differentiation maturation and their proliferation and functional capacity, potentially affecting bone health. Given the widespread exposure to this contaminant, further human studies are warranted to determine the long-term risk to bone health posed by BPA.	Int J Mol Sci. 2022 May 11;23(10):5349.	10.3390/ijms23105349	35628159	in vitro	-	-	-	-	-	-	-	-	-	1	0	10E-12, 10E-11, 10E-10, 10E-9, 10E-8, 10E-7, 10E-6, 10E-5 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1968	N. García-Gutiérrez, G. Lura-Bárcenas, G. Herrera-Hernández, R. Campos-Vega, S. L. Luzania-Hernández, K. A. Sánchez-Tuirán, P. García-Solís and H. A. Vergara-Castañeda	2023	Quercetin and Its Fermented Extract as a Potential Inhibitor of Bisphenol A-Exposed HT-29 Colon Cancer Cells' Viability	Bisphenol A (BPA) promotes colon cancer by altering the physiological functions of hormones. Quercetin (Q) can regulate signaling pathways through hormone receptors, inhibiting cancer cells. The antiproliferative effects of Q and its fermented extract (FEQ, obtained by Q-gastrointestinal digestion and in vitro colonic fermentation) were analyzed in HT-29 cells exposed to BPA. Polyphenols were quantified in FEQ by HPLC, and their antioxidant capacity by DPPH and ORAC. Q and 3,4-dihydroxyphenylacetic acid (DOPAC) were quantified in FEQ. Q and FEQ exhibited antioxidant capacity. Cell viability with Q (BPA and FEQ) BPA was 80% and 50%, respectively. Q and FEQ (BPA) were 60% and 50%, respectively. Q and FEQ (BPA) induced cell cycle arrest in the G0/G1 phase and apoptosis in 20% of cells. Q and FEQ (BPA) inhibited colony formation. Q and FEQ modulated ERβ and PPARγ genes. Using a gene microarray of the 84 genes related to Q, Q-BPA, FEQ, and FEQ-BPA would modulate related genes involved in cancer. Q and FEQ inhibited the expression of pro-apoptotic and cell cycle-repressor genes. In silico analyses demonstrated the binding affinity of Q + BPA > DOPAC molecules for ERα and ERβ. Further studies are needed to understand the role of dioxybenz in colon cancer.	Int J Mol Sci Vol.24 Issue 6	10.3390/ijms24065604	36982678	in vitro	-	-	-	-	-	-	-	-	-	1	0	4.4-8.8 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1969	P. Gao, L. Wang, N. Yang, J. Wen, M. Zhao, G. Su, J. Zhang and D. Wang	2020	Peroxisome proliferator-activated receptor gamma (PPAR γ) activation and metabolism disturbance induced by bisphenol A and its replacement analog bisphenol S using in vitro macrophages and in vivo mouse models	Bisphenol A (BPA) and its replacement analog, bisphenol S (BPS), have been proposed as environmental damagers to disrupt the lipid metabolism through regulating peroxisome proliferator-activated receptor gamma (PPARγ) nowadays. However, there is a dearth of information on better the biological effect and cause in human macrophages and type which closely interacts with adipocytes and hepatocytes to control lipid metabolism. Here, we for the first time investigate the activity of BPA and BPS on PPARγ pathway in human macrophages. The results demonstrated that BPA and BPS served as activators of PPARγ in human macrophages. Besides, BPA and BPS induced the expression of PPARγ and its target genes (CD36 and FABP4) in a dose-dependent manner. Moreover, BPA and BPS induced the lipid accumulation in human macrophages by using Oil Red O staining. Consistently, the knockdown of PPARγ by siRNA significantly inhibited BPA- and BPS-induced lipid accumulation and the expression of PPARγ target genes in human macrophages. Furthermore, we found that BPA and BPS induced the expression of PPARγ and its target genes in mice adipose tissue and the results confirmed the induction of PPARγ and its respective target genes in mice following exposure to BPA or BPS. Moreover, the observed alteration of PPARγ expression highly correlated with the disturbance of metabolism profiles in liver tissues as detected by 1D Nuclear Magnetic Resonance (NMR)-based metabonomics. Overall, this study provided the first evidence that BPA and BPS activated PPARγ and its target genes in human macrophages, and provided comprehensive information to confirm that BPA and BPS disturb the metabolism through targeting PPARγ via both in vitro assays and in vivo animal models.	Environ Int Vol.134 Pages 105328	10.1016/j.envint.2019.105328	31778932	動物、in vitro	-	1	1	1	1	0	10 μg/kg bw, 1000 μg/kg bw	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1970	J. Gao, T. Song, D. Chu, C. Li, I. Jiang, J. Pang, Y. Yang, Goma and P. Li	2019	The effect of bisphenol a exposure onto endothelial and decidualized stromal cells on regulation of the invasion ability of trophoblastic spheroids in in vitro co-culture model	Bisphenol A (BPA) is a kind of environmental endocrine disruptors (EDCs) that interfere embryo implantation. Trophoblast invasion plays a crucial role during embryo implantation. In this study, the effects of BPA on trophoblast invasion were investigated by using a co-culture model of trophoblastic spheroids and endothelial cells or decidualized stromal cells. Trophoblastic spheroids were formed by JEG-3 cells in 96-well plates. After 24 and 48 h of co-culture with the endothelial cells or decidualized stromal cells, BPA at 1.100 μM also activated ERK 1/2 can express expression in the transfected cells, which was through the ERα, but not ERβ and GPR30 binding. Endothelial receptivity ability was harmed by BPA treatment since receptivity markers of L1P, E1P, MUC1 and integrin α1β3 were decreased after BPA treatment. The invasion ability of trophoblastic spheroids penetrated into top Ecell line was inhibited by BPA and this effect was mediated through secretion of PL pathway and MAPK/ERK/MMP-9/uPA signaling. Besides, BPA treated decidualized stromal cells suppressed Jeg-3 spheroid outgrowth and invasion in an in vitro co-culture assay. Our study could give a better understanding on the possible mechanisms of BPA effect on human embryo implantation process.	Biochem Biophys Res Commun Vol.516 Issue 2 Pages 506-514	10.1016/j.bbrc.2019.06.066	31230753	in vitro	-	-	-	-	-	-	-	-	-	1	0	1—100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1971	M. D. Garzarella, N. C. Indolfo, L. C. M. Oliveira, T. N. Dorabiatu, T. M. Avellino, R. J. de Kawabata, L. B. Tofani, M. F. Terra, G. B. Elias, L. L. de Souza, M. R. Alkuzaguti, S. A. Rocco, K. F. Arndova and A. C. M. Figueira	2024	Unveiling the intricacies of BPA and BPS: comprehensive insights into its toxic effects using a cutting-edge microphysiological system	Concerns over Bisphenol A (BPA) and its substitute, Bisphenol S (BPS), have led to innovative exploration due to potential adverse health effects. BPS, replacing BPA in some regions to avoid toxic impacts, remains inadequately studied. Traditional in vitro models, relying on monolayer cell cultures, struggle to accurately predict in vivo responses. Microphysiological systems (MPS), or organ-on-chip technology, offer a reliable reference or animal models, by integrating diverse tissues and dynamic cell environments enhances precision in predicting organ function. Here, we employ a 3-organ-on-chip microphysiological system with skin, intestinal, liver cultures to assess the effects of BPA and BPS via topical and oral administration. Our evaluation focused on gene markers associated with carcinogenicity, systemic toxicity, and endocrine disruption. BPA exhibited significant cytotoxicity in skin and liver tissues, while BPS showed minimal impact. Notably, BPA induced substantial changes in gene expression, particularly in hepatic pathways, such as the downregulation of the cytochrome P450 family and alterations in steroid hormone synthesis. Skin tissues also displayed sensitivity to BPA, with changes in genes related to cell proliferation and differentiation. Our findings underscore the urgency of addressing BPA toxicity concerns, highlighting the crucial role of organ-on-a-chip technology in understanding exposure-specific risks. The study promotes the organ-on-a-chip methodology as a valuable tool for safe drug development and disease treatments, offering a novel alternative to traditional animal tests. This contributes to advancing comprehensive of the biological effects of these compounds, fostering improved safety assessments in human health.	Toxicol In Vitro. 2024 Jun:98:105849.	10.1016/j.tiv.2024.105849	38772494	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1972	G. Gaggi, A. Di Credico, F. Barbagallo, B. Ghinassi and A. Di Baldassarre	2023	Bisphenols and perfluoroalkyls alter human stem cells integrity: A possible link with infertility	Bisphenols and Perfluoroalkyls are chemical compounds widely used in industry known to be endocrine disruptors (EDCs). Once ingested through contaminated aliments, they mimic the activity of endogenous hormones, leading to a broad spectrum of diseases. Due to the extensive use of plastic in human life, particular attention should be paid to antenatal exposure to Bisphenols and Perfluoroalkyls since they cross the placental barrier and accumulate in developing embryo. Here we investigated the effects of Bisphenol A (BPA), Bisphenol S (BPS), perfluorooctanoic sulfonate (PFOS) and perfluorooctanoic acid (PFOA), alone or combined, on human stem cells (hSCs) integrity. Our results showed that exposure to BPA, BPS, PFOS, PFOA, and their mixture, induced a significant increase in cell death and a decrease in cell proliferation. Moreover, we found that the mixture of the four chemicals was involved in the maintenance of pluripotency, germline specification, and epigenetic regulation. We also evidenced that these chemicals, when combined, may have additive, synergistic but also negative effects. All these data suggest that antenatal exposure to these EDCs may affect the integrity of stem cells in the developing embryo, interfering with critical stages of early human development that might be determinant for fertility. The observation that the effects of exposure to a combination of these chemicals are not easily foreseeable further highlights the need for wider awareness of the complexity of the EDCs effects on human health and of the social and economic burden attributable to these compounds.	Environ Res. 2023 Oct 15:235:116487.	10.1016/j.envres.2023.116487	37419196	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1973	U. B. Gadgoli, C. S. Y, D. Kumar, M. M. Pai, S. Pulya, B. Ghosh and G. P. Kulkarni	2022	Estrogenic Activity of Tetrazole Derivatives Bearing Bisphenol Structures: Computational Studies, Synthesis, and In Vitro Assessment	The classification of bisphenol A (BPA) as an industrial endocrine disruptor has led to a ban of this ubiquitous critical starting material from food and medical applications. Thus, scientists worldwide are researching to develop non-EDG-ating starting compounds to fulfill unmet market needs. In line with this trending research topic, the current paper highlights the development of tetrazole derivatives bearing a bisphenol structure (TetB) as potential BPA substitutes. Computational studies, including molecular docking, ADMET prediction, and molecular dynamics simulations, were performed to assess the binding affinity, ADMET predictions, and in vitro studies identified TetBs as privileged substitutes for BPA. Four TetB ligands were successfully synthesized and subjected to biological testing comparing radioligand competitive binding and functional cellular assays. The measured IC50 value for BPA was found to be 4.24 μM, whereas all the inhibitions were less than 35% for the four TetB ligands. 2Cl and 2,5-Cl, bi-these TetB ligands did not meet the established acceptance criteria of 50% inhibition; they are considered as extremely weak binders to ERα. Steric clashes, the deactivation effect, and the increased total polar surface area (TPSA) of TetB ligands to the hydrophobic binding site are hypothesized to be possible reasons for low binding. Modeling studies complemented by bioassays highlight TetB compounds as privileged prospective BPA replacements. However, more research on TetB ligand toxicity is needed to understand and substantiate that the endocrine effects on the hormonal system, for example, via metabolic activations are not elicited.	J Chem Inf Model. 2022 Feb 28;62(4):854-873.	10.1021/acs.jcim.1c01077	35143200	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1974	J. Fujiki, M. Uchida, S. Tsunoda, N. Maeda, H. Inoue, H. Yokota and H. Iwano		Bisphenol A-sulfate conjugate disrupts AURKA transcription and cell cycle in BeWo cytotrophoblasts	Bisphenol A (BPA) has been shown to exhibit various toxic effects, including the induction of reproductive disorders. Generally, BPA is converted to conjugated metabolites, leading to its inactivation. On the other hand, the toxicity of conjugated metabolites is not fully understood. Notably, the placenta develops the sulfate sulfatase pathway, which transports and reactivates sulfated steroids. Therefore, we investigated the potential adverse effects of the BPA-sulfate conjugate (BPA-S) on human placental trophoblast BeWo cells. Cytotoxicity assay revealed that BPA-S (50 μM) induced cytotoxic inhibition of BeWo growth, with effects similar to those seen with unconjugated BPA (100 μM and 200 nM). This growth inhibition was restored by treatment of the cells with an inhibitor of the organic anion transporting peptides (OATPs). Transcriptome analysis revealed that BPA-S (50 μM) significantly altered the expression of 1,000 genes, whereas BPA (100 μM) affected the expression of 2,000 genes. BPA-S suppressed cell growth activity via the sulfatase pathway. In addition, cell cycle analysis revealed that BPA-S (50 μM) increased the fraction of cytotrophoblasts in the G2/M phase and significantly decreased the accumulation of the transcript encoding Aurora kinase A (AURKA), which is a critical regulator of cellular division. These results suggested that BPA-S triggers cell cycle arrest and inhibits proliferation of BeWo cytotrophoblasts by decreased AURKA, an effect that is mediated by the sulfatase-sulfatase pathway. Overall, these findings provide insights into the mechanism of sulfated endocrine-disrupting chemicals and subsequent adverse effects.	J Chem Inf Model. 2022 Feb 28;62(4):854-873.	10.1016/j.mce.2022.111561	35041905	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1975	N. Franko and M. Sollner Dolenc	2024	Evaluation of THP-1 and Jurkat Cell Lines Coculture for the In Vitro Assessment of the Effects of Immunosuppressive Substances	The group agreed to reduce animal testing calls for the development and validation of in vitro, in chemico and in silico models that would replace the need for in vivo testing and ex vivo materials. A category that requires such more approach methods in the assessment of immunosuppression that can be induced by chemicals including environmental pollutants. To assess the immunosuppressive action on monocytes and lymphocytes, we established a coculture of human tumor cell lines in direct contact. THP-1 and Jurkat cells were used in the ratio 1:1. The cocultures were stimulated to activation and investigated the effects of known immunosuppressive drugs with different mechanisms of action on the release of proinflammatory cytokines. Chemicals were also tested in human peripheral blood mononuclear cells as an appropriate reaction of immunosuppression. A set of recommendations concerning dexamethasone, BPA, BPAF, BPF, BPZ, BPS, TCDMA and BPA NAC were then applied to the model and BPF and BPZ were found to act as potent immunosuppressants at micromolar concentrations.	Toxics. 2024 Aug 19;12(8):607.	10.3390/toxics12080607	39195709	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1976	N. Franko, T. Markovič, P. Žižek, A. Kadlia, I. Milisavić Rašlćan and M. Sollner Dolenc	2025	Unravelling immunomodulatory effects of bisphenol A substitutes on human macrophages, T and B lymphocytes using in vitro models	This study investigates the immunomodulatory effects of BPA substitutes using in vitro and in vivo approaches. A comprehensive in vitro screening with Endocrine Disruptome of BPA and its 25 substitutes revealed that BPG, BPH, BAS, BPS, BPF, BPAF and PC1 have the highest potential to bind nuclear receptors. Based on the in vitro ranking, 12 compounds were selected and tested in vitro to investigate their effects on THP-1 derived macrophages, Jurkat T cells and CLL. The metabolic activity tests showed that BPA has IC50 values of 99-160 μM, while the values for BPG, BPH and BPF are 5-10times lower. Comparison of the IC50 values with the half of the tested concentrations revealed that the BPA analogues affect cell viability in a similar way. Cytokine profiling revealed that BPA and its substitutes generally stimulated the proinflammatory response in THP-1 macrophages in a statistically significant manner when exposed to the environmentally relevant concentrations and suppressed it in the stimulated Jurkat T cells. Similarly, BPA and its substitutes suppressed the activation of CLL cells. The EC50 values for BPA, BPG, BPH, BPF, BPAF, BPZ, BPS, TCDMA and PC1 were 1.5-3.5 μM, 0.5-1.5 μM, 0.5-1.5 μM, 1.5-3.5 μM, 0.5-1.5 μM, 1.5-3.5 μM, 0.5-1.5 μM, 1.5-3.5 μM and 0.5-1.5 μM, respectively. The lowest EC50 values were predicted in silico in the TOXLINE database. The overall results of this study identify BPG, BPF, BPAF, BPZ and TCDMA as BPA analogues within the highest immunomodulatory potential in addition, the immunomodulatory potential of the BPA alternatives Pergaflex201 and BT168 was confirmed in vitro for the first time. This study emphasizes the need for cautious evaluation of BPA substitutes due to their potential immunomodulatory effects, which could significantly affect public health.	Ecotoxicol Environ Saf. 2025 Jul 15:300:118406.	10.1016/j.ecoenv.2025.118406	40449052	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1977	S. Fouget, E. Olivier, P. Lepeuz, M. Dutot and P. Rat	2021	Bisphenol A, Bisphenol F, and Bisphenol S: The Bad and the Ugly. Where Is the Good?	BACKGROUND: Bisphenol A (BPA), a neurotoxic and endocrine-disrupting chemical, has been substituted by alternative bisphenols such as bisphenol F (BPF) and bisphenol S (BPS) in the plastic industry. Despite their detection in placenta and amniotic fluids, the effects of bisphenols on human placental cells have not been investigated. OBJECTIVE: Our objective was to evaluate in vitro and to compare the toxicity of BPA to its substitutes BPF and BPS to highlight their potential risks for placenta and then pregnancy. METHODS: Human placenta cells (JEG-3cc cells) were incubated with BPA, BPF, and BPS for 72 h. Cell stability, cell death, and degenerated FOS/JUN activity were evaluated using the neutral red uptake assay, propidium iodide staining, and AP-1 transactivation assay, respectively. RESULTS: BPA, BPF, and BPS induced cytotoxicity, cell death, and activation of AP-1 transactivation with similar potency. Cytotoxicity and AP-1 activation were enhanced in combination. BPA and BPF induced more caspase-3, caspase-9, and caspase-1 activation than BPS. Only BPF enhanced caspase-8 activity. CONCLUSIONS: BPA, BPF, and BPS are all toxic to human placental cells, with the FOS/ transcription factor as a common key element. BPA substitutes to BPF and BPS does not appear to be a safe alternative for human health, particularly for pregnant women and their fetuses.	Life (Basel) Vol.11 Issue 4	10.3390/life11040314	33916708	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1978	A. Flores, P. Moyano, E. Sola, J. M. Garcia, J. Garcia, M. J. Anadon, M. T. Frejo, M. Y. Naval, M. C. Fernadez and J. D. Pino	2022	Single and repeated bisphenol A treatment induces ROS, Aβ and hyperphosphorylated-tau accumulation, and insulin pathways disruption, through HDAC2 and PTP1B overexpression, leading to SN56 cholinergic apoptotic cell death	Bisphenol-A (BPA), a polymer component extensively used, produces memory and learning alterations after acute and long-term exposure. However, the mechanisms are not well known. Cortex and hippocampus neuronal networks control cognitive functions, which are interrupted by basal forebrain cholinergic neurons (BFCN), and their neurodegeneration induces cognitive dysfunctions. BFCN lose or protein/receptor phosphatase 1B (PTP1B), histone deacetylase 2 (HDAC2), beta-A amyloid precursor protein (βAPP) silenced SN56 cells treated with BPA (0.001 μM–100 μM) with or without N-acetylcysteine (NAC; 1 mM), following 1 and 14 days, were used, as a model of BFCN to determine the insulin pathway dysfunction, oxidative stress (OS) generation and amyloid-β (Aβ) and tau proteins accumulation involvement in the BFCN cell death induction, as a possible mechanism that could produce the cognitive disorders reported. BPA induced BFCN cell death, after 30 h and 14 days of treatment, through insulin pathway dysfunction, OS generation, mediated by HNF2 and PTP1B overexpression, leading to Aβ and hyperphosphorylated-tau accumulation, and finally, to BFCN cholinergic apoptosis. This is relevant information to explain the BFCN neurodegeneration mechanisms that could trigger the neurodegeneration in the rest of the regions innervated by them, leading to cognitive disorders.	Food Chem Toxicol. 2022 Dec:170:113500.	10.1016/j.fct.2022.113500	36374790	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1979	Y. Fischer, A. Pieruchalski, S. Riedbeck, A. S. Aldraihi, V. A. Castaneda-Montalvo, S. B. Haarge, M. von Bergen, U. E. Rolle-Kampczyk, N. Jehmlich, K. C. Zanclussen and G. Herbarth	2024	An in vitro model system for testing chemical effects on microbiome-immune interactions - examples with BPX and PFAS mixtures	INTRODUCTION: More than 350,000 chemicals make up the chemical universe that surrounds us every day. The impact of this vast array of compounds on our health is still poorly understood. Manufacturers are required to test the toxicity of their products, but these tests rarely consider the microbiome. The microbiome is the community of microbes that live in and on our bodies. Disruptions in the microbiome's composition can cause or be due to a variety of illnesses or be risk factors. In offsets, we either potentially affected organ systems. This is the case for the microbiome-immune interaction, which is not yet included in any public studies. METHODS: A high-throughput in vitro model was used to elucidate the potential effects of environmental chemicals and chemical mixtures on microbiome-immune interactions. Therefore, a modified human intestinal microbiota (SIHUMIx) consisting of eight bacterial species was cultured in vitro to microbiome that partially mimics intestinal conditions. The bacteria were continuously exposed to mixtures of representative and widely distributed environmental chemicals, i.e. bisphenols (BPX) and (per- and polyfluoroalkyl substances (PFAS) at concentrations of 22 μM and 4 μM, respectively. Furthermore, changes in the immunostimulatory potential of exposed microbes were investigated using human peripheral blood mononuclear cells (PBMCs) from healthy donors. RESULTS: Exposure to BPX and PFAS mixtures altered the composition of the bacterial community in SIHUMIx in vitro. However, it altered the potential of the consortium to stimulate human immune cells. In particular, activation of CD8(+) T/NKT cells was affected by the exposure to BPX- and PFAS mixtures treated bacteria. DISCUSSION: The present study provides a model to investigate how environmental chemicals can indirectly affect immune cells via exposed microbes. It contributes to the much-needed knowledge on the effects of EDCs on an organ system that has been little explored in this context, especially from the perspective of cumulative exposure.	Front Immunol Vol.15 Pages 1298971	10.3389/fimmu.2024.1298971	38953021	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1980	Y. Fischer, M. R. Eimer, J. Howaniak, Z. Yin, M. Bauer, M. Wagner, B. Fink, A. C. Zenclussen and A. Schumacher	2024	Single and mixture effects of bisphenol A and benzophenone-3 on in vitro T helper cell differentiation	Immune homeostasis is key to guarantee that the immune system can elicit effector functions against pathogens and at the same time retain tolerance towards other antigens. A disbalance of this delicate balance may underlie or at least trigger pathologies. Endocrine-disrupting chemicals (EDCs) are increasingly recognized as risk factors for immune dysregulation. However, the immunotoxic potential of especially EDCs, and their mixtures is still poorly understood. Thus, we aimed to investigate the effect of bisphenol A (BPA) and benzophenone-3 (BP-3), alone and in combination, on in vitro differentiation of T helper (Th)17 cells and regulatory T (Treg) cells. Naïve T cells were isolated from mouse lymphoid tissues and differentiated into the respective Th populations in the presence of 0.001–10 μM BPA and/or 0.01–100 μM BP-3. Cell viability, proliferation and the expression of Th lineage-specific transcription factors and cytokines was measured by flow cytometry and CBA/Th1/2/17 assay. Moreover, the transcription of hormone receptors as direct targets of EDCs was quantified by RT-qPCR. Our results show that BPA and BP-3 affected Th17 cell differentiation in vitro, with BP-3 showing a stronger impact than BPA. Co-exposure to BPA and BP-3 mixtures at environmentally relevant concentrations of EDCs, however, EDC exposure modulated the emergence of Th17 and Treg cell intermediate states. While BPA and BP-3 promoted the development of Th1-like Th17 cells, under Th17-differentiating conditions, Th1-like Treg cells occurred under Treg polarization. Interestingly, differential effects, visible for observed in mixtures of the two tested compounds compared with the individual compounds. Notably, estrogen receptor β expression was decreased under Th17-differentiating conditions in the presence of BPA and BP-3 as mixture. In conclusion, our study provides solid evidence for both, the immune disruptive potential and the existence of immediate effects of real-future EDC mixtures on T cell in vitro differentiation.	Chem Biol Interact. 2024 May 25:395:111011.	10.1016/j.cbi.2024.111011	38653352	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1981	S. Fical, A. Papait, M. Magatti, A. Massardotti, M. Gaida, A. R. Silini and O. Parolini	2025	Bisphenol-A disrupts mitochondrial functionality leading to senescence and apoptosis in human amniotic mesenchymal stromal cells	In today's context, microplastic pollution has become an increasingly pressing issue not only for the environmental fallout but also for the assumed negative effects on human health. It is now well established that microplastics (<5 mm in size) can enter the human body through ingestion, inhalation, dermal contact and also maternal-fetal transmission. Alarming were the recent findings of microplastics within the human term placenta. The amniotic membrane surrounds the fetus, playing a fundamental protective role toward toxic chemicals and pollutants that the mother may encounter. Our research revealed toxic exposure to increasing concentrations of BPA compromise mitochondrial functionality in hAMSC, resulting in enhanced production of reactive oxygen species at mitochondrial level (mROS). This, in turn, leads to the stabilization of p53, which triggers an increased expression of p21 and p27 encoding genes, and an imbalance in the genetic expression of Bax and Bcl-2. Additionally, our observed upregulated expression of cytokines and chemokines associated with senescence-associated secretory phenotype (SASP) further supports the induction of premature senescence. Furthermore, the observed activation of BPA-mediated toxicity investigate the mechanism of the mitochondrial dysfunction, as cells likely due to the overwhelming stress conditions. Therefore, our results provide novel insights into the mechanism of action of BPA and elucidates its impact on the functionality of hAMSC. This underscores the pressing need to reconsider the use of BPA as a plastic additive, mitigating the potential adverse effects on babies.	Cell Death Discov. 2025 Jul 16;11(1):327.	10.1038/s41420-025-02620-8	40670380	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1982	R. Ferreira, C. Amaral, G. Correia-da-Silva, M. Almeida, M. Augusto, S. C. Cunha, J. O. Fernandes and N. Teixeira	2022	Bisphenols A, F, S and AF trigger apoptosis and/or endoplasmic reticulum stress in human endometrial stromal cells	Disruption of non-differentiated endometrial stromal cells could have serious consequences in female reproduction, impairing endometrial remodelling and implantation. Following the classification of bisphenol A (BPA) as an endocrine disruptor, BPA analogues, namely bisphenol S (BPS), bisphenol F (BPF) and bisphenol AF (BPAF), have been used as substitutes in many consumer products. Herein, we investigated the effects of BPA, BPS, BPF and BPAF on immortalized human endometrial stromal cell line (St-T1b) to study the effects of BPA and its three most commercialized structural analogues. Tested bisphenols S, F and AF induced stromal cells to undermined their effects on female reproductive function. Bisphenols showed dissimilar effects. All four compounds generated endoplasmic reticulum (ER) stress. In addition, bisphenols A, F and AF induced apoptosis through different mechanisms, with bisphenol AF causing cell cycle arrest at G2/M phase. Bisphenol AF decreased mitochondrial transmembrane potential and bisphenols A, F and AF produced oxidative stress.	Toxicology. 2022 Aug:478:153282.	10.1016/j.tox.2022.153282	35940389	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1983	L. Ferreira Azevedo, M. M. Masiero, S. Cherkaoui, M. F. Hornos Carneiro, F. Barbosa, Jr. and N. Zamboni	2022	The alternative analog plasticizer BPS displays similar phenotypic and metabolomic responses to BPA in HepG2 and INS-1E cells	Bisphenols A (BPA) and S (BPS) are endocrine-disrupting chemicals that affect energy metabolism, leading to impairment of glucose and lipid homeostasis. We aimed at identifying metabolic pathways regulated by both compounds in human liver cells and rat pancreatic β-cells that could impair energy homeostasis regulation. We assessed the effects on growth, proliferation, and viability of hepatocarcinoma (HepG2) and insulinoma (INS-1E) cells exposed to either BPA or BPS in a full range concentration between 0.001 and 200 μM. Both the dose and duration of exposure caused a differential response on growth and viability of both cells. Effects were more pronounced on HepG2, as these cells exhibited non-linear dose responses following exposure to xenobiotics. For INS-1E cells, BPA was observed only at the highest concentration. In addition, we profiled how BPA and BPS modulated the metabolome of HepG2 cells. Principal component analysis revealed that BPA and BPS induced similar metabolic changes. Moreover, metabolite set enrichment analysis identified that some differentially expressed metabolites, such as metabolites participating in histidine and linoleic acid metabolic pathway. In summary, this study shows that BPS also disrupts molecular functions in cells that regulate energy homeostasis, displaying similar but less pronounced responses than BPA.	Food Chem Toxicol. 2022 Sep:167:113266.	10.1016/j.fct.2022.113266	35779701	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1984	M. M. Fay, O. Columbu, C. Cotter, C. Friend, S. Henry, M. Hoppe, P. Kadaikkal, C. Lamy, M. Lawell, S. Mortelliti, C. Noyes, P. Salerno, J. Wu, M. M. Zhang, P. J. Anderson, N. Kedersha, P. Ivanov and N. G. Fahy	2021	Bisphenol A promotes stress granule assembly and modulates the integrated stress response	Bisphenol A (BPA) is a ubiquitous precursor of polycarbonate plastics that is found in the blood and serum of >92% of Americans. While BPA has been well documented to act as a weak estrogen receptor (ER) agonist, its effects on other cellular pathways are poorly understood. Here, we report that BPA induces the assembly of stress granules (SGs), which are cytoplasmic biomolecular condensates that form in response to cellular stress. BPA SG induction is not via the ER pathway. We also tested other structurally related environmental xenobiotics, including the common BPA substitutes BPS and BPF. Only BPA and BPF induced SG assembly. Using 17 structurally related compounds (2 BP and 6 BF, as well as the pesticide 2,4-dichlorophenoxyacetic acid (2,4-D). The variable results from these related compounds suggest that structural homology is not a reliable predictor of the necessity or sufficiency to cause SGs. Also, we demonstrate that BPA activity primarily through the PERK pathway to promote canonical SGs. Finally, we show that chronic exposure to a low physiologically relevant dose of BPA suppresses SG assembly upon subsequent acute stress. Interestingly, this SG inhibition does not affect phosphorylation of eIF2α or translation inhibition, thus uncoupling the physical assembly of SGs from translational control. Our work identifies additional effects of BPA beyond endocrine disruption that may have consequences for human health.	Biol Open. 2021 Jan 10:10(1):bio057539.	10.1242/bio.057539	33431410	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1985	M. Farahani, M. Rezaei-Tavirani and B. Arjmand	2021	A systematic review of microRNA expression studies with exposure to bisphenol A	Bisphenol A (BPA), as a common industrial component, is generally consumed in the synthesis of polymeric materials. To gain a deeper understanding of the detrimental effects of BPA, BPA-induced microRNA (miRNA) alterations were investigated. A systematic search was performed in the PubMed, SCOPUS and Web of Science databases to order relevant published data up to August 30, 2020. We identified altered miRNAs that have been reported in at least three studies. Moreover, miRNA homology analysis between human and nonhuman species was performed to determine the toxicity signatures of BPA in human exposure. In addition, to inform in vitro and in vivo experimental models, the miRNA-BPA network was constructed. Finally, the miRNA-related pathways, shared the BPA-exposed cells, were identified. Our findings showed that 15 miRNAs were identified that were differentially expressed in at least three independent studies. Upregulating miR-16b and downregulating miR-30c, miR-21b, miR-27b and miR-223 were found in three studies. MiR-30c and miR-16b were upregulated in four studies, after BPA exposure, and miR-21 was upregulated in six studies. The results indicate that BPA at low-level exposures can also alter miRNA expression in response to toxicity. Finally, the miRNA-related pathways, shared the BPA-exposed, can affect human health through various cell signaling pathways, which were predictable and consistent with existing studies. Overall, our findings suggest that further studies should be conducted to examine the role of miRNA-level changes in human BPA exposure.	J Appl Toxicol. 2021 Jan;41(1):4-19.	10.1002/jat.4025	32662106	in vitro	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1986	H. Fan, L. Jiang, Y. L. Lee, C. K. C. Wong, E. H. Y. Ng, W. S. B. Yeung and K. F. Lee	2020	Bisphenol compounds regulate decidualized stromal cells in modulating trophoblastic spheroid outgrowth and invasion in vitro	Bisphenol A (BPA) is commonly found in epoxy resins used in the manufacture of plastic coatings in food packaging and beverage cans. There is a growing concern about BPA as a weak estrogenic compound that can affect human endocrine function. Chemicals structurally similar to BPA, such as bisphenol F (BPF) and bisphenol S (BPS), have been developed as substitutes in the manufacturing industry. Whether these bisphenol analogs have similar effects on human reproductive functions remains unclear. In this study, we investigated the effects of BPA, BPF and BPS on the decidualization of human primary endometrial stromal cells an trophoblast outgrowth and invasion by Ishikawa and Jeg-3 cells in a co-culture models. At three bisphenols did not affect the survival and decidualization process. However, BPA- and BPF-treated decidualized stromal cells stimulated trophoblastic spheroid invasion in the indirect co-culture model. The BPA-treated decidualized stromal cells had upregulated expressions of several invasion-related molecules including leukemia inhibitory factor (LIF), urokinase-type PA (uPA) and BPF-treated decidualized stromal cells had downregulated expressions of anti-invasive molecules including plasminogen activator inhibitor-type 1 (PAI-1) and tumor necrosis factor (TNF-α). Taken together, BPA and BPF altered the expression of invasive and anti-invasive molecules in decidualized stromal cells modulating its function on trophoblast outgrowth and invasion, which could affect the implantation process, and subsequent pregnancy outcome.	Biol Reprod. 2020 Mar 13;102(3):693-704.	10.1093/biolre/ioz212	31742322	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1987	H. Fan, S. R. Ferrardo, L. Jiang, Z. Wang, S. P. Kodithuwakku, C. K. C. Wong, E. H. Y. Ng, W. S. B. Yeung and K. F. Lee	2021	Bisphenol A Analogues Suppress Spheroid Attachment on Human Endometrial Epithelial Cells through Modulation of Steroid Hormone Receptors Signaling Pathway	Bisphenol A (BPA) is a well-known endocrine disruptor, widely used in various consumer products and ubiquitously found in air, water, food, dust, and sewage leachates. Recently, several countries have restricted the use of BPA and replaced them with bisphenol S (BPS) and bisphenol F (BPF), which have a similar chemical structure to BPA. Compared to BPA, both BPS and BPF have similar estrogenic effects, but their effects on human reproductive function including endometrial receptivity and embryo implantation still remain largely unknown. We used an in vitro spheroid (blastocyst surrogate) co-culture assay to investigate the effects of BPA, BPS, and BPF on the attachment competency of human endometrial epithelial cells. Ishikawa cells were treated with BPA, BPS, and BPF at concentrations ranging from 0.1 nM to 10 μM. BPF or the homocysteine-endometrial cells. We found that bisphenol treatment in human endometrial Ishikawa cells altered estrogen receptor alpha (ERα) signaling and steroid progesterone receptor (PR). Bisphenols suppressed spheroid attachment onto Ishikawa cells, which was reversed by the downregulation of PR through PR siRNA. Overall, we found that bisphenol compounds can affect human endometrial epithelial cell receptivity through the modulation of steroid hormone receptor function leading to impaired embryo implantation.	Cells. 2021 Oct 26;10(11):2882.	10.3390/cells10112882	34831106	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.01-100 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1988	E. Evgelahi, M. D. M. van Schijndel, D. Vaudagna, M. Di Ciccio, K. A. Ramsbottom, D. J. Rigden, A. Herland and J. Rüegg	2021	Bisphenol A Inhibits the Transporter Function of the Blood-Brain Barrier by Directly Interacting with the ABC Transporter Breast Cancer Resistance Protein (BCRP)	The breast cancer resistance protein (BCRP) is an important efflux transporter in the blood-brain barrier (BBB), protecting the brain from a wide range of substances. In this study, we investigated if BCRP function is affected by bisphenol A (BPA), a high production volume chemical used in common consumer products, as well as by bisphenol F (BPF) and bisphenol S (BPS), which are used to substitute BPA. We employed a transwell assay with MDCK II cells overexpressing human BCRP and found that BPA, BPF, and BPS inhibited BCRP function at concentrations relevant for human exposure. Using the intracellular accumulation of the substrate Hoechst 33342, BPA was found to inhibit BCRP at the luminal membrane of the BBB. In silico modeling further predicted the bisphenols could directly interact with BCRP. Our results showed that BPA significantly inhibits the transport function of BCRP. Additionally, BPA was predicted to bind to the key cavity that is targeted by known BCRP inhibitors. Taken together, our findings demonstrated that BPA inhibits BCRP function in vitro, probably by direct interaction with the transporter. This effect might contribute to BPA's known impact on neurodevelopment.	Int J Mol Sci Vol.22 Issue 11	10.3390/ijms22115534	34073890	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	500 nM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1989	M. A. Elmetwally, A. A. Halawa, W. Tang, G. Wu and F. W. Bazer	2020	Effects of Bisphenol A on expression of genes related to amino acid transporters, insulin- like growth factor, aquaporin and amino acid release by porcine trophectoderm cells	The peri-implantation period of pregnancy is critical for conceptus development, implantation, and signaling for establishment of pregnancy. This study evaluated the effects of bisphenol A (BPA) on proliferation, adhesion and migration of porcine trophectoderm (pTr) cells, expression of transporters of arginine and synthesis of amino acids, (E) concentrations of BPA decreased proliferation and adherence of pTr cells after BPA compared to the control group. Lower concentrations of BPA (1 × 10(-6), 1 × 10(-8), (5) (100) increased (P < 0.05), but higher concentrations of BPA (1 × 10(-5), 1 × 10(-4)) decreased migration of pTr cells. BPA increased expression of SLC7A1 mRNA at lower concentrations (1 × 10(-6), 1 × 10(-8)) and SLC7A5, another concentrations (1 × 10(-5), 1 × 10(-4)). BPA also lower regulated the expression of SLC7 and IGF1 receptor at concentrations of 1 × 10(-5) to 1 × 10(-4) compared to the control group. The expression of mRNAs for aquaporins (AQP) 3 and 9 were reduced at all concentrations of BPA. Abundance of mRNA for AQP3 was greater (P < 0.05) in pTr cells exposed to 1 × 10(-6) and 1 × 10(-8) BPA than in cells exposed to 1 × 10(-5) and 1 × 10(-4) BPA. Expression of mRNAs for synthases of cytoplasmic (nitric oxide synthase 1) and mitochondrial (nitric oxide synthase 3) forms of nitric oxide synthase, and nitrite/nitrate concentrations in culture media of pTr cells, (Collectively, BPA adversely affected the expression of transporters for substrate amino acids (but arginine, as well as AQPs, IGF1, and IGF1R associated with proliferation, migration, and adhesion of pTr cells. These adverse effects would likely increase pregnancy losses during the peri-implantation period of pregnancy.	Reprod Toxicol. 2020 Sep;96:241-248.	10.1016/j.reprotox.2020.07.008	32710935	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	1 nM, 10 nM, 100 nM, 1 μM, 10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1990	R. Sarlings, X. Y. Lee, W. Van Eynde, L. Moris, S. El Kharraz, E. Smeets, W. Devles, F. Claessens, K. J. Vanclooper, A. Voet and C. Helsen	2025	Rewiring Estrogen Receptor α into Bisphenol Selective Receptors Using Darwin Assembly-Based Directed Evolution (DADE) in Saccharomyces cerevisiae	Bisphenols are widely used in manufacturing plastics and resins, but their environmental persistence raises concerns to human health and ecosystems. Accurate measurements for bisphenols are crucial for effective monitoring and risk assessment. Current detection methods rely on costly and complex analytical techniques, highlighting the need for simple, cost-effective biosensors for widespread environmental contamination. Our strategy leverages Saccharomyces cerevisiae with increased structural plasticity and specificity for bisphenols. In our previous work, we demonstrated the successful creation of more than 1 million integrated estrogen receptor variants. By mutating the estrogen receptor α towards recognition of bisphenol A in yeast, we determined the preBEAT variant (S422Q, I423Q, V533Q) with elevated bisphenol A sensitivity (EC50:639 nM) and low estrogen responsiveness (EC50:4.17 mM). Further engineering yielded an off-target mutant, identified as the Bisphenol Affinity and Specificity Enhanced (BASE) variant (S422Q, I423Q, V533Q, L539Q, Y537L, I426Q) that uses bisphenols as its primary agonist (EC50:53 nM) and impaired estrogen sensitivity (EC50:5566). The resulting into a bisphenol receptor was confirmed in ligand binding assays in purified ligand-binding domains. Taken together, the identified variants form stepping stones for further protein engineering to generate bisphenol-specific high-throughput yeast-based biosensors.	ACS Synth Biol. 2025 Jun 20;14(6):2254-2269.	10.1021/acssynbio.5c00163	40347189	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1991	Y. Ebrahimi-Kia, A. Nouri-Zadeh, F. Rajaei, S. Darabi, L. Darabi and H. Ghasemi Hamidabadi	2022	The Effect of bisphenol A and photobiomodulation Therapy on Autophagy-Related Genes Induction in Adipose Tissue-Derived Stem Cells	Introduction: As adipose tissue-derived stem cells (ADSCs) can divide rapidly and be prepared non-invasively, they have extensively been used in regenerative medicine. On the other hand, a new method of therapy, known as photobiomodulation (PBM), has been used in recent years. Bisphenol A (BPA) is a chemical substance that is widely used in the production of plastics. BPA can induce autophagy and lead to autophagy. This study investigated the effects of BPA and PBT on the expression of autophagy-related genes, including LC3, MAP1, PEG 3 on ADSCs as a model. Methods: ADSCs isolated adipose tissue were confirmed by immunocytochemistry (ICC). The cells were then treated with different concentrations of BPA and also subjected to PBT. Reverse transcription polymerase chain reaction (RT-PCR) was used for the evaluation of LC3, MAP1 and PBT gene expressions. 3) and 5 staining was used to investigate apoptosis-caused formation. Results ICC showed that the isolated cells over CD 34 positive but CD 31 and CD 45 negative. The viability test indicated that the number of live cells after 24 hours in the BPA groups at concentrations of 0, 1, 10, 100 and 200 μM was 100%, 95%, 81%, 72%, and 65% respectively. The difference in cell viability between the BPA groups at 0 and 1 μM was not significant ($P > 0.05$), but the difference between 0 and 10, 100, and 200 μM was significant ($P < 0.05$). However, in the treatment group at the concentration of 500 μM of BPA, the LC3 gene was expressed, but MAP1 and PEG genes were downregulated. Conclusion: BPA and PBT induce autophagy and adipocytes in ADSCs in a dose-dependent manner.	J Lasers Med Sci Vol.13 Pages e15	10.34172/jlms.2022.15	35996481	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0, 1, 50, 100, 200 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1992	R. Ebrahimi, M. Shokrzadeh and N. Ghasemi Baghi	2021	Effects of melatonin on the Bisphenol-A- induced cytotoxicity and genetic toxicity in colon cancer cell lines, normal gingival cell lines, and bone marrow stem cell lines	Bisphenol A (BPA) is a synthetic chemical that has widely been used in the production of polycarbonate plastic and epoxy resins. In the manufacture of consumer products. The most common path of human exposure to BPA is by oral intake that involves genotoxicity, oxidative stress, endocrine disruption, mutagenicity, and carcinogenicity in both in vitro and in vivo models. Melatonin is known as a free radical scavenger and a powerful antioxidant agent. This study aimed to investigate the effects of melatonin on viability and genetic alterations of normal human Gingival Fibroblasts (HGF), colon cancer (SW480), and bone marrow stem cell (KS1) lines exposed to BPA. For this purpose, MTT and Comet assays were performed to evaluate the cytotoxicity and genotoxicity properties of BPA and the role of melatonin. The results showed that BPA exposure resulted in increased oxidative stress parameters, including GSH and MDA, and decreased SOD content. The comet study demonstrated the cytotoxicity and genotoxicity effects of BPA and the protective role of melatonin in preventing cytotoxicity and DNA damage are induced by BPA.	Cancer Inform. 2021 Nov 17;20:11769351211056295	10.1177/11769351211056295	34819716	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	1	0.5, 5, 50, and 100 μg/ml	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1993	I. Čunovová, E. Goffa, Z. Šerštková, D. Mánišo a, K. Gaplovská-Kyselá, M. Chovanec and A. Šesto ňová	2021	Acute Exposure to Bisphenol A Causes Oxidative Stress Induction with Mitochondrial Origin in Saccharomyces cerevisiae Cells	Bisphenol A (BPA) is a major component of the most commonly used plastic products, such as disposable plastics, Tetra Paks, cans, spot protective equipment, or medical devices. Due to the accumulation of excessive amounts of plastic in the environment, BPA is released into the environment, where it can be found in water, soil, and air. Its presence in the environment and its ability to affect the endocrine system of living organisms due to its binding to estrogen receptors (ERs), are relatively well described. However, the exact physiological effects on living organisms may result from this action. Since evidence of the potential pro-oxidizing effects of BPA has accumulated over the last years, herein, we focus on the detection of oxidative stress and its origin following BPA exposure using yeast-based cell pharmacotests, flow cytometry, fluorescent microscopy, and Western blot analysis. Saccharomyces cerevisiae cells served as a model system, as these cells lack ERs affecting us to discern the ER-dependent and -independent effects of BPA. Our data show that high concentrations of BPA affect cell survival and cause increased intracellular oxidation in yeast, which is primarily generated in the mitochondrion. However, at acute BPA exposure does not lead to significant oxidative damage to DNA or proteins.	J Fungi (Basel) Vol.7 Issue 7	10.3390/jof7070543	34356922	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	500 and 1000 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1994	M. Duvnik, L. Hiti, T. Tomašič and L. P. Mašič	2022	New bisphenol A and bisphenol S analogs: Evaluation of their hERα agonistic and antagonistic activities using the OECD 455 in-vitro assay and molecular modeling	Bisphenol A (BPA) and bisphenol S (BPS) are agonists of hERα receptors and due to BPA regulations in many countries, several substitutes that are close analogs to BPA and BPS were developed. In the presented study, we have determined human estrogen receptor (hER) α agonistic and antagonistic activities with the validated OECD assay with the hERα-HeLa-9903 cell line for a different mixtures of BPA and BPS analogs. The study also defined clear structural activity relationships for agonist and antagonist activities, of the 22 bisphenols, six hERα, which are supported by molecular docking studies. These data show that chemical analogs of BPA and BPS, which are in use, have similar hormonal activities and should be regulated in the same manner as BPA and BPS. Bisphenol analogs with the highest agonistic activity were 4,4'-(1,4-phenylenebis(propan-2-yl-2-ylidene))diphenol (BPP) and 4,4'-(1,4-phenylenebis(propan-2-yl-2-ylidene))bis(2-methylphenol) (BPP-2) with EC50 values of 0.31 μM and 0.48 μM, respectively. Among these validated bisphenols, 2,2'-methylenebis-(octylphenol)diol was the most potent hERα antagonist, with an IC50 of 0.39 μM. The antagonistic agonist and antagonistic potencies of these different chemical classes of BPA and BPS analogs are mutually comparable and can be used as a basis for further structure-activity relationships studies and human risk assessment.	Chem Biol Interact. 2022 Feb 25:354:109820.	10.1016/j.cbi.2022.109820	35077665	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1995	M. Duvnik, D. Gramec Skledar, T. Tomašič, J. Trontelj and L. Peterlin Mašič	2023	Last piece in the puzzle of bisphenols BPA, BPS and BPF metabolism: Kinetics of the in vitro sulfation reaction	Bisphenols are endocrine disrupting chemicals ubiquitously present in the environment, with the consequent exposure to humans. In humans, bisphenols are metabolized to glucuronide and sulfate conjugates. Recent studies indicate that sulfation represents an important bisphenol metabolic pathway for the most vulnerable humans, such as the growing fetus. So we was to evaluate sulfation kinetics of commonly detected bisphenols. In biological samples: bisphenol S (BPS), bisphenol S (BPS), and bisphenol F (BPF). Furthermore, we evaluated estrogenic agonist potencies and long-term stability of these bisphenol sulfates. BPS and BPF sulfates were synthesized using the SO3-pyridine complex and characterized by NMR and HRMS analysis. Sulfation kinetics was evaluated using pooled human liver S9 fraction and PAPS as a cofactor. Quantification by LC-MS/MS. A validated transactivation assay using the MVLN-hERα-HeLa-9903 cell line was used to determine estrogenic agonist potencies. Moreover, BPA, BPS, and BPF sulfates were examined under various conditions and during storage. In vitro sulfation of BPS and BPF followed Michaelis-Menten kinetics. BPF sulfation followed substrate inhibition model. Sulfation rates were comparable for these bisphenols, although their K(M) values indicated some large differences. In synthesis, BPS and BPF sulfates are not hERα agonists. The bisphenol sulfates can be considered stable for at least 2 days under these normal body conditions. These data indicate that bisphenol sulfation is an important route in their biotransformation. Compared to glucuronidation, these bisphenols show slower sulfation rates but similar K(M) values. BPA and BPS metabolic biotransformation by sulfation provides their detoxification as they are inferior estrogenic activities.	Chemosphere. 2022 Sep;303(Pt 2):135133.	10.1016/j.chemosphere.2022.135133	35636595	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1996	R. Dragone, G. Grasso and C. Frazzoli	2020	Amperometric Cytosensor for Studying Mitochondrial Interferences Induced by Plasticizers Bisphenol B and Bisphenol A	The widespread presence of plastic-born Bisphenol B (BPB) and Bisphenol A (BPA) in food-contact materials, medical equipment, and common household products is a toxicological risk factor for health due to internal exposure after environmental dietary exposure. This work describes the use of an amperometric cytosensor (i.e., a whole-cell-based amperometric biosensor) to detect for studying mitochondrial interferences of BPA and BPB. The HepG2 cell line was employed as a biological recognition element. The cytosensor was exposed to BPA and BPB at concentrations ranging from 0.1 to 100 μg/mL. Mitochondrial interferences were evaluated by comparison of aerobic respiration of exposed and control (i.e., unexposed) cells in suspension. Results suggested the hypothesis of a dose-dependent or action of two mechanisms: uncoupling of oxidative phosphorylation and oxidative stress. These mechanisms, respectively matched with opposite effects of hyperstimulation and inhibition of cellular respiration. While uncoupling of oxidative phosphorylation and oxidative stress have been previously described as coupled effects from in vitro BPA exposure using other biochemical endpoints and biological systems, effects of BPB on cellular aerobic respiration are here reported for the first time. Results highlighted a similar hyperstimulation effect after exposure to 5 μg/mL BPA and BPB. About a 2-fold higher cellular respiration inhibition potency was observed after exposure to 10, 50, and 100 μg/mL BPB compared to BPA. 2,6-Dichlorophenol (2,6-DCP) was used as model uncoupling agent. A time-dependent mechanism of mitochondrial interference was also highlighted.	Molecules Vol.25 Issue 21	10.3390/molecules25215185	33171786	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	5-100 μg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1997	R. S. Dos Santos, R. M. Medina-Gali, I. Babiloni-Chust, L. Marroqui and A. Nadal	2022	In Vitro Assays to Identify Metabolism-Disrupting Chemicals with Diabetogenic Activity in a Human Pancreatic β-Cell Model	There is a need to develop identification tools for Metabolism Disrupting Chemicals (MDCs) with diabetogenic activity. Here we used the human EndoC-βH1 β-cell line, the rat β-cell line INS-1E and dispersed mouse pancreatic islets to identify MDCs with diabetogenic activity. Bisphenol A (BPA) and Bisphenol S (BPS) were used as reference MDCs. Bisphenol A (BPA) and Bisphenol S (BPS) were used as reference MDCs. Bisphenols A (BPA) and bisphenol S (BPS) have a similar chemical structure, exert estrogenic activity via ERα and ERβ, impair glucose-stimulated insulin secretion (GSIS), induce pancreatic β-cell dysfunction and diabetes in rodents, and increase the risk of developing type 2 diabetes (T2D) in humans. Regarding cell viability, BPA and "BS" increased cell death as previously observed. Their mode of action involved the activation of estrogen receptors and PPARγ, respectively. ROS production was a consistent key event in BPA and "BS"-treated cells. None of the other MDCs tested modified viability or ROS production. Conclusions: Exposing EndoC-βH1 cells to a human β-cell model for testing diabetogenic MDCs. Optimization of the two methods proposed here could be incorporated into a set of protocols for the identification of MDCs.	Int J Mol Sci. 2022 May 1;23(9):5040.	10.3390/ijms23095040	35563431	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1 pM−1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_1998	R. S. Dos Santos, I. Babiloni-Chust, L. Marroqui and A. Nadal	2022	Screening of Metabolism-Disrupting Chemicals on Pancreatic α-Cells Using In Vitro Methods	Metabolism disrupting chemicals (MDCs) are endocrine disruptors with stereogenic and/or diastereogenic action. There is mounting evidence linking exposure to MDCs to increased susceptibility to diabetes. Despite the important role of glucagon in glucose homeostasis, there is little information on the effects of MDCs on α-cells. Furthermore, there are no methods to identify and test MDCs with the potential to alter α-cell viability and function. Here, we used the mouse α-cell line α-TC1-9 to evaluate the effects of MDCs on cell viability and glucagon secretion. We tested six chemicals at concentrations within human exposure (from 0.1 pM to 1 µM). Bisphenol A (BPA) and bisphenol S ("BS") were used as reference MDCs. Bisphenols A (BPA) and bisphenol S ("BS") have a similar chemical structure, exert estrogenic activity via ERα and ERβ, impair glucose-stimulated insulin secretion (GSIS), induce pancreatic β-cell dysfunction and diabetes in rodents, and increase the risk of developing type 2 diabetes (T2D) in humans. Concerning GSIS, "BS" increased insulin secretion while BPA reduced secretion. While BPA decreased ROS, suggesting that this chemical could be a "new" diabetogenic agent. Our results indicate that the EndoC-βH1 cell line is a suitable human β-cell model for testing diabetogenic MDCs. Optimization of the two methods proposed here could be incorporated into a set of protocols for the identification of MDCs.	Int J Mol Sci. 2022 Dec 23;24(1):231.	10.3390/ijms24010231	36613676	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.1 pM−1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成根拠評価への追加。当該物質評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_1999	C. F. Durán, M. El Heiba, A. Wielnicka, B. Gyllfy, S. Aires, A. Escanilla, S. Cross, P. Clausella, J. Lachuer, M. Diab-Assaf, S. E. Ghayad, B. Ferrara, V. Cavaillès, Y. Maguer-Satta and F. A. Cohen	2020	Long-Term Exposure of Early-Transformed Human Mammary Cells to Low Doses of Benzo[a]pyrene and/or Bisphenol A Enhances Their Cancerous Phenotype via an AhR/GPR30 Interplay	It is of utmost importance to decipher the role of chronic exposure to low doses of environmental carcinogens on breast cancer progression. The early-transformed triple-negative human mammary MCF10AT1 cells were chronically (60 days) exposed to low doses (10−10 M) of Benzo[a]pyrene (B[a]P), a genotoxic agent, and/or Bisphenol A (BPA), an endocrine disruptor. Our study revealed that exposed MCF10AT1 cells developed, in a time-dependent manner, an atypical phenotype characterized by (a) increase in cancerous properties, (anchorage independent growth and stem like phenotype). Co-exposure of MCF10AT1 cells to B[a]P and BPA led to a significant increase in the cancerous properties of MCF10AT1 cells. Mechanistically, we demonstrated that the cancerous phenotype induced by B[a]P and/or BPA is dependent on the G protein coupled receptor 30 (GPR30) by which chronic and low doses exposure of B[a]P and/or BPA increase the cancerous properties of MCF10AT1 cells. Also, a more aggressive subclone (Exp) was isolated from exposed MCF10AT1 cells and characterized by a mesenchymal phenotype, enhanced migration, and invasion properties. Experiments using AhR or GPR30 antagonists, siRNA strategies, and RNAseq analysis led us to propose a model in which AhR signaling plays a "driver role" in the AhR/GPR30 cross-talk in mediating long-term and low-dose exposure of B[a]P and/or BPA. Retrospective analysis of two independent breast cancer cohorts revealed that the AhR/GPR30 mRNA expression signature resulted in poor breast cancer prognosis, in particular in the ER-negative and the triple-negative subtypes. Finally, the study identified targeting AhR and/or GPR30 as hit-specific antagonistic as a strategy capable of inhibiting carcinogenesis associated with chronic exposure to low doses of B[a]P and BPA in MCF10AT1 cells. Altogether, our results indicate that the engagement of both AhR and GPR30 functions, in particular in an ER-negative/triple-negative context of breast cells, favors tumor progression and leads to poor prognosis.	Front Oncol. 2020 May 29;10:712.	10.3389/fonc.2020.00712	32670863	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10（-10）M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2000	P. Dong, G. Ye, X. Tu, Y. Luo, W. Cui, Y. Ma, L. Wei, X. Tian and Q. Wang	2022	Roles of ERRα and TGF-β signaling in stemness enhancement induced by 1 μM bisphenol A exposure via human neural stem cells	Bisphenol A (BPA) is a common industrial chemical widely used to produce various plastics and is known to impair neural stem cells (NSCs). However, the effects of low- dose BPA exposure on the stemness maintenance and differentiation fate of NSCs remain unclear in the relevant fields. The present study demonstrated that 1 μM BPA promoted human NSC proliferation and stemness, without significantly increasing apoptosis. The Chip-seq experiments demonstrated that both the cell cycle and the TGF-β signaling pathway were accelerated after treatment with 1 μM BPA. Subsequently, estrogen-related receptor α (ERRα) gene knockout cell lines were established by CRISPR/Cas9 technology to investigate the potential mechanisms underlying the promotion of stemness induced by 1 μM BPA. The results revealed that ERRα mediated the TGF-β1 signaling pathway, including the downstream factors Activin A receptor, type I (ACVR1) and serine/threonine kinase 6 (Smad6). In conclusion, the stemness of NSCs could be maintained by BPA at 1 μM through the activation of the ERRα and TGF-β1 signaling pathways and could increase the differentiation of NSCs into neurons. The present research further clarified the mechanism of BPA toxicity on NSCs from the novel perspective of ERRα and TGF-β1 signaling pathways regulated by BPA and provided insights into potential novel methods of prevention and therapy for neurogenic diseases.	Exp Ther Med Vol.23 Issue 2 Pages 164	10.3892/etm.2021.11087	35069845	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2001	A. Di Cerdico, G. Gaggi, I. Bucci, B. Ghirardi and A. Di Baldassarre	2023	The Effects of Combined Exposure to Bisphenols and Perfluoroalkyls on Human Perinatal Stem Cells and the Potential Implications for Health Outcomes	The present study investigates the impact of two endocrine disruptors, namely Bisphenols (BPs) and Perfluoroalkyls (PFCs), on human stem cells. These chemicals leach from plastic, and when ingested through contaminated food and water, they interfere with endogenous hormone signaling, causing various diseases. While the ability of BPs and PFCs to cross the placental barrier and accumulate in fetal tissue has been documented, the exact consequences for human development require further elucidation. The present research work explored the effects of combined exposure to BPs (BPA or BPS) and PFCs (PFOS and PFOA) on human placental (Hora) mesenchymal stromal cells, hPSMSCs) and amniotic fluid (AFSCs) derived stem cells. The effects of the xenobiotics were assessed by quantifying cell viability, mitochondrial functionality, and the expression of genes involved in pluripotency and epigenetic regulation, which are crucial for early human development. Our findings demonstrate that extended exposure to BPs and to PFs may alter the biological characteristics of perinatal stem cells and fetal epigenome, with potential implications for health outcomes at birth and in adulthood. Further research is necessary to comprehend the full extent of these effects and their long-term consequences.	Int J Mol Sci. 2023 Oct 9;24(19):15018.	10.3390/ijms241915018	37834465	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2002	P. Deng, M. Tan, W. Zhou, C. Chen, Y. Xi, P. Gao, Q. Wu, Y. Liang, M. Chen, L. Tian, J. Xia, M. Liu, Y. Luo, Y. Li, L. Zhang, L. Wang, Y. Zeng, H. Yi, Z. Yu and Z. Zhou	2021	Bisphenol A promotes breast cancer cell proliferation by driving miR-381-3p-PTTG1-dependent cell cycle progression	Bisphenol A (BPA) is a high-production-volume industrial chemical that facilitates the development of breast cancer. However, the molecular mechanism associated with BPA-induced breast cancer cell proliferation and migration remains elusive. In our study, we exposed MCF-7 cells to different concentrations of BPA (0.1, 1 and 10 μM) for 24, 48, or 72 h. We found that BPA exposure significantly promoted MCF-7 cell proliferation and migration but not invasion. To elucidate the mechanisms, the differentially expressed genes between the BPA and control groups were investigated with the Gene Expression Omnibus (GEO) database through GEO2R, Kyoto Encyclopedia of Genes and Genomics (KEGG) and cellular component analyses demonstrated that the cell cycle was one of the cell cycle pathway in the effects of BPA exposure in MCF-7 cells. Importantly, miR-381-3p with the core/hub phylogram of Cytoscape software coupled with analysis of enriched genes in the cell cycle pathway identified PTTG1 and CDC20 in four hub genes as key targets associated with BPA-induced MCF-7 cell proliferation. Furthermore, BPA exposure significantly downregulated miR-381-3p and upregulated PTTG1 and CDC20 mRNA and protein expression. Dual-luciferase reporter assays revealed that miR-381-3p directly targeted PTTG1 to regulate cell cycle progression. In addition, we confirmed that the increased expression of PTTG1 and BPA exposure was caused by miR-381-3p inhibition. Moreover, we verified that miR-381-3p inhibition was low and reversed, correlated with PTTG1 expression in breast cancer tissues. Together, these findings demonstrate that BPA promotes high PTTG1 expression and alters the cell cycle to enhance MCF-7 cell proliferation by inhibiting miR-381-3p expression.	Chemosphere. 2021 Apr;268:129221.	10.1016/j.chemosphere.2020.129221	33352510	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1、1、10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2003	G. Del Favero, J. Berger, L. Pahn, C. Fellinger, M. Mattewa, A. Szabadi, A. S. Fernandes, N. Saraiva, C. Schröder and D. Marko	2024	Short-Term Exposure to Foodborne Xenoestrogens Affects Breast Cancer Cell Morphology and Motility Relevant for Metastatic Behavior In Vitro	Breast cancer is highly susceptible to metastasis formation. During the time of disease progression, tumor pathophysiology can be impacted by endogenous factors, like hormonal status, as well as by environmental exposures, such as those related to diet and lifestyle. Next lines of evidence point to a potential risk for foodborne endocrine disruptive chemicals in this respect. However, mechanistic understanding remains limited. At the molecular level, crucial steps toward metastasis formation include cell-structural changes, alteration of adhesion, and reorganization of cytoskeletal proteins involved in motility. Hence, this study investigates the potential of dietary xenoestrogens to impact advanced aspects of breast cancer cell mechanobiology. Using the onset of the metastatic cascade as a model, experiments focused on cell-matrix adhesion, organ migration, and adaptation of cell morphology. Dietary mycoestrogens, alternariol (AOH, 1 μM) and α-zearalenol (α-ZEL, 10 nM), soy isoflavone genistein (GEN, 1 μM), and food packaging plasticizer bisphenol A (BPA, 10 nM) were applied to MCF-7 cells for 72 h. Cell viability, proliferation, and migration were assessed by real-time impedance measurements. Immunofluorescence staining was performed comparing the MCF-7 cell line to the triple-negative breast cancer cells MDA-MB-231. Indeed, the two compounds functionally affected the motility and the adhesion of both cell types. These responses were coherent with rearrangements of the actin cytoskeleton and with the modulation of the expression of integrin β1 and cadherin-13. Mechanistically, metabolic-dynamic simulations confirmed a potential interaction with fragments of the α1 and β1 integrin subunits. In sum, dietary xenoestrogens posed effective in modifying the motility and adhesion of breast cancer cells, as predictive risk points for metastatic behavior in vivo. These effects were measurable after short incubation times (1 or 8 h) and contribute to shed novel light on the activity of compounds with hormonal-mimicry potential in breast cancer progression.	Chem Res Toxicol. 2024 Oct 21;37(10):1634-1650.	10.1021/acs.chemrestox.4c00061	39262136	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2004	S. C. de Aguiar Greca, I. Kyriva, R. Pink, H. Ranveer, D. Grammatopoulos, E. Silva and E. Karteris	2020	Involvement of the Endocrine-Disrupting Chemical Bisphenol A (BPA) in Human Placentation	MACROMOLECULES: Endocrine-disrupting chemicals (EDCs) are environmental chemicals/toxicants that humans are exposed to, interfering with the action of multiple hormones. Bisphenol A (BPA) is classified as an EDC and is widely used in the manufacture of polycarbonate plastics and epoxy resins. Exposure to BPA has been associated with the molecular progression of diseases such as obesity, metabolic syndrome, and hormone-regulated cancers. In the present study, we examined the effects of physiologically relevant doses of BPA in vitro, METHODS: BPA (Sigma-Aldrich), ethinylestradiol (EE2), and bisphenol F (BPF) using human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM). Cardiac parameters were evaluated using microelectrode array (MEA) technology and live cell imaging. Cytotoxicity was assessed by lactate dehydrogenase (LDH) release and cell viability assays. Apoptosis was evaluated by caspase 3/7 activity and immunofluorescence staining. Mitochondrial depolarization was quantified, and mitochondrial membrane potential was assessed using tetramethylrhodamine methyl ester (TMRM). Cardiomyocyte structure was investigated by immunofluorescence staining of α-actinin. Calcium transient dynamics (CTD) of BPA + BPF + EE2. Cardiomyocyte physiology was largely unaffected by BPA. BPA-induced effects were exaggerated when coadministered with an L-type calcium channel (LTCC) antagonist or E2, and reduced when coadministered with an LTCC agonist or an estrogen receptor alpha antagonist. E2-induced effects were not exaggerated by coadministration with an LTCC antagonist. Although the observed cardiac effects of E2 and BPA were similar, a few distinct differences suggest that these chemicals may act in part through different mechanisms. hiPSC-CM are a useful model for screening cardiotoxic chemicals; nevertheless, the described findings should be validated using a more complex ex vivo and/or in vivo model.	J Clin Med. 2020 Feb 3;9(2):405.	10.3390/jcm9020405	32028606	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	3 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2005	O. S. Davis, G. L. M. Scandlyn, E. A. Potestio, C. Robinson, K. D. Hickey, M. Ross and L. A. Favetta	2025	Impact of BPA and its analogs on sperm hyperactivity, acrosome reaction, epigenetic profiles and in vitro embryo development	Bisphenols, particularly BPA, are ubiquitous environmental contaminants known to affect male reproductive health. However, their specific impacts on sperm function and subsequent embryo development remain understudied especially for BPA's commonly used replacements, BPS and BPF. This study investigated the effects of short sperm exposure to BPA, BPS, and BPF on fertilization capacity and embryo development using a bovine in vitro fertilization (IVF) model. Sperm were exposed to 0.05 mg/mL of BPA, BPS, or BPF during capacitation and fertilization. Sperm motility, viability, and acrosome integrity were assessed using computer-assisted sperm analysis and flow cytometry, while fertilization and embryo development were evaluated up to Day 8. Short exposure to BPA, BPS, and BPF had no significant effect on fertilization rates or embryo development rates, and blastocysts on Day 8. However, sperm exposed to BPA showed a significantly increased sperm hyperactivity, and BPS decreased acrosome reaction levels ($p < 0.05$). Cleavage and blastocyst rates were also notably decreased in embryos derived from BPS-exposed sperm ($p < 0.05$). Furthermore, blastocysts produced from BPA, BPS and BPF treated sperm all had significantly lower cell counts and increased DNA fragmentation ($p < 0.05$). Although no statistically significant changes in mRNA levels were observed, this study highlights some of the detrimental effects of bisphenols on bovine sperm and subsequent embryo development, with potential implications for human reproductive health.	Mol Cell Endocrinol Vol.604 Pages 112555	10.1016/j.mce.2025.112555	40252911	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.05 mg/mL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2006	M. D'Almeida, O. Sire, S. Lardjane and H. Dusel	2020	Development of a new approach using mathematical modeling to predict cocktail effects of micropollutants of diverse origins	A wide variety of micropollutants (MP) of diverse origins is present in waste and surface waters without knowing the effect of their combination on ecosystems and human. The impact of chemical mixtures is poorly documented and often limited to binary mixtures using MP of the same category. Knowing that it is not realistic to test every possible combination found in mixtures, we aimed to develop a new method helping to predict cocktail effects of MP of diverse origins. The approach combines experimental designs, mathematical modeling, and optimization algorithms. Single effects of 20 MP were first characterized by concentration at which 20% Effective Concentration (EC20) or 20% (EC/IC)-of their maximal effect on bacterial growth was observed. Using an Ecological Structure Activity Relationship (ECOSAR), relevant complex mixtures were then binned. Multiple linear regression was applied to response surface modeling in order to evaluate and visualize the influence of the different MP in mixtures and their potential interactions. The comparison of predicted and experimental toxicities of validation mixtures proved the efficiency of the approach. Then, the most relevant mixtures identified by ECOSAR were experimentally tested and successfully modeled. The cocktail effect in mixtures of 5 MP was investigated by considering mixture/effect response surface reduction. It was deduced that there was a neutrality/synergism between bisphenol A and isoniazid. In conclusion, our approach is relevant to predict complex mixture of MP the combinations likely involved in cocktail effects. The proposed methodology coupling experimental data acquisition and mathematical modeling can be applied to all kind of relevant bioassays using lower concentrations of MP. Situations at high ecological risk and potentially hazardous for humans will then be identified, which will allow to improve legislation and policies.	Environ Res. 2020 Sep;188:109897.	10.1016/j.envres.2020.109897	32846655	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2007	D. Crump, T. Shrim, S. Chiu and J. M. O'Brien	2021	In Vitro Screening of 21 Bisphenol A Replacement Alternatives: Compared with Bisphenol A, the Majority of Alternatives Are More Cytotoxic and Dysregulate More Genes in Avian Hepatocytes	An adaptive in vitro screening approach was used to determine the effects of 21 bisphenol A (BPA) alternatives. Cytotoxicity and dysregulation of genes associated with estrogen response and other toxicologically relevant pathways evoked by these alternatives were compared with BPA. Most of the BPA alternatives (16/21) were more cytotoxic than BPA in chicken embryonic hepatocytes, with cytotoxicity in cell viability tests associated with chemical structure and the log octanol-water partition coefficient (logP) values. A negative linear relationship ($r^2 = -0.705$; $p < 0.001$; $n = 18$) was observed between logP and the log median lethal concentration (LC50) values. Bisphenol AF (BPAF) was the most cytotoxic alternative tested, with a mean LC50 value of 0.3 μM (approximately 10 times more cytotoxic than BPA in this assay). This overall approach shows promise for use as a screen for hazard-based prioritization of BPA replacement alternatives and to identify chemicals that may be less harmful and for more sophisticated toxicity testing. Environ Toxicol Chem 2021;40:2624–2633. © 2021 Her Majesty the Queen in Right of Canada Environment Toxicology and Chemistry © 2021 SETAC. Reproduced with the permission of the Minister of Environment and Climate Change Canada.	Environ Toxicol Chem. 2021 Jul;40(7):2026-2033.	10.1002/etc.5032	33683738	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2008	J. Cronhwall, S. Sydden and E. Atlas	2025	The obesogenic effects of Bisphenol A and its analogues are differentially regulated via PPARγ transactivation in mouse 3T3-L1 cells	Exposure to environmental pollutants with obesogenic activity is being recognized as one of the contributing factors to the obesity epidemic. Bisphenol A (BPA) has been shown to stimulate adipogenesis in both human and mouse preadipocytes, to increase body weight and affect lipid metabolism in animal and epidemiological studies. Regulatory actions and public concern has prompted industry to replace BPA with other structurally similar bisphenol analogues. However, the obesogenic activity of these BPA analogues is largely unknown. In this study, we investigated the adipogenic activity of BPA and 11 of its analogues (BPA analogues) activity relative to BPA. 3T3-L1 cells were treated with increasing concentrations of BPA and replacements and mRNA expression of the mature adipocyte markers fatty acid binding protein 4 (Fabp4), perilipin (Plin) Diacylglycerol O-acyltransferase 2 (Dgat2) and peroxisome proliferator activated receptor (Pparγ) and lipid accumulation were assessed. In addition, a luciferase reporter assay for PPARγ transactivation was employed to investigate mechanism of action. Our results show that BPC, BPG BADGE, BPE BPZ and TDSG, were the most adipogenic Bisphenols, as shown by an robust increase in lipid accumulation and mRNA expression of adipogenic marker. BPG MPP, BPC BPAIB, TDSG and DB increased PPARγ transcriptional activity. Despite its ability to activate PPARγ in the transcriptional assay DB did not affect adipogenesis in this cell model.	Toxicol In Vitro. 2025 Apr;104:106009.	10.1016/j.tiv.2025.106009	39842701	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1-20 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2009	J. C. Carton, G. Mattes, B. Charley, J. Liu, B. Vallarat, L. Everett, E. Atlas, M. J. Meier, A. Williams and C. L. Yauk	2024	A 50-gene biomarker identifies estrogen receptor-modulating chemicals in a microarray compendium	High-throughput transcriptomic (HTTr) profiling has the potential to rapidly and comprehensively identify molecular targets of environmental chemicals that can be linked to adverse outcomes. We describe here the construction and characterization of a 50-gene expression biomarker designed to identify estrogen receptor (ER) active chemicals in HTTr datasets. Using microarray compendium, the genes in the biomarker were selected for their consistent and reproducible response to 17β-estradiol (E2) and ER antagonist fulvestrant (FULV) co-exposures in MCF-7 cells, and their lack of response to androgen receptor agonist and antagonist treatments. ER50 classifier performance was evaluated in a training set of 1,167 chemicals and a test set of 1,000 chemicals from the ToxCast/Tox21 phase 1 library. The biomarker was evaluated as a predictive tool using the Running Fisher algorithm by comparison to annotated previous microarray datasets including those evaluating the transcriptional effects of hormones and chemicals in MCF-7 cells. Depending on the reference dataset used, the biomarker had a predictive accuracy for activation of up to 96%. To demonstrate applicability for HTTr data analysis, the biomarker was used to identify ER activators in a set of 55 chemicals that are considered potential Bisphenol A (BPA) alternatives. Assessed at six 24 h concentrations in MCF-7 cells and analyzed by full-genome TempO-Seq, Using benchmark dose (BMD) modeling, the biomarker genes stratified the ER potency of BPA alternatives consistent with previous studies. These results demonstrate that the ER biomarker can be used to accurately identify ER activators in transcriptomic profile data derived from MCF-7 cells.	Chem Biol Interact. 2024 May 1:394:110952.	10.1016/j.cbi.2024.110952	38570061	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2010	S. A. Cortés-Ramírez, A. M. Salazar, M. Sordo, P. Ostrosky-Wegman, M. Morales-Pacheco, M. Cruz-Burgos, A. Losada-García, G. Rodríguez-Martínez, I. González-Ramírez, K. Vaquiz-ue-Santillán, V. González-Covarrubias, V. Maldonado-Lagunas and M. Rodríguez-Dorantes	2023	Transcriptome-Wide Analysis of Low-Concentration Exposure to Bisphenol A, S, and F in Prostate Cancer Cells	Bisphenol A (BPA) is a ubiquitous synthetic compound used as a monomer in the production of polycarbonate plastics and epoxy resins. Even at low doses, BPA has been associated with the molecular progression of diseases such as obesity, metabolic syndrome, and hormone-regulated cancers due to its activity as an endocrine-disrupting chemical (EDC). Consequently, the use of BPA has been regulated worldwide by different health agencies. BPA structural analogs such as bisphenol S and bisphenol F (BPS and BPF) have emerged as industrial alternatives, but their biological activity in the molecular progression of cancer remains unclear. Prostate cancer (PCa) is a hormone-dependent cancer, and the role of BPA's structural analogs in PCa progression is still controversial. In this work, we use an in vitro model to characterize the transcriptomic effect of low concentration exposure to bisphenol A, S, or F in the two main stages of the disease: androgen-dependent (LNCaP) and metastasic (PC-3). Our findings demonstrated that the low concentration exposure to each bisphenol induced a differential effect over PCa cell lines, which made the relevance of studying the effect of EDC compounds through all the stages of the disease.	Int J Mol Sci. 2023 May 30;24(11):9462.	10.3390/ijms24119462	37298413	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1, 5, and 10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2011	B. L. Cooper, S. Salameh and N. G. Posnack	2024	Comparative cardiotoxicity assessment of bisphenol chemicals and estradiol using human induced pluripotent stem cell-derived cardiomyocytes	Bisphenol A (BPA) is commonly used to manufacture consumer and medical grade plastics. Due to health concerns, BPA substitutes are being incorporated including bisphenol S (BPS) and bisphenol F (BPF) without a comprehensive understanding of their toxicological profile. Previous studies suggest that bisphenol chemicals perturb cardiac electrophysiology in a manner that is similar to 17β-estradiol (E2). We aimed to compare the effects of E2 with BPA, BPF, and BPS using human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM). Cardiac parameters were evaluated using microelectrode array (MEA) technology and live cell imaging. Cytotoxicity was assessed by lactate dehydrogenase (LDH) release and cell viability assays. Apoptosis was evaluated by caspase 3/7 activity and immunofluorescence staining. Mitochondrial depolarization was quantified, and mitochondrial membrane potential was assessed using tetramethylrhodamine methyl ester (TMRM). Cardiomyocyte structure was investigated by immunofluorescence staining of α-actinin. Calcium transient dynamics (CTD) of BPA + BPF + EE2. Cardiomyocyte physiology was largely unaffected by BPA. BPA-induced effects were exaggerated when coadministered with an L-type calcium channel (LTCC) antagonist or E2, and reduced when coadministered with an LTCC agonist or an estrogen receptor alpha antagonist. E2-induced effects were not exaggerated by coadministration with an LTCC antagonist. Although the observed cardiac effects of E2 and BPA were similar, a few distinct differences suggest that these chemicals may act in part through different mechanisms. hiPSC-CM are a useful model for screening cardiotoxic chemicals; nevertheless, the described findings should be validated using a more complex ex vivo and/or in vivo model.	Toxicol Sci. 2024 Mar 26;198(2):273-287.	10.1093/toxsci/kfae015	38310357	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1—1000 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき判定。

引用評価機関
● ：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	単独ばく露試験	適応毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2012	J. C. Cohen, E. R. Cohencur, K. G. Hamett and S. M. Schuh	2021	BPA, BPAF and TMBPF Alter Adipogenesis and Fat Accumulation in Human Mesenchymal Stem Cells, with Implications for Obesity	Bisphenol A (BPA) is an endocrine disrupting chemical used in the production of plastics, and is linked to developmental, reproductive, and metabolic disorders including obesity. Manufacturers have begun using BPA substitutes, such as BPAF and TMBPF, in consumer products labeled as BPA-free. However, the safety of these substitutes is unknown. BPA is commonly found in the lining of food metal cans and in food-contact coatings. Here, we used human female adipose-derived stem cells (hASCs), a type of adult mesenchymal stem cell, to compare the effects of BPA and BPA alternatives on adipogenesis at low cell development in vitro. We focused on two commonly used BPA replacements, bisphenol AF (BPAF) and tetramethyl bisphenol F (TMBPF), monomer of the two-coffee UV-heat contact coating). Human ASCs were differentiated into adipocytes in the presence of vehicle (0.1% DMSO), BPA, BPAF, or TMBPF at 0.1 nM, 1 nM, 10 nM, 0.1 μM, 1 μM, 10 μM, 20 μM, 50 μM, 100 μM, 100 μM, 300 μM, 500 μM, or 900 μM. Treatments were performed in triplicate in 1 and 0.1 mM, or TMBPF (0, 0.02, and 0.1 μM). After differentiation, the cells were stained and imaged to quantify lipid accumulation. Cell viability was measured to quantify the concentration of lipid vesicles and number of developing the cells. Treated cells were also examined for cell viability and apoptosis (programmed cell death) using the respective cellular assays. Dosing to 0.1 BPA at 0.1 μM and BPAF at 0.1 nM, significantly increased adipogenesis and lipid production by 25% compared to control differentiated cells (based on total lipid vesicle number to cell number ratio), whereas higher levels of BPA and BPAF significantly decreased adipogenesis by ~2-3000. All tested doses of TMBPF significantly reduced adipogenesis, and lipid production by 50–80%, likely at least partially through toxic effects on stem cells, as viable cell numbers decreased and apoptosis levels increased throughout differentiation. These findings indicate that low, environmentally relevant doses of BPA, BPAF, and TMBPF have significant effects on fat cell development and lipid accumulation, with TMBPF having non-monotonic, anti-adipogenic effects. These and other recent results may provide a potential cellular mechanism between exposure to bisphenols and human obesity, and underscore the likely impact of these chemicals on fat development in vivo.	Int J Mol Sci. 2021 May 19;22(10):5363.	10.3390/ijms22105363	34069744	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0、0.1、1 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2013	A. Citarella, Z. M. Benhamé, L. Coppola, C. Sabato, T. M. Aiello, E. Visentini, V. M. Bimonte, G. Catanzaro, N. Pediconi, A. Fabi, S. Migliaccio, M. Milella, R. Bei, E. Ferretti and A. Po	2025	Bisphenol A drives nuclear factor-kappa B signaling activation and enhanced motility in non-transformed breast cells	Bisphenol A (BPA) is a chemical compound found in a wide range of everyday consumer products, resulting in human exposure. BPA has been described as an endocrine disruptor, affecting different systems of the human body. Notably, carcinoma levels of BPA have been detected in human mammals, including plasma and milk. BPA exposure has been associated with the development of breast cancer, and the increase in breast cancer incidence prompted us to investigate the effects of BPA in MCF10A, a model of non-transformed mammary epithelium. Cells were treated with 10 nM BPA for 24 h to capture early molecular alterations preceding phenotypic transitions. Comprehensive transcriptomic analyses were conducted to differentially expressed genes and enriched signaling pathways. Subsequent validation focused assessment of cytoskeletal release, protein expression, immunofluorescence for subcellular localization of Nuclear Factor-Kappa B (NF-κB), and evaluation of actin cytoskeletal organization. Transcriptome analysis revealed enrichment in pathways related to cytoskeleton remodeling, cell adhesion, and NF-κB signaling. Functional assays confirmed increased cell migration and invasion following BPA exposure. The inhibition of NF-κB effectively mitigated BPA-induced effects, including augmented cell motility, nuclear translocation of NF-κB, and cytoskeletal rearrangements. Notably, inhibition of the Mitogen-Activated Protein Kinase (MAPK) pathway, and to a lesser extent of the JNT pathway, counteracted BPA-induced NF-κB activation and the associated increase in cell motility. In conclusion, we show that nanomolar concentration of BPA induces significant changes in the molecular setting and behavior of non-transformed breast cells, activating NF-κB signaling that in turn controls inflammation, cell cycle, proliferation and cell motility. Our findings indicate that nanomolar concentrations of BPA can induce significant molecular and behavioral changes in non-transformed breast epithelial cells. These results contribute to a deeper understanding of how environmental pollutants like BPA may perturb breast epithelial cell function and potentially contribute to carcinogenesis.	Environ Pollut. 2025 Jul 1:376:126422.	10.1016/j.envpol.2025.126422	40360080	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2014	R. Qnar and M. Nazıroğlu	2025	Bisphenol A Induces Neuronal Apoptosis and Oxidative Stress Through TRPV4 Channel Signaling Pathways: Protective Role of Alpha-Lipoic Acid	Bisphenol A (BPA), an environmental toxin, exerts adverse effects by increasing mitochondrial (mROS) and intracellular (ROS) reactive oxygen species, apoptosis, and Ca2+/J reflex in neurological diseases. However, antioxidants can mitigate these detrimental effects. This study aimed to investigate the protective role of antioxidant alpha-lipoic acid (ALA) against BPA-induced TRPV4 channel stimulation, oxidant, and apoptotic changes in SH-SY5Y neuronal cells. Five experimental groups were established (control, ALA, BPA, BPA + ALA, and BPA + TRPV4 antagonist (ruthenium red; RuR). BPA increased intracellular Ca2+/J influx and TRPV4 current density, while BPA- and TRPV4 agonist (GSK1016790A)-induced TRPV4 stimulations were decreased by ALA and RuR. BPA-induced increases in intracellular ROS, mROS, JH2O2, apoptotic markers (caspase-3, -9, and -7), Δψ(-), and cell death were reduced by ALA and RuR treatment. Conversely, BPA-induced reductions in cell viability, glutathione, and glutathione peroxidase levels were restored following treatment. In summary, ALA attenuated BPA-induced excess Ca2+/J influx, ROS/J accumulation, apoptosis, and oxidative neurotoxicity via TRPV4 inhibition. Therefore, ALA may offer protection against BPA-induced neuronal cell death associated with oxidative neurotoxicity.	Environ Toxicol. 2025 Nov;40(11):1261-1276.	10.1002/tox.24541	40396745	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2015	I. Cimmino, F. Oriente, V. D'Esposito, D. Liguoro, P. Liguoro, M. R. Ambrosio, S. Cabaro, C. D'Andrea, F. Beguinot, P. Formisano and R. Valentino	2019	Low-dose Bisphenol-A regulates inflammatory cytokines through GPR30 in mammary adipose cells	The dramatic rise in obesity and metabolic syndrome can be related, at least in part, to environmental chemical factors such as Bisphenol A (BPA). In this study, we aimed to understand the effects of low-dose Bisphenol A on the human mature adipocytes and stromal vascular fraction (SVF) cells, obtained from subcutaneous mammary adipose tissue of overweight female patients, undergoing surgical mammary reduction. 24 and/or 48 h exposure to 0.1 nM BPA induced a significant increase in the expression and release of IL-6, IL-8, MCP-1, and TNF-α in mature adipocytes and SVF cells. Similar results were obtained with the selective GPR30 agonist G1. Moreover, 48 h BPA treatment increased 3D SPHERE levels more than two-fold both in mature adipocytes and SVF cells. These effects were not observed with 10 nM BPA and were prevented by G15, a GPR30-selective antagonist. As a result of BPA GPR30 signaling activation, fatty acid synthase (FASN) and leptin mRNA levels were significantly higher upon BPA exposure ($P < 0.05$) in mature adipocytes, with an opposite effect on adiponectin (ADIPOQ). In addition, an increase in SVF cell proliferation and CRE-Luc2 stimulation was observed, compared to untreated cells. 0.1 nM was the set of all these effects. Interestingly, the action of BPA on SVF cell growth was mimicked by IL-6 treatment and was reverted by incubation with anti-IL6 antibodies. All these data suggest that BPA at 0.1 nM, a non-toxic, lower concentration than environmental exposure, increases the expression of pro-inflammatory cytokines via GPR30 both in mature mammary adipocytes and in SVF cells with a possible involvement of IL-6.	J Mol Endocrinol. 2019 Nov;63(4):273-283.	10.1530/jme-18-0265	31546233	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2016	B. Qiji and K. Yildizhan	2020	Resveratrol diminishes bisphenol A-induced oxidative stress through TRPM2 channel in the mouse kidney cortical collecting duct cells	Bisphenol A (BuPh-H) is a latent danger that threatens our health, which we frequently exposure in our modern life (e.g. the widespread use of drinking water in plastic pot bottles). But the BuPh-H induced transient receptor potential melastatin 2 (TRPM2)-mediated oxidative stress and apoptosis in these cells has not been studied yet. Calcium (Ca2+) plays an important role in a versatile intracellular signal transduction that works over a wide range to regulate oxidative stress processes. TRPM2 is activated under oxidative stress and is highly permeable to Ca2+. Ca2+ is a signaling mechanism in a variety of cells, contributing many cellular functions, including cell death. Resveratrol (RES), which belongs to the polyphenol group, acts as an antioxidant, eliminating cellular oxidative stress, and increasing the body's resistance to diseases. The current study aimed to investigate the protective effects of RES against BuPh-H-induced TRPM2 activation and cell death in mouse kidney cortical collecting duct cells. The cell viability was measured via cell counting kit-8 (CCK-8). BuPh-H (100 μM) for 6 and/or 24 h. RES. Intracellular Ca2+/J concentrations and TRPM2 channel currents were high in BuPh-H-treated cells, but decreased with resveratrol treatment. In addition, BuPh-H induced mitochondrial membrane depolarization, reactive oxygen species (ROS) / caspase-3, caspase-9 and apoptotic values were decreased by the resveratrol treatment. In conclusion, resveratrol protected cells from BuPh-H induced oxidative damage. In this study, we characterized TRPM2 channel mediates this protective effect of resveratrol.	J Recept Signal Transduct Res Vol.40 Issue 6 Pages 570-583	10.1080/10799893.2020.1769657	32515636	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2017	Y. G. Choi, W. S. Choi, J. Y. Song, Y. Lee, S. H. Lee, J. S. Lee, S. Lee, S. R. Choi, C. H. Lee and J. Y. Lee	2023	Antiinflammatory effect of the ethanolic extract of Korean native herb Potentilla rugulosa Nakai in Bisphenol-a-stimulated AS49 cells	Potentilla rugulosa Nakai (P. rugulosa) is a perennial herb in the Rosaceae family and found in the Korean mountains. Previously, our findings demonstrated that P. rugulosa contains numerous polyphenols and flavonoids exhibiting important antioxidant and anti-obesity bioactivities. Bisphenol A (BPA) is a xenoestrogen that can cause chronic exposure to produce pulmonary inflammation in humans. However, the mechanisms underlying BPA-induced inflammation remain to be determined. The aim of this study was to examine whether ethanolic extract of P. rugulosa exerted an inhibitory effect on BPA-induced inflammation utilizing an adenocarcinoma human alveolar basal epithelial cell line (A549). The P. rugulosa extract inhibited BPA-mediated cytotoxicity by reducing levels of reactive oxygen species (ROS). Further, P. rugulosa extract suppressed the upregulation of various pro-inflammatory mediators induced by activation of the nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB) and mitogen-activated protein kinase (MAPK) signaling pathways. In addition, inhibition of the BPA-induced NF-κB and MAPK signaling pathways by P. rugulosa extract was associated with the suppression of the receptor for advanced glycation end products (RAGE) and cyclooxygenase-2 (COX-2) and stress-activated protein kinase/c-Jun N-terminal kinase (SAPK/JNK) was noted. Thus, our findings suggest that the ethanolic extract of P. rugulosa may act as a natural anti-inflammatory therapeutic agent.	J Toxicol Environ Health A. 2023 Oct 18;86(20):758-773.	10.1080/15287394.2023.2240835	37527000	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2018	S. I. Choi, J. S. Lee, S. Lee, W. S. Sin, Y. C. Kim and O. H. Lee	2020	Potentilla rugulosa Nakai Extract Attenuates Bisphenol A-, S- and F-Induced ROS Production and Differentiation of 3T3-L1 Preadipocytes in the Absence of Dexamethasone	Endocrine-disrupting chemicals (EDCs) disrupt the physiological metabolism, thus playing an important role in the development of obesity. EDCs, the so-called 'obesogens', might predispose some individuals to gain weight. This study investigated the effects of bisphenol A (BPA) and its alternatives, BPS and BPF, on adipocyte differentiation and the effects of the leaves of Potentilla rugulosa Nakai extract (PR) on a functional food that prevents obesity induced by BPA and its alternatives. Treatment with BPA, BPS, and BPF (0.1–10 μM) significantly increased the accumulation of lipid droplets and triglyceride (TG) content ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively) in 3T3-L1 cells exposed to dexamethasone (DEX). However, PR ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively) suppressed the BPA-, BPS-, and BPF-induced increases in TG content in 3T3-L1 cells. Furthermore, PR significantly ($p < 0.05$) reduced the BPA-, BPS-, and BPF-induced increases in the expression of adipogenic transcription factors (CCAAT/enhancer-binding protein-alpha, peroxisome proliferator-activated receptor-gamma, and adipocyte protein 2) was reduced by PR. Additionally, PR significantly ($p < 0.05$) reduced the BPA-, BPS-, and BPF-induced increases in the mRNA and protein levels, as demonstrated through reverse transcription-polymerase chain reaction and western blot assays. Taken together, the results reveal that adipocyte differentiation can be induced by obesogens, and PR can alleviate them. Therefore, PR can alleviate them alternatives in the absence of DEX.	Antioxidants (Basel). 2020 Jan 28;9(2):113.	10.3390/antiox9020113	32012803	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1～10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2019	S. I. Choi, H. Y. Kwon, K. Han, X. Men, Y. E. Choi, G. W. Jang, K. T. Park, J. Han and O. H. Lee	2021	Environmental obesogens (bisphenols, phthalates and parabens) and their impacts on adipogenic transcription factors in the absence of dexamethasone in 3T3-L1 cells	Endocrine-disrupting chemicals (EDCs) are exogenous compounds that are capable of blocking or mimicking the action of biodentical hormones. Obesogenic EDCs, commonly called obesogens, play an important role in adipogenesis. This study was carried out to determine the effects of select obesogens and their alternatives on adipogenesis in 3T3-L1 cells under dexamethasone (DEX)-free conditions. Preadipocytes were treated with a cocktail of 3-isobutyl-1-methylxanthine (IBMX) and insulin in which one obesogen (ie., bisphenol A (BPA) or its analogs BPS and BPF; dibutyl phthalate (DBP) or its alternatives Di (2-ethylhexyl) terephthalate or various parabens) had been added. A mixture containing IBMX, insulin, and DEX, which constitutes the typical hormonal cocktail required for adipocyte differentiation, was used as the control against which the other groups were measured. The differentiation of preadipocytes was evaluated by measuring the lipid accumulation and triglyceride (TG) content. Exposure to BPA, BPS, and BPF (0.1–10 μM) significantly ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively) increased the expression of adipogenic transcription factors (CCAAT/enhancer-binding protein-alpha, peroxisome proliferator-activated receptor-gamma, and adipocyte protein 2) was reduced by PR. All of BPA, BPS, or BPF activities in mRNA and protein levels, as demonstrated through reverse transcription-polymerase chain reaction and western blot assays. Taken together, the results reveal that adipocyte differentiation can be induced by obesogens, and PR can alleviate them alternatives in the absence of DEX.	J Steroid Biochem Mol Biol Vol.214 Pages 105994	10.1016/j.jsbmb.2021.105994	34481040	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	20 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2020	N. Cho, D. M. Jang, E. M. Kim and K. K. Kim	2024	Establishment of a stress granule reporter system for evaluating in vitro colon toxicity	Exposure to toxic molecules from food or oral medications induces toxicity in colon cells that cause serious human diseases; however, in vitro monitoring systems for colon cell toxicity are not well established. Stress granules are membraneless foci that form in cells exposed to stress. When cells sense toxic environments, they acutely and systemically promote stress granule formation with the G3BP1 protein activating protein binding protein 1 (G3BP1) acting as a core component to protect them mRNA from chemical degradation. Here, we knocked in green fluorescent protein (GFP)-coding sequences into the C-terminal region of the G3BP1 gene in human colon cells (HCT116) using CRISPR/Cas9 genome editing technology to establish a stress granule reporter system for evaluating colon cell toxicity. Treatment with sodium arsenite (SA) demonstrated the formation and dissociation of stress granules in G3BP1-GFP-expressing colon cells, through real-time monitoring using a fluorescence microscope. Furthermore, we established the toxicity monitoring system in the established colon cell line by observing stress granule formation following exposure to dihydroxyacetone, bisphenol A, and sorbitol. Taken together, we established a stress granule reporter system in a colon cell line, providing a novel assessment for the real-time monitoring of colon toxicity in response to various chemicals.	Anim Cells Syst (Seoul) Vol.28 Issue 1 Pages 315-325	10.1080/19768354.2024.2364673	38895161	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	100, 300, 500, 900 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2021	C. H. Chiu, S. H. Sun, Y. J. Yao, Y. Chuang, Y. T. Lee and Y. J. Lin	2025	Concentrations, composition profiles, and in vitro-in silico-based mixture risk assessment of bisphenol A and its analogs in plant-based foods	The substitution of bisphenol A (BPA) with structurally similar analogs has raised concerns due to their comparable estrogenic activities. Considering the high consumption of plant-based foods, assessing the risks posed by bisphenols (BPs) in such dietary sources is essential. However, limited exposure and animal toxicological data on BP analogs hinder comprehensive risk assessment. This study investigated 16 BPs in 72 plant-based foods from Taiwan and reviewed their dietary exposure across age groups. High-throughput toxicokinetic modeling was used to convert in vitro ToxCast estrogen receptor (ER) bioactive concentrations into equivalent human oral doses, enabling in vitro-in silico-based risk characterization. BPA was detected in 19 % of samples, with concentrations ranging from 0.0001 to 0.0016 μg/g. Bisphenol AF (BPAF) was frequently detected (14 %), while BPS was detected, and most samples (88.9 %) contained detectable concentrations. Total concentrations of the 16 BPs (Σ16BPs) ranged from 0.001 to 0.021 μg/g (median: 0.002 μg/g), with BPS being the most predominant (57 % of the mean Σ16BP concentrations), followed by bisphenol S (19 %) and 4,4-bisphenol F (7 %). In vitro-in silico-derived PODs were comparable to or even more protective than in vivo-derived derived PODs. For most population groups, combined exposure to multiple BPs from plant-based foods is generally not a risk concern for 50 % safety confidence, although potential concerns in acute case scenarios cannot be excluded. This study advances the understanding of the dietary risks associated with BP mixtures and illustrates the potential of in vitro-in silico approaches for assessing human health risks from environmental contaminants.	Environ Int. 2025 Jan;195:109229.	10.1016/j.envint.2024.109229	39740268	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2022	Y. W. Chiang, C. H. Su, H. Y. Sar, S. P. Chen, C. J. Chen, W. Y. Chen, C. C. Chang, C. M. Chen and Y. H. Kuan	2022	Bisphenol A induced apoptosis via oxidative stress generation involved Nrf2/HO-1 pathway and mitochondrial dependent pathways in human retinal pigment epithelium (ARPE-19) cells	Bisphenol A (BPA) is an estrogen-like compound, and an environmental hormone, that is commonly used in daily life. Therefore, it may enter the human body through food or direct contact, causing BPA residues in blood and urine. Because most studies focused on the analysis of BPA in reproductive cells or tissues, regarding evidence the effect of BPA on human retinal pigment epithelium (HRPE-19) cells unavailable. Accordingly, the present study investigated the cytotoxicity of BPA in HRPE-19 cells. The results revealed that BPA significantly decreased cell viability in a dose- and time-dependent manner. Moreover, the production of ROS was increased. Then the mitochondrial membrane potential was altered. BPA changed in mitochondrial membrane potential led to the release of cytochrome C, which activated caspase 9 to promote downstream caspase 3 leading to cytotoxicity. The nuclear factor (erythroid-derived 2)-like 2 (Nrf2) and heme oxygenase 1 (HO-1) pathway play a major role in age-related macular degeneration. Our results showed that expression of HO-1 and Nrf2 suppressed by BPA. Superoxide dismutase and catalase, which Nrf2 downstream antioxidants, were degraded by BPA. ABP-activated kinase (ASPK), which can regulate the phosphorylation of Nrf2, and the phosphorylation of ASPK expression was reduced by BPA. Finally, BPA-induced ROS generation and cytotoxicity were reduced by N-acetyl-l-cysteine. Taken together, these results suggest that BPA-induced ARPE-19 cells via oxidative stress, which was associated with down-regulated Nrf2/HO-1 pathway, and the mitochondria dependent apoptotic signaling pathway.	Environ Toxicol. 2022 Jan;37(1):131-141.	10.1002/tox.23384	34664771	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2023	W. Chang, Y. Zhou, Y. Xia, Y. Li, R. Zhou, H. Wang, Y. Feng and Y. Wang	2023	Combined effect of polystyrene microplastics and bisphenol A on the human embryonic stem cells-derived liver organoids: The hepatotoxicity and lipid accumulation	Human are exposed to microplastics (MP) via inhalation or ingestion daily and inevitably. The liver is an important target organ of MP. Bisphenol A (BPA) is one of commonly used plastic ions. It is added in plastics, but also generally detected in the biological samples of human beings. However, the combined toxic effect of MP and BPA on human liver is unclear. In this study, a novel 3D in vitro model, the liver organoid (LO) derived from human embryonic stem cells (hESCs), was established to investigate the combined effect of polystyrene MP (PS) and BPA on human liver. The LOs were treated with PS (1 μm, 10 mg/L), BPA (50 μg/L), or co-exposure to PS and BPA for 7 days. The results showed that the LOs could be successfully induced from hESCs by three-step differentiation method, which was regarded the strong supplement. Specifically, Oct4, cytokeratin 8 (CK8), albumin (ALB), and hepatocyte nuclear factor 4 alpha (HNF4α) were highly expressed in the LOs, indicating the successful differentiation as well as progenitors, epithelium and hepatocytes. The LOs exposed to PS, BPA, or co-exposure to PS and BPA for 7 days showed comparable to previous study. The BPA levels in the culture medium were declined by the added PS. The combined adverse effects of PS and BPA on the LOs was identified to be synergistic upon determined hepatotoxicity and identified the gene-level related to multiple processes of toxic mechanism. Co-exposure to PS and BPA induced the most significant changes in the DEGs number, enrichment of GO terms and KEGG pathways together with the positive of HNF4A, CDH2, ACC1, CYP1A, CYP3A1, TP53, and ALB. Specifically, PS didn't change the BPA or ERβ2. Individually, but when the LOs were co-exposed to PS and BPA, the ERα further showed significantly and synergistically. Our findings highlight the metabolic-related health risk due to co-exposure to MP and BPA, even at low doses equivalent to human internal exposure level. Based on these findings, the potential adverse outcome pathway related to PS and BPA singly and jointly were proposed, predicting two possible outcomes to be hepatic steatosis. Moreover, the ERα- and HNF4A-axis proposed to be potential candidate markers to investigate the "sector-like effect" of PS in the present of BPA.	Sci Total Environ. 2023 Jan 1:854:158585.	10.1016/j.scitotenv.2022.158585	36089014	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2024	W. Chang, S. Yang, X. Li, F. Liang, R. Zhou, H. Wang, Y. Feng and Y. Wang	2020	Low doses of BPA induced abnormal mitochondrial fission and hypertrophy in human embryonic stem cell-derived cardiomyocytes via the calcineurin-DRP1 signaling pathway: A comparison between XX and XY cardiomyocytes	Humans are inevitably exposed to bisphenol A (BPA) via multiple exposure ways. Thus, attention should be raised to the possible adverse effects related to low doses of BPA. Epidemiological studies have outlined BPA exposure and the increased risk of cardiovascular diseases (such as cardiac hypertrophy), which has been confirmed in the sex-specific in rodent animals and presents in the in vitro studies, although the molecular mechanism is still unclear. However, whether BPA at low doses equivalent to human internal exposure level could induce cardiac hypertrophy via the calcineurin (CNP)-signaling pathway by disrupting calcium homeostasis and the sex-specific effects remain unknown. Here, we established the human embryonic stem cell-derived cardiomyocytes (hESC-CMs) to investigate the effects of BPA on cardiac hypertrophy. In our study, either ES- and HF-CM were exposed to two physiological BPA (0 ng/mL, naturally elevated hypertrophic-related mRNA expression levels (such as NPPB and NPPB), enhanced cellular area and reduced ATP supplementation, demonstrated the hypertrophic cardiomyocyte phenotype in vitro. The monocrine factor produced by BPA was promoted by Ca2+ mediated dephosphorylation of DRP1. At the molecular level, the increase in cytosolic Ca2+ levels by low doses of BPA could discriminate between XY- and HF-CM, which may suggest a potential non-specific hypertrophic risk in cardiomyocytes in terms of abnormal mitochondrial fission and ATP production by impairing Ca2+/P-DRP1 signaling. In Ca2+ blockdown cardiomyocytes, these changes were highly presented in XX human pacemaker cells, rather than in XY human pacemaker cells.	Toxicol Appl Pharmacol. 2020 Feb 1:388:114850.	10.1016/j.taap.2019.114850	31830493	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2025	Y. Chen, S. Zhang, Y. Sun, J. Zou, X. Qiu, H. Xi, Y. Xu, Y. Li, B. Chen, J. Fan and M. Zhu	2025	Bisphenol A impairs oocyte maturation by dysfunction of cumulus cells	Bisphenol A (BPA) is a well-known environmental endocrine disruptor that has detrimental effects on reproduction. This study aimed to investigate whether BPA exposure could disrupt the function of cumulus cells and influence oocyte maturation and development. Vector-coupled and the germinal vesicle-stage were exposed to BPA (in EX). The results revealed that BPA exposure had no function in cumulus cells by inhibiting mitotic division, inducing metaphasic reticulum stress, and disrupting steroid synthesis. Furthermore, BPA exposure significantly increased reactive oxygen species and caused abnormal distribution of mitochondria in the oocytes. Notably, matured oocytes in the BPA stage from the BPA-treated groups showed significantly reduced development in the blastocyst stage, along with increased autophagy and apoptosis. These findings suggest that cumulus oocyte complexes are sensitive to BPA exposure during the germinal vesicle stage, and the toxic effects of BPA on cumulus cells can severely inhibit oocyte and parthenogenetic embryos development.	Theriogenology. 2025 Feb:233:139-146.	10.1016/j.theriogenology.2024.11.023	39615448	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2026	Y. Chen, Z. Hu, M. Tang, F. Huang, Y. Xiang, D. Ouyang, J. Ma, S. Hu, H. Xiao and D. Hu	2023	Lysosome-related exosome secretion mediated by miR-26b / Rab31 pathway was associated with the proliferation and migration of MCF-7 cells treated with BPA	Bisphenol A (BPA), one of the typical environmental endocrine disruptors (EDCs), can promote the proliferation and migration of cancer cells, but the mechanism of which remains largely unclear. Exosome secretion plays an important role in the proliferation and migration of cells. In environmental stress, This study aimed to investigate whether exosome secretion was involved in the effect of BPA on the proliferation and migration of MCF-7 cells, and the related mechanism. Our data shows that the IC50 value of MCF-7 exposure to BPA was about 81.82 μM. The exposure of MCF-7 to 10 μM BPA resulted in a decreased miR-26b expression and the increased Rab31 expression. Meanwhile, BPA exposure significantly increased the number and activity of lysosomes and the secretion of exosomes. Moreover, the exosomes from 10 μM BPA-treated MCF-7 cells showed a significantly increased ability to promote the proliferation and migration of MCF-7 cells. Treatment with GW4869, an exosome secretion inhibitor, for 48 h not only reduced the number and activity of lysosomes via miR-26b/Rab31 pathway, but also inhibited the exosome secretion of MCF-7 treated with BPA, their proliferation and migration were also down-regulated. Herein, we concluded that the stimulating effect of BPA on the proliferation and migration of MCF-7 cells was associated with the lysosome - related exosome secretion via miR-26b/Rab31 pathway.	Ecotoxicol Environ Saf Vol.252 Pages 114563	10.1016/j.ecoenv.2023.114563	36701876	in vitro	-	-	-	-	-	-	-	-	1	0	10 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2027	P. Chen, Y. Hu, Z. Dou, X. Feng, N. Zhao, C. Ban and Q. Wang	2025	Exploring the toxicity of bisphenol A and its analogue bisphenol S-MPE to Escherichia coli K12 from integrated AutoQSAR and transcriptomics analysis	Bisphenol (BPX) analogues are a group of emerging contaminants as substitutes for BPA. Bacteria are acknowledged as indispensable parts of the ecosystem, whereas the bacterial toxicity data for BPX analogues is still lacking. Herein the still-type and Escherichia coli resistance (E.coli) strains of K- and K12 were exposed to BPX and bisphenol S-MPE (BPS-MPE), a BPX analogue already detected in environmental compartments for the first time. Results showed that BPX and BPS-MPE could severely inhibit the growth of the wild-type strain was significantly promoted by BZ test (≤ 0.1 BPA and BPS-MPE at a stationary phase, while that of the Δ-efflux pump strain was significantly inhibited by BZ test (≤ 0.1 BPA and BPS-MPE at a stationary phase. Besides, BPX could induce the production of reactive oxygen species (ROS) in both wild-type and Type I replacements and a concentration-dependent increase in the ICP levels. The predictive binding concentrations of BPA and BPS-MPE by Escherichia coli K12 were double to each type of cell with the measured values. Transcriptomics showed that BPA and BPS-MPE not only resulted in significant enrichment of Gene ontology terms relevant to transport, ATPase activity, binding and cell membrane, but also inhibited oxidative phosphorylation and ATP-binding cassette transporters pathways. Transcriptics revealed the presence of three significant clusters, all of which showed higher changes in gene expression caused by 0.5 mmol L-1 BPX-MPE compared to 0.5 mmol L-1 D BPA consistently. Our results unveiled BPA-like toxicity of BPS-MPE to K. coli K12 at environmentally relevant concentrations.	Environ Pollut. 2025 Sep 15:381:126589.	10.1016/j.envpol.2025.126589	40467001	in vitro	-	-	-	-	-	-	-	-	1	0	50 nmol/L	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2028	M. Chen, S. Yang, D. Yang and X. Guo	2024	Bisphenol A and its metabolites promote white adipogenesis and impair brown adipogenesis in vitro	Bisphenol A (BPA), an obesogen, can disrupt adipogenesis in vitro, but these studies did not distinguish adipocytes as white or brown. BPA can be metabolized into BPA-glucuronide (BPA-G) and BPA-sulfate (BPA-S). These metabolites are not completely inactive in the body, but the related results remain limited. In this study, preadipocytes isolated from mouse white and brown adipose tissues were treated with 0.1, 1, and 10 μ M of BPA and its metabolites for 8 days, which are equivalent to the exposure level of general and occupational populations, to investigate and compare the effects of BPA and its metabolites on white and brown adipogenesis. The results showed that BPA and BPA-G increased lipid accumulation during white adipogenesis, whereas BPA-S did not. BPA induced this same effect during brown adipogenesis. Moreover, BPA and its metabolites up-regulated the expression of pan-adipogenic markers, such as peroxisome proliferator-activated receptor gamma (PPARγ), during white adipogenesis, whereas they down-regulated that of PPARγ during brown adipogenesis. Additionally, BPA and its metabolites up-regulated the expression of uncoupling protein 1 (UCP1), a thermogenic marker, during brown adipogenesis, but not during white adipogenesis. Besides, during brown adipogenesis, we BPA-S also reduced the mRNA expression levels of Ppar γ and Ucp1. These findings indicated that BPA induced different effects on white and brown adipogenesis, whereas the former and its metabolites the latter. Despite less potent than BPA, BPA-G and BPA-S might also affect white and brown adipogenesis. This research provides in-depth insights into the obesogenic effects of BPA and the biological activities of its metabolites.	Toxicology. 2024 Dec:509:153995.	10.1016/j.tox.2024.153995	39537008	in vitro	-	-	-	-	-	-	-	-	1	0	0.1、1、10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2029	L. Chen, D. Tao, M. Qi, T. Wang, Z. Jiang and S. Xu	2022	Cineole alleviates the BPA-inhibited NETs formation by regulating the p38 pathway-mediated programmed cell death	Bisphenol A (BPA) is an endocrine disruptor, that can cause immune dysfunction. Cineole (CIN) has that effect of regulating immune function and mild oxidation. Neutrophil extracellular traps (NETs) are one of the ways to resist pathogen invasion. In order to explore the effects of BPA and CIN on the release of chicken NETs and the antagonistic effect of CIN, take chicken peripheral blood neutrophils as object of study grouping as: NC, BPA, CIN, BPA + CIN, SB203580 + BPA. The results showed that BPA could induce the release of NETs, and CIN could inhibit the release of NETs induced by BPA. BPA can increase the contents of ROS and NO, increase the activity of iNOS, BPA exposure inhibited the expression of Nrf2 and HO-1 mRNA, reduced the expression of MPO, elastase (NE) and histone, and inhibited the release of NETs. BPA activates the disinfectant apoptotic and necroptosis through the p38 mitogen-activated protein kinase (p38 MAPK) pathway, which increased the expression of cytochrome C (Cyt C), bcl-2 associated X protein gene (bax), cysteine aspartate-specific proteinase-3 caspase-3), cysteine aspartate-specific proteinase-9 caspase-9), receptor-interacting protein kinase 1 (RIP1), receptor-interacting protein kinase 3 (RIP3) and mixed lineage kinase domain like protein (MLKL), decreased the expression of B cell lymphoma 2 (bcl-2). However, the co-exposure of CIN and BPA partially recovered the release of NETs, alleviated BPA-induced oxidative stress, and inhibited the activation of p38 MAPK pathway, necroptosis, and mitochondrial apoptosis pathway. These results indicated that CIN modulated p38 pathway alleviated BPA-induced neutrophil necroptosis, and apoptosis, and increased NETs formation.	Ecotoxicol Environ Saf. 2022 Jun 1:237:113558.	10.1016/j.ecoenv.2022.113558	35483150	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2030	H. Chen, J. Chen, X. Shi, L. Li and S. Xu	2022	Naringenin protects swine testis cells from bisphenol A-induced apoptosis via Keap1/Nrf2 signaling pathway	Bisphenol A (BPA) has caused serious pathologies to varying organs of humans and animals, especially reproductive organs. Naringenin (NRG) is a flavanone compound that has shown protective effects against several environmental chemicals through suppression of oxidative stress and activation of nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. Herein, we described the discovery path of NRG inhibition on apoptosis in BPA-exposed swine testis (ST) cells through targeting Kelch-like ech-associated protein (Keap1). We found that NRG could specifically bound to the active residues of 0308 domain in Keap1 and activated Nrf2 signaling pathway, and then increasing the levels of GSH, SPX and CAT, and finally inhibiting oxidative stress and mitochondrial apoptosis induced by BPA in ST cells. Altogether, our results showed that NRG inhibits oxidative stress and mitochondrial apoptosis induced by BPA in ST cells by targeting Keap1-Nrf2 signaling pathway, indicating that NRG could serve as an antagonistic therapy against BPA.	Biofactors. 2022 Jan;48(1):190-203.	10.1002/biof.1814	34914851	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2031	C. Champmartin , F. Marquet, L. Chedik, M. J. Dilger, M. Aubertin, E. Ferrari, M. C. Grandclaude and F. Cossier	2020	Human in vitro percutaneous absorption of bisphenol S and bisphenol A: A comparative study	Bisphenol A (BPA) is widely used in industrial products. Due to the toxicity of this compound, and to comply with restrictions and regulations, manufacturers have progressively replaced it by substitutes. One of the main substitutes used is bisphenol S (BPS). Despite increasing use in many products, the effects of BPS on human health have been little investigated, and studies on percutaneous BPS absorption and particularly toxicokinetic data are lacking. However, the endocrine-disrupting activity of BPA and BPS appears comparable. Dermal contact is a significant source of occupational exposure and is the main route during handling of bisphenol-containing receipts by cashiers. Here, we assessed BPA absorption was investigated and compared to that of BPS. Experiments were performed according to OECD guidelines. Two receipts were formulated to which a solution, artificial sebum or water - were applied in vitro to fresh human skin samples in static Franz diffusion cells. Then, cumulative absorbed dose and distribution of dose recovered were measured. BPA absorption was significantly greater than BPS absorption, regardless of the receipt matrix. Indeed, BPA absorption was 2.5 times greater than BPS absorption when receipts were applied in water. However, depending on the receipt matrix, 10% to 47% of the applied BPS dose remained in the skin, and was consequently potentially absorbable. Both BPA and BPS were mainly absorbed without biotransformation. Taken together, these results indicate that cashiers may be exposed to BPS through skin when handling products containing it. This exposure is of concern as its toxicity is currently incompletely understood.	Chemosphere. 2020 Aug:252:126525.	10.1016/j.chemosphere.2020.126525	32220717	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2032	A. Cayir, T. M. Barrow, L. Guo and H. M. Byun	2019	Exposure to environmental toxicants reduces global N6-methyladenosine RNA methylation and alters expression of RNA methylation modulator genes	The spliceosome/polysome complex: more than 100 forms of RNA modifications. Of these, N6-methyladenosine (m6A) is the most abundant form of RNA methylation, with roles in modulating mRNA transcript processing and regulation. The aims of the study: overtemperature changes (ambient RNA methylation (m-AEM-Seq) epithelial cells in response to environmental toxicants, and differential gene expression of m6A modulator genes. Treatment: human- and mouse/C57 mouse subjects exposed quantitative reverse PCR) and to lung cancer-housecleaning activity available non-survey datasets. Global m6A methylation decreased in m6A/mRNA after organochlorines carcinogen. (PA) and sodium arsenite (iAs) and endocrine disruptors (bisphenol A and simulated for 24 h) Global m6A methylation level significantly decreased with exposure to ≥0.1 μM BPA, ≥0.5 μM PA, and ≥5 μM iAs in human bronchial epithelial cells (BEAS-2B). Consistently, m6A dot blot analysis showed that ≥0.1 μM BPA, ≥0.5 μM PA, and ≥5 μM iAs (P < 0.05). Further, the m6A-seq (MeRIP-Seq) analysis revealed that 1,175 and 614 (MeRIP) and readers. UNIMPUTE showed significantly higher expression among participants in the High (PAEC) Manpower group compared to those in the low-exposure control group (all p < 0.05). Further, the m6A-qPCR (METTL3/ukaro reduced expression in lung tumors. In comparison to normal lung epithelial (p < 0.0001). Our findings reveal that m6A/RNA methylation can be modified by exposure to environmental toxicants, and exposure to particulate matter is associated with differential expression level of m6A/RNA methylation modification machinery.	Environ Res Vol.175 Pages 228-234	10.1016/j.envres.2019.05.011	31146095	in vitro	-	-	-	-	-	-	-	-	1	0	1 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2033	Y. Cao, Z. Chen, M. Zhang, L. Shi, S. Qin, D. Lv, D. Li, L. Ma and Y. Zhang	2022	Maternal exposure to bisphenol A induces fetal growth restriction via upregulating the expression of estrogen receptors	Bisphenol A (BPA) accumulation in the placenta leads to fetal growth restriction (FGR). Here we aimed to explore the effect and the underlying mechanism of BPA exposure on fetal development. ELISA was performed to detect the concentrations of estradiol (E2) and BPA in the serum of pregnant women and umbilical cord blood. Immunohistochemistry was performed to detect the expression of estrogen receptors (ERs) and enzymes for ER synthesis, and ERs methyltransferases (DNMTs). Bisulfite-sequencing PCR analysis was performed to measure CpG methylation in ER genes. Mice systemic exposure was used to examine ER expression. We found that human FGR placentae had significantly increased BPA and estrogen levels and decreased DNMT levels compared with healthy placentae. BPA downregulated DNMT expression via ERα, and ADNP silencing promoted ER expression in BeWo cells. Compared with vehicle treatment, BPA treatment significantly enhanced the expression of key enzymes for estrogen synthesis and ERs in BeWo cells. BPA treatment inhibited CpG methylation in ER genes, along with downregulated DNMT1 expression and upregulated DNMT3a and DNMT3b expression. BPA treatment significantly promoted BeWo cell apoptosis compared with vehicle treatment. Importantly, ER inhibitor ICI 182780 significantly reversed all the BPA-induced effects on BeWo cells. In conclusion, BPA promotes estrogen production and cell apoptosis in BeWo cells via upregulating ER expression, leading to FGR.	Chemosphere. 2022 Jan;287(Pt 3):132244.	10.1016/j.chemosphere.2021.132244	34537452	in vitro	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2034	M. Cao, Y. Qian, Z. Sun, S. Liu, R. Zheng, L. Zhao and G. Chen	2025	Preparation, characterization, and stability of selenium nanoparticles decorated with Mori Fructus polysaccharide and its protective effects in bisphenol A-induced Sertoli cells	Bisphenol (BPA) is an endocrine disruptor universally present in food packaging, which may cause oxidative stress and reproductive toxicity through migration to food and ingestion then. Both Mori Fructus and selenium have excellent antioxidant ability and good therapeutic effects on reproductive improvement. Hence, in this work, Mori Fructus polysaccharide (MFP) was selected as a stabilizer to synthesize MFP-selenium nanoparticles (MFP-SeNPs). The MFP-SeNPs were characterized by UV-vis spectrophotometer, FT-IR, SEM, TEM, DLS, and XPS, respectively, and showed a spherical and dispersed structure. The stability experiment showed that spherical MFP-SeNPs (average size 50.72 nm) was potential. 12.8 mM) cells were viable and cell dispersion was successfully synthesized with 1 mg/mL the MFP as a stabilizer. Additionally, the MFP-SeNPs showed the ABTS and DPPH scavenging activities. Compared with MFP and SeNPs, MFP-SeNPs had stronger radical scavenging ability. It could also decrease the levels of MDA and ROS and enhance the SOD and GSH-Px activities through PI3K/Akt pathways in BPA-induced TM4 cells. Taken together, MFP-SeNPs could become a potential antioxidant to improve male reproductive functions in the future food field.	Int J Biol Macromol Vol.294 Pages 139463	10.1016/j.ijbiomac.2025.139463	39756730	in vitro	-	-	-	-	-	-	-	-	0	0	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2035	M. Caglayan and S. Ozden	2024	Potential impacts of bisphenols on prostate cells: An overview of cytotoxicity, proliferation, oxidative stress, apoptosis, and ER-stress response activation	This study aimed to evaluate the toxic effects of Bisphenol A (BPA), Bisphenol F (BPF) and Bisphenol S (BPS) on PNT1A and PC-3 cells, focusing on their effects on endoplasmic reticulum (ER) stress and related pathways. PNT1A and PC-3 were treated with BPA, BPF, and BPS at concentrations of 0.1, 1, and 10 μM for 48 h cytotoxicity, BrdU cell proliferation, ROS generation, apoptosis detection, gene expression analysis and Western blot analysis were performed. BPS induced proliferation but apoptosis in PNT1A cells, whereas it induced both apoptosis and early apoptosis in PC-3 cells. BPF and BPS induced late apoptosis in PC-3 cells. Increased ROS levels were observed in PNT1A cells exposed to 1-10 μM BPA, BPF, BPF and BPS increased the expression levels of ER stress related genes in PNT1A cells. Furthermore, exposure to BPA increased the expression of ER stress-related CHOP/GADD153 proteins in PNT1A cells. These findings highlight the potential health risks associated with BPA, BPF and BPS exposure, emphasizing the importance of investigating the underlying mechanisms by which these chemicals may affect human health. Further research is required to comprehensively understand the role of ER stress pathways in cellular responses to these substances.	Food Chem Toxicol. 2024 Feb:184:114416.	10.1016/j.fct.2023.114416	38134982	in vitro	-	-	-	-	-	-	-	-	1	0	0.1、1、10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2036	P. Burkhardt, S. A. Palma-Duran, A. R. R. Tuck, K. Norgren, X. Li, V. Nikiforova, J. L. Griffin and V. Manlio Kos	2024	Environmental chemicals change extracellular lipidome of mature human white adipocytes	Certain environmental chemicals affect the body's energy balance and are known as metabolism-disrupting chemicals (MDCs). MDCs have been implicated in the development of metabolic diseases, such as obesity and type 2 diabetes. In contrast to their well-known impact on developing adipocytes, MDC effects leading to altered energy balance and development of insulin resistance in mature white adipocytes, constituents of adult adipose tissue, are largely unclear. Here, we investigated the effects of six well-established environmental MDCs: bisphenol A (BPA), perfluorooctanoic acid (PFOA), tributyltin (TBT), p,p-dichlorodiphenyl-dichloroethylene (DDE), mono-(2-ethylhexyl) phthalate (MEHP), and tetrabromobisphenol A (TBBPA) on mature human white adipocytes. Exposure to MDCs induced changes in the extracellular lipidome, metabolism-disrupting effects. While most of the tested exposures had no effect on adipocyte glucose consumption, hydrolysis, lipid storage, and basal glucose transport stimulation. Differences in the total lipid storage and adipocyte size, as well as glucose consumption and mRNA expression of the glucose transporter GLUT1, leptin and adiponectin. Additionally, an increased expression of adiponectin was observed with TPP and the positive control PPARγ agonist rosiglitazone. In contrast, the lipidomic analysis of the cell culture medium after a 5-day exposure was extremely sensitive and revealed concentration-dependent changes in the extracellular lipidome of adipocytes exposed to nearly all studied chemicals. While none of the extracellular lipidome changes were specific for the MDC used, some effects were found common to several known chemicals and included increases in lysophosphatidylcholines, glycosphingolipids and ceramides, and a decrease in fatty acids, with possible implications in inflammation, lipid and glucose uptake. This study points to early signs of metabolic disruption and likely systemic effects of mature adipocytes exposure to environmental chemicals, as well as to the need to include lipidomic endpoints in the assessment of adverse effects of MDCs.	Chemosphere Vol.349 Pages 140852	10.1016/j.chemosphere.2023.140852	38048832	in vitro	-	-	-	-	-	-	-	-	1	0	1—100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2037	F. Burkhardt, S. D. Schulz, E. Hellwig, K. Vach, P. Tomakidi and D. Polydorou	2021	Low-dose Bisphenol A and its analogues Bisphenol F and S activate estrogen receptor ß and slightly modulate genes in human gingival keratinocytes	OBJECTIVES: This study investigated the putative activation of estrogen receptor ß (ERβ) and possible effects related on gene expression in oral mucosal cells in response to the endocrine disruptor Bisphenol A (BPA) and its analogues Bisphenol F and S (BPF, BPS). MATERIALS AND METHODS: Human gingival keratinocytes (HGK) were exposed to BPA, BPF, BPS, 17β-estradiol (E2) and ICI 182,780 (ICI) as well as DMSO and 100 nM estradiol (E2/1) for 6 h, 24 h and 6 d, before immunofluorescence (IF) was performed to detect a possible ERβ activation. Additionally, transcription of keratinocyte-relevant biomarkers was analysed by quantitative real-time PCR (qRT-PCR). A linear mixed model and pairwise comparisons were applied for statistical analysis. RESULTS: The tested concentrations of BPA, BPF, BPS and E2 revealed distinct activation of ERβ at all time periods, whereas 100 nM E2/1 induced the most pronounced activation. Despite the detected ERβ activation, the concentrations of BPA and its analogues induced only moderate modulations of the tested keratinocyte-relevant biomarker genes at all time periods. This also applied to 200 nM E2/1, while in none of 100 nM E2/1 significant changes (p > 0.05) were detected for almost all analysed genes. CONCLUSIONS: Despite the ERβ activation, BPA and its analogues BPF and BPS showed only slight modulations of the gene expression of the tested keratinocyte-relevant biomarker genes at all time periods. This also applies to 200 nM E2/1, while in none of 100 nM E2/1 significant changes (p > 0.05) were detected for almost all analysed genes. Although limited to a selected number of genes, the sparse modulation of gene expression may give a hint that the substances do slightly affect homeostasis of gingival keratinocytes. Although limited to a selected number of genes, the sparse modulation of gene expression may give a hint that the substances do slightly affect homeostasis of gingival keratinocytes. Interestingly, the concentrations applied to HGK were of physiological importance.	Dent Mater. 2021 Apr;37(4):625-635.	10.1016/j.dental.2021.01.008	33558057	in vitro	-	-	-	-	-	-	-	-	1	0	1.3 μM、0.16 μM、11.4 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価へ進め、当該物質関連報告が原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	適応毒性試験	適応毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2038	C. F. Burgos, D. Méndez, S. Quintana, S. Gonkowski, A. Tvorchanskiy and M. Alarcón	2025	Acrylamide and bisphenol A: two plastic additives increase platelet activation, via oxidative stress	BACKGROUND: Since the mid-20th century, the widespread use of plastics has led to the buildup of harmful byproducts in the environment most notably acrylamide (AA) and bisphenol A (BPA). These chemicals are now commonly detected in human tissues, raising concerns about their potential health effects. While their presence as environmental pollutants is well known, their specific impact on platelet function and the associated cardiovascular risks remains poorly understood. METHODS: To explore how AA and BPA affect platelet physiology, we performed in vitro assays to assess platelet activation and aggregation following exposure to these substances. Platelets were isolated from healthy donors and treated with AA and BPA at concentrations ranging from 0.1 to 10 mM. Flow cytometry was used to measure platelet activation, while ELISA tests and RT-PCR analyses were performed to quantify increases in oxidative stress markers, apoptosis, and signaling pathways regulated by protein kinase C (PKC), cyclin-dependent kinase 5 (CDK5), and the protein targets, with ERS affected by AA and CDN by BPA. These proteins are primarily involved in oxidative stress

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則に基づき除去。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物飼及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2051	Z. Awada, R. Nasr, R. Akika, V. Cahais, C. Cuenin, M. Zhivagui, Z. Herceg, A. Ghantous and N. K. Zgheib	2019	DNA methylome-wide alterations associated with estrogen receptor-dependent effects of bisphenols in breast cancer	BACKGROUND: Bisphenol A (BPA), an estrogen like endocrine disruptor used in plastics, has been associated with development and promotion of breast cancer; so plastic manufacturers shifted towards less studied analogs, BPF and BPS. Studying the associated DNA methylome-wide mechanisms of these derivatives is timely, particularly in comparison with BPA. METHODS: We evaluated proliferation, cell cycle, and migration of estrogen receptor positive (ER+) breast cancer cells (MCF-7 and T47D) exposed to BPA, BPF and BPS. Using the Illumina Infinium MethylationEPIC BeadChip, we then performed DNA (de)methylation analyses and GSE-2 methylation event-specific PCR. Bioinformatics and statistical analysis was evaluated in bisphenol-exposed cells and compared to clinical breast cancer data. RESULTS: The three bisphenols caused ER-dependent increased proliferation and migration of MCF-7 but not MDA-MB-231 cells, while BPS being ER-lower, less potent than BPA and BPF. Although they have similar chemical structures, the three bisphenols induced distinct DNA methylation changes, with BPF showing the greatest number of differentially methylated positions (DMPs) and differentially methylated regions (DMRs). Bisphenol-driven DMPs had the strongest effects on the methylome, followed by BPS then BPF. No pathways were enriched for BPF-solely DMPs and BPS-induced methylome alterations were restricted to the bisphenol-driven DMRs. Importantly, bisphenol-dysregulated methylome-wide alterations, comparing ER-positive breast cancer samples to adjacent normal tissues, CORGI/LUDWIG. The three bisphenols have important epigenetic effects in breast cell lines, with those of BPA and BPS overlapping with cancer-related pathways in clinical breast cancer models. Hence, further investigation of their safety is warranted.	Clin Epigenetics. 2019 Oct 10;11(1):138.	10.1186/s13148-019-0725-y	31601247	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10－8 M	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2052	E. Atlas and V. Dimitrova	2019	Bisphenol S and Bisphenol A disrupt morphogenesis of MCF-12A human mammary epithelial cells	Breast cancer is one of the most common cancers diagnosed in women worldwide. Genetic predisposition, such as breast cancer 1 (BRCA1) mutations, account for a minor percentage of the total breast cancer incidence. And thus, many life style factors have also been linked to the disease such as smoking, alcohol consumption and obesity. Emerging studies also link the environment to breast cancer development and adversely affected. The aim of this study is to investigate the possible effects of BPA on the development of the nervous system and neural tube in 48 hr chicken embryos. SETTINGS: Thirty-specific pathogen free (SPF) fertilized eggs were used in the study. Eggs were incubated at 37.5°C and 60% humidity for 48 hours. DESIGN: Eggs were divided into three groups: Control, Vehicle (Ethanol 96%) and BPA (50 µg/egg). Eggs were windowed and each group was examined macroscopically with the Hamilton-Hamburger system. At the end of 48hr of incubation, eggs were sacrificed and separated from the embryo. Embryos were examined morphologically and histopathologically. RESULTS: As the BPA dose increased, delays in the development of the nervous system and midline closure increased in the early period of chicken embryos. Depending on the dose, it was found that the embryo's cranio-caudal length and somite number decreased (p < .05). CONCLUSION: It was determined that BPA application on early chicken embryos adversely affected neural tube development. It was also found to delay midline closure.	Sci Rep. 2019 Nov 5;9(1):16005.	10.1038/s41598-019-52505-x	31690802	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2053	E. Atay, A. Emekin, E. Bozkurt and E. Aslan	2020	Impact of Bisphenol A on neural tube development in 48-hr chicken embryos	OBJECTIVES: Bisphenol A (BPA) is one of the most heavily produced chemicals in the world. BPA is involved in the production of many substances such as cosmetics, various foodstuffs, toys, personal care products, detergents and plastic bottles of that are frequently used in daily life. Depending on BPA exposure, neural maturation and reproductive function, and bone and brain development are adversely affected. The aim of this study is to investigate the possible effects of BPA on the development of the nervous system and neural tube in 48 hr chicken embryos. METHODS: Thirty-specific pathogen free (SPF) fertilized eggs were used in the study. Eggs were incubated at 37.5°C and 60% humidity for 48 hours. DESIGN: Eggs were divided into three groups: Control, Vehicle (Ethanol 96%) and BPA (50 µg/egg). Eggs were windowed and each group was examined macroscopically with the Hamilton-Hamburger system. At the end of 48hr of incubation, eggs were sacrificed and separated from the embryo. Embryos were examined morphologically and histopathologically. RESULTS: As the BPA dose increased, delays in the development of the nervous system and midline closure increased in the early period of chicken embryos. Depending on the dose, it was found that the embryo's cranio-caudal length and somite number decreased (p < .05). CONCLUSION: It was determined that BPA application on early chicken embryos adversely affected neural tube development. It was also found to delay midline closure.	Birth Defects Res. 2020 Oct;112(17):1386-1396.	10.1002/bdr2.1791	32864885	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2054	A. Arora, M. Becker, C. Marques, M. Oksanen, G. Li, F. Mastropasqua, M. E. Watts, M. Arora, A. Falk, C. O. Daub, J. Lanekoff and K. Tanninen	2023	Screening autism-associated environmental factors in differentiating human neural progenitors with fractional factorial design-based transcriptomics	Research continues to identify genetic aetiation, environmental exposures, and their mixtures underlying different diseases and conditions. There is a need for screening methods to understand the molecular outcomes of such factors. Here, we investigate a highly efficient and multiplexable, fractional factorial experimental design (FFED) to study six environmental factors (lead, valproic acid, bisphenol A, ethanol, fluoxetine hydrochloride, and polyinosinic:polycytidylic acid) and their interactions in differentiating human neural progenitor cells (hNPCs). Using a resolution IV FFED, we performed RNA-seq after 24 h exposure to these environmental factors and put the results in the context of autism spectrum disorder (ASD). We performed this effort 3 by exposure of differentiating neural progenitors to a layered analytical approach and detected several convergent and divergent, gene and pathway level responses. We revealed significant upregulation of pathways related to synaptic function and lipid metabolism following neuronal fluoxetine exposure, respectively. Moreover, fluoxetine exposure elevated several fatty acids when validated using mass spectrometry-based metabolomics. Our study demonstrates that the FFED can be used as a multiplexed transcriptomics analysis to detect relevant pathway-level changes in human neural development caused by low-grade environmental risk factors. Future studies will require multiple cell lines with different genetic backgrounds for characterizing the effects of environmental exposures in ASD.	Sci Rep Vol.13 Issue 1 Pages 10519	10.1038/s41598-023-37488-0	37386098	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.00-50.00 µM or 0.00-200.00 mM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2055	Y. Arita, H. J. Park, A. Cantillon, D. Getahun, R. Mercer and M. B. Peltier	2019	Effect of bisphenol-A (BPA) on placental biomarkers for inflammation, neurodevelopment and oxidative stress	Background: Bisphenol-A (BPA) is a ubiquitous pollutant whose effects on pregnant women are poorly understood. Therefore, we investigated the effects of BPA on basal and bacteria-stimulated production of proinflammatory cytokines (interleukin (IL)-1β', tumor necrosis factor-α' (TNF-α') and IL-6), and inflammatory mediators (soluble glycoprotein 130 (sgp-130, tumor necklace-1 (HO-1) and IL-10) and biomarkers for neurodevelopment (brain-derived neurotrophic factor (BDNF)) in placental explants. Methods: Placental explant cultures were treated (0.01 (0.002) (0.01) (0.1) (1) (10) (100) (1000) nM) in the presence or absence of 107 colony-forming unit (CFU)/mL heat-killed Escherichia coli for 24 h. Biomarker concentrations in conditioned medium were quantified by the enzyme-linked immunosorbent assay (ELISA). Results: Under basal conditions, BPA at 0.01 (0.002), 0.1, 1, 10, 100, 1000 nM significantly increased the production of IL-1β' (0.01 nM), TNF-α' (0.01 nM), IL-6 (0.01 nM), sgp-130 (0.01 nM), HO-1 (0.01 nM), BDNF (0.01 nM), and IL-10 (0.01 nM). BPA at 0.01 nM significantly increased the production of IL-1β' (0.01 nM), TNF-α' (0.01 nM), IL-6 (0.01 nM), sgp-130 (0.01 nM), HO-1 (0.01 nM), BDNF (0.01 nM), and IL-10 (0.01 nM) in bacteria-stimulated explants. BPA increased IL-6 production at 100 nM and reduced sgp130 at 1000 nM in bacteria-stimulated explants. BPA at 0.01 nM significantly increased the production of IL-1β', TNF-α', BDNF, HO-1, IL-6 and IL-10. Conclusion: BPA may increase placental inflammation by promoting IL-1β' and IL-6 but inhibiting sgp130. It may also disrupt oxidative balance and neurodevelopment by increasing IL-6' and BDNF production.	J Perinat Med. 2019 Sep 25;47(7):741-749.	10.1515/jpm-2019-0045	31339859	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0－10,000 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2056	M. I. Ansari, N. Bano, K. M. Kainat, V. K. Singh and P. K. Sharma	2022	Bisphenol A exposure induces metastatic aggression in low metastatic MCF-7 cells via PGC-1 α mediated mitochondrial biogenesis and epithelial-mesenchymal plasticity	ABSTRACT: The frequency of estrogen receptor alpha (ERα+) positive breast cancers and their metastatic progression is prevalent in females globally. Aberrant interaction of estrogen like endocrine disrupting chemicals (EDCs) is highly implicated in breast carcinogenesis. Studies have shown that single or acute exposures of weak EDCs such as bisphenol A (BPA) may not have a substantial per-carcinogenic/metastatic effect. However, repeated exposure to EDCs, is reported to strongly induce carcinogenic/metastatic progression, which remains to be studied. AIMS/METHODS: Low metastatic ERα+ positive human breast cancer cells (MCF-7) were exposed to noticeable doses of BPA every 24 h (up to 200 days) to study the effect of repeated exposure on metastatic potential. Following the designated treatment of BPA, markers of epithelial-mesenchymal transition (EMT), mitochondrial biogenesis, and mitochondrial ROS were evaluated. Mitochondrial biogenesis was inhibited by PGC-1α siRNA to confirm the role of PGC-1α in BPA induced metastatic aggression. RESULTS: Long-term exposure of low-dose BPA induced subtle epithelial-mesenchymal plasticity in MCF-7 cells, to augment migration and invasion in the ERα dependent pathway. Repeated exposures of BPA increased levels of several mesenchymal markers such as N-cadherin, vimentin, cluster of differentiation 44 (CD44), slug, and alpha-smooth muscle actin (α-SMA), whereas reduced the level of E-cadherin drastically. BPA induced mitochondrial biogenesis, favored metastatic aggression by fulfilling bioenergetics demand via PGC-1 α /NRF2/ERRα signaling. Knockdown of PGC-1α resulted in suppressing both mitochondrial biogenesis and EMT in BPA exposed MCF-7 cells. SIGNIFICANCE: Repeated exposures of low dose BPA may induce metastatic aggression in ERα+ positive breast cancer cells via PGC-1 α mediated mitochondrial biogenesis and epithelial-mesenchymal plasticity.	J Life Sci. 2022 Aug 1:302:120649.	10.1016/j.lfs.2022.120649	35597549	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2057	I. A. Anastasiou, I. Eleftheriadou, A. Tentolouris, P. Sarantis, A. Angelopoulou, A. Katsaounis, I. Mourouzis, M. V. Karamouzis, V. Gerogiatis, C. Pantos and N. Tentolouris	2022	Low concentrations of bisphenol A promote the activation of the mitochondrial apoptotic pathway on Beta-TC-6 cells via the generation of intracellular reactive oxygen species and mitochondrial superoxide	The natural history of type 2 diabetes mellitus is characterized by a progressive loss of pancreatic beta cell function and insulin resistance. Bisphenol A (BPA) is an endocrine disrupting chemical that is used widely in industry; people are exposed to BPA and its products daily. Studies have delineated that BPA alters the function of pancreatic beta cells. Herein, we examined the effect of low doses of BPA on pancreatic beta cell viability and apoptosis and we tried to elucidate the mechanisms involved in these processes. Beta-TC-6 (ATCC® CRL-11506™) cells were cultured in a medium containing the following dilutions of BPA: 0.002, 0.02, 0.1, 0.2, 2 µM up to 72 h. We examined the viability and existence of intracellular ATP levels of cells. Then, we measured apoptosis, cell cycle, and insulin levels. We quantified the levels of several proteins implicated in the mitochondrial pathway of apoptosis, and finally, we quantified the intracellular reactive oxygen species and mitochondrial superoxide. We found that the exposure of Beta-TC-6 cells to BPA results in a decrease in cell viability, ATP levels, and insulin secretion. Moreover, BPA induces apoptosis through a decrease in cell cycle G0/G1 phase. In addition, BPA activates the mitochondrial pathway of apoptosis. Finally, our results increase the intracellular reactive oxygen species and mitochondrial superoxide production. Exposure to low concentrations of BPA triggers the mitochondrial pathway of apoptosis via the generation of intracellular reactive oxygen species and mitochondrial superoxide on Beta-TC-6 cells in a dose-dependent way.	J Biochem Mol Toxicol. 2022 Aug;36(8):e23099.	10.1002/jbt.23099	35593412	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0.002、0.02、0.1、0.2、2 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2058	S. K. Anand, A. Sharma, N. Singh and P. Kakkar	2020	Activation of autophagic flux via LKB1/AMPK/mTOR axis against xenoestrogen Bisphenol-A exposure in primary rat hepatocytes	Bisphenol A, an endocrine disruptor chemical widely used to manufacture polycarbonate plastics and epoxy resins, acts via multiple mechanisms that perturb cellular and molecular functions. BPA has the potential to induce hepatotoxicity via generation of ROS and oxidative stress. However, the mechanism of BPA-induced oxidative stress and autophagy is still ambiguous at molecular and cellular levels. This study aims to elucidate the impact of BPA exposure (50 and 100 µM) in primary rat hepatocytes. BPA-induced accumulation of autophagosomes and LC3-II/LC3-I ratio, a key regulator in autophagy signaling were found to be associated during BPA exposure. The increased AMP/ATP ratio and subsequent phosphorylation by its upstream mediator Liver Kinase B1 (LKB1) activates AMPK. BPA down-regulated AMPK downstream molecule i.e. mammalian target of rapamycin (mTOR) by activating tuberous sclerosis complex 2 (TSC2) and inhibiting Ras homolog enriched in brain (Rheb). Activated AMPK also induces autophagy by phosphorylating Unc-51 like autophagy activating kinase 1 (ULK1) at Ser555 and translocation of Parkin to damaged mitochondria, culminating in decreased mitochondrial mass. Ultra-structural changes also confirmed mitochondrial disintegration, enhanced autophagic induction as evident from autophagosome formation. Findings confirm that BPA-induced oxidative stress, which eventually triggered LKB1/AMPK mediated autophagy and maintains cellular energy balance by rethydrogic removal of unhealthy mitochondria is primary rat hepatocytes.	Food Chem Toxicol Vol.141 Pages 111314	10.1016/j.fct.2020.111314	32305408	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	50 µMおよび100 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2059	G. Ampem, A. Jungjohan, H. Yu, L. Balogh, J. Thunduyil, M. E. Schneider and T. Rösser	2019	The environmental obesogen bisphenol A increases macrophage self-renewal	Self-renewal of macrophages is important for the healthy development and replenishment of tissue-resident macrophage pools. How this mechanism is controlled by endocrine signals is still largely unexplored. Here, we show that the endocrine disruptor bisphenol A (BPA) increases macrophage self-renewal. This effect was associated with phosphorylation of extracellular signal-regulated kinase (ERK) and a slight increase in the expression of liver X receptor alpha (LXRα). We found that LXRα inhibition reduced, while LXRα activation impeded, macrophage self-renewal. LXRα signaling hence may protect from excessive macrophage expansion. Self-renewing macrophages, however, had negligible LXRα expression when compared with quiescent macrophages. Accordingly, tissue-resident macrophage pools, which are dominated by quiescent macrophages, were not in LXRα-expressing macrophages. Overall, we show that BPA increases macrophage self-renewal and that this effect, at least in part, can be inhibited by increasing LXRα expression. Since BPA is accumulated in fat-adipose tissue, it has the potential to increase self-renewal of adipose tissue macrophages, leading to a condition that might negatively impact adipose tissue health.	Cell Tissue Res. 2019 Oct;378(1):81-96.	10.1007/s00441-019-03019-5	31011801	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2060	R. Al-Abdulla, H. Ferrero, S. Soriano, T. Borrell-Badia and P. Alonso-Magdalena	2022	Screening of Relevant Metabolism-Disrupting Chemicals on Pancreatic β -Cells: Evaluation of Murine and Human In Vitro Models	Endocrine disrupting chemicals (EDCs) are chemical substances that can interfere with the normal function of the endocrine system. EDCs are ubiquitous and can be found in a variety of consumer products such as food packaging materials, personal care and household products, plastic additives, and flame retardants. Over the last decade, the impact of EDCs on human health has been widely acknowledged as they have been associated with different endocrine diseases. Among them, a subset called metabolism-disrupting chemicals (MDCs) is able to promote metabolic changes that can lead to the development of metabolic disorders such as diabetes, obesity, hepatic steatosis, and metabolic syndrome, among others. Despite this, today, there are still no definitive and standardized in vitro tests to support the metabolic risk assessment of existing and emerging MDCs. Therefore, the present study aimed to establish a battery of in vitro tests to identify MDCs and to characterize their mechanisms of action. For this purpose, murine EndoC-βH1 cells and human EndoC-βH3 cells were challenged with the following top range of relevant concentrations of seven well-known EDCs: bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), perfluorooctanesulfonic acid (PFOS), di(2-ethylhexyl) phthalate (DEHP), cadmium chloride (CdCl2), and dichlorodiphenyldichloroethylene (DDE). The screening revealed that most of the tested chemicals have detectable, deleterious effects on glucose-stimulated insulin release, insulin content, mitochondrial activity, gene expression, and/or viability. For data provider new molecular information on the direct effects of the selected chemicals on key aspects of pancreatic β -cell function, such as the insulin secretion machinery and ion channel activity. In addition, we found that, in general, the sensitivity and responses were comparable to those from other in vivo studies reported in the literature. Overall, our results suggest that both models can serve as effective tools for the rapid screening of potential MDC effects on pancreatic β -cell physiology as well as for deciphering mechanisms underpinning the molecular mechanisms that underlie their action.	Int J Mol Sci. 2022 Apr 10;23(8):4182.	10.3390/ijms23084182	35457000	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	100 pM－10 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2061	R. Al-Abdulla, H. Ferrero, T. Borrell-Badia, S. Soriano, I. Quesada and P. Alonso-Magdalena	2023	Exploring the Effects of Metabolism-Disrupting Chemicals on Pancreatic α -Cell Viability, Gene Expression and Function: A Screening Testing Approach	Humans are constantly exposed to many environmental pollutants, some of which have been largely acknowledged as key factors in the development of metabolic disorders such as diabetes and obesity. These chemicals, have been classified as endocrine disrupting chemicals (EDCs) and, more recently, since they can interfere with metabolic functions, they have been renamed as metabolism-disrupting chemicals (MDCs). MDCs are present in many consumer products, including food packaging, personal care products, plastic bottles and containers, and detergents. The scientific literature has, ever increasingly focused on insulin-releasing pancreatic β -cells as the main MDC target. However, α -cells, which are responsible for glucagon secretion, are also crucial players in glucose homeostasis and, therefore, in the development of diabetes. Hence, the aim of this study was to establish a battery of in vitro tests to identify MDCs and to characterize their mechanisms of action. For this purpose, murine EndoC-αN1 cells and human EndoC-αH1 cells were challenged with the following top range of relevant concentrations of seven well-known EDCs: bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), perfluorooctanesulfonic acid (PFOS), di(2-ethylhexyl) phthalate (DEHP), cadmium chloride (CdCl2), and dichlorodiphenyldichloroethylene (DDE). The screening revealed that most of the tested chemicals have detectable, deleterious effects on glucose-stimulated insulin release, insulin content, mitochondrial activity, gene expression, and/or viability. For data provider new molecular information on the direct effects of the selected chemicals on key aspects of pancreatic α -cell function, such as the insulin secretion machinery and ion channel activity. In addition, we found that, in general, the sensitivity and responses were comparable to those from other in vivo studies reported in the literature. Overall, our results suggest that both models can serve as effective tools for the rapid screening of potential MDC effects on pancreatic α -cell physiology as well as for deciphering mechanisms underpinning the molecular mechanisms that underlie their action.	Int J Mol Sci. 2023 Jan 5;24(2):1044.	10.3390/ijms24021044	36674557	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	10 nM to 10 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2062	G. Aichinger, F. Pantasi and D. Marko	2020	Combinatory estrogenic effects of bisphenol A in mixtures with alternariol and zearalenone in human endometrial cells	Humans are typically exposed to mixtures of substances, whereby their bioactivity can be significantly altered by co-occurring compounds. Thus, over the last years, research on combinatory effects has gained increasing attention. In particular, steroid xenoestrogens have been recently reported to interact synergistically, among them alternariol (AOH) and zearalenone (ZEN). Due to toxins produced by molds which contaminate crops or food products, AOH and ZEN are frequently co-occurring in food and feed. Bisphenol A (BPA) is a well-known xenoestrogen, which is widely used in consumer products and can be found in the environment, food and human tissues. Its impact on the bioactivity of other xenoestrogens, well-established or not, is rarely investigated. Therefore, we investigated the combinatory effects of BPA with AOH and ZEN in MCF-7 cells, which represent a well-established estrogen-sensitive human cell model. Estrogenic stimuli of the single compounds and binary combinations in constant concentration ratios were measured by assessing the activity of alkaline phosphatase, a natural reporter gene for estrogen receptor activation. In parallel, cytotoxicity was monitored via assay. For statistical analysis of combinatory effects the "combination index" model was applied. In combination with ZEN, BPA was found to cause additive estrogenic effects. Mixtures of BPA with AOH expressed moderately antagonistic to nearly additive combinatory effects, depending on the concentration ratio. Although no synergistic effects were measured in the applied chemical mixtures, additive estrogenic stimuli were observed, underlining the importance to consider the cumulative impact of endocrine active toxins out of different sources and structural classes.	Toxicol Lett. 2020 Feb 1:319:242-249.	10.1016/j.toxlet.2019.10.025	31733320	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2063	J. S. Ahn, J. H. Won, D. Y. Kim, S. E. Jung, B. J. Kim, J. M. Kim and B. Y. Ryu	2022	Transcriptome alterations in spermatogonial stem cells exposed to bisphenol A	During to their self-renewal and differentiative abilities, spermatogonial stem cells (SSCs) are essential for maintaining male fertility and species preservation through spermatogenesis. With an increase in exposure to xenobiotics, the risk of endocrine-disrupting chemicals exerting-mimetic effects on estrogen receptors, such as bisphenol A (BPA), has also increased. This has led to concerns regarding the preservation of male fertility. BPA impairs spermatogenesis and the maintenance of SSCs; however, the transcriptome differences caused by BPA in SSCs are poorly understood. Thus, this study aimed to investigate the transcriptome differences in SSCs exposed to BPA, using RNA-sequencing (RNA-Seq) analysis. We found that cell proliferation and survival were suppressed by SSC exposure to BPA. Therefore, we investigated transcriptome differences through RNA-Seq, functional annotation, and gene-set enrichment analysis. Our results showed imperfect and abundant terms related to loss genes of lysosomal acidification and five genes of glycosaminoglycan degradation. Furthermore, we identified 10 candidate genes (Ccnd1, Cdkn1a, Ddit3, Gadd45a, Hspa5, Jun, Myc, Nr4a1, Pmaip1, Tnfrsf12a, and Tnfrsf19) that were differentially expressed in the presence of BPA. Taken together, our report that the identified DEGs and lysosomal mechanisms could provide new insights into the preservation of male fertility and related research.	Anim Cells Syst (Seoul) Vol.26 Issue 2 Pages 70-83	10.1080/19768354.2022.2061592	35479511	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	0, 10, 100 µM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2064	F. Ahmad, A. Sanserbayeva, P. Katsoglannis, C. Apaer and M. J. Pereira	2020	The effects of bisphenol A and bisphenol S on adipokine expression and glucose metabolism in human adipose tissue	PURPOSE: The environmental endocrine disruptors, bisphenol A (BPA) and bisphenol S (BPS) are associated with the development of type 2 diabetes. We aim to study the effects of BPA or BPS exposure on adipokine expression in human adipose tissue and on adipocyte glucose uptake. METHODS: Human subcutaneous adipose tissue was treated for 24 or 72 h with environmentally relevant and supraphysiological concentrations of BPA or BPS (0.1 nM–10 μM). Adipokine expression was measured by RT-qPCR and ELISA. Glucose uptake was measured by 2-deoxy-D-[1,2-3H(N)]-glucose uptake in adipocytes isolated and cultured in isolated adipocytes. Following adipose tissue culture with BPA for 24 h, RNA-Seq. Adipose tissue treated with BPA for 24 h had reduced expression of the proinflammatory genes (LIF, IL1B, TNFB) and adipokines (NAMPT, FABP4). BPA and BPS had no effect on the expression of other proinflammatory genes (IL1B), adipokines (LEP), or receptors (ESR1, ESR2) after 72 h exposure. Adipose tissue treated with environmentally relevant concentrations of BPA for 24 h had reduced insulin-stimulated glucose uptake, without altered gene and protein levels of key insulin signalling pathway markers. CONCLUSIONS: We found that human adipose tissue treated with environmentally relevant concentrations of BPA for 24 h, but not BPS, reduced expression of proinflammatory genes and adipokines. Furthermore, BPA-reduced glucose uptake in adipocytes. Independently of insulin signalling. Such mechanisms can contribute to the development of insulin resistance associated with BPA exposure.	Toxicology. 2020 Dec 1:445:152600.	10.1016/j.tox.2020.152600	32976960	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1—10 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2065	F. Ahmad, L. Chahadi, L. Gamwea, A. Caron and C. Apaer	2020	The effects of acute BPA exposure on skeletal muscle mitochondrial function and glucose metabolism	Bisphenol A (BPA) is an environmental pollutant that has been associated with adverse health effects including skeletal muscle insulin resistance, a major contributor to the pathogenesis of type 2 diabetes (T2D). Early, acute exposure to environmentally relevant concentrations of BPA may contribute to the development of insulin resistance. However, the mechanisms underlying this remain poorly understood. Mitochondrial sensitivity. Lb myotubes were treated with BPA (1 nM–100 nM) during the last 24 h of differentiation. Following exposure to 100 nM of BPA, resting and insulin-stimulated glucose uptake were decreased, whereas mitochondrial protein load was increased. Overall metabolic activity, measured by resazurin reduction, was decreased in Lb myotubes exposed to 1000 nM of BPA. At this concentration, insulin-stimulated glucose uptake was increased, which corresponded to an increased phosphorylation of the insulin signalling protein Akt, and increased glycolysis, measured by extracellular acidification rate (ECAR). Acute BPA exposure did not alter levels of oxidative stress markers in muscle cells, but significantly increased mitochondrial protein load, which is known to be involved in decreased ROS production. The effects of BPA on glucose uptake, but not mitochondrial function, were reversed by co-treatment with the oestrogen receptor antagonist ICI 182,780. These results suggest that acute exposure of LA myotubes to only high concentrations of BPA alters glucose metabolism, which is likely a compensatory response to reduced mitochondrial energy production capacity.	Mol Cell Endocrinol. 2020 Jan 1:499:110580.	10.1016/j.mce.2019.110580	31536778	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1 nM—10（5） nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2066	S. M. Abdullah and H. Rashid	2020	Melatonin Ameliorates BPA Induced Oxidative Stress in Human Red Blood Cells: An In vitro Study	BACKGROUND: Bisphenol A (BPA) is a xenobiotic that causes oxidative stress in various organs in living organisms. Blood cells are also an endpoint where BPA is known to cause oxidative stress. Blood cells, especially red blood cells (RBCs), are crucial for maintaining homeostasis and overall wellbeing of the organism. They are highly susceptible to oxidative stress induced by xenobiotics. However, there is limited data about the oxidative stress induced by BPA in blood, especially in red blood cells. This study was carried out to evaluate BPA induced oxidative stress in human RBCs in vitro and its ameliorative by melatonin. OBJECTIVE: To find the ameliorative effect of melatonin against BPA induced oxidative stress in human RBCs in vitro. METHODS: Human RBCs were incubated with BPA (100, 200, 300, 400, 500 µg/ml) for 2 hours at 37°C. Another set of erythrocytes was pre-treated with melatonin (1 mM) for 30 minutes and then co-incubated with BPA for 2 hours. Control RBCs were incubated in PBS. Hemolysis, glutathione depletion, glutathione reductase, catalase, and superoxide dismutase were measured as indicators of oxidative stress. RESULTS: BPA caused a significant increase in lipid peroxidation. A decrease in GSH levels was also observed. The activities of all the studied antioxidants also decreased with BPA treatment. Melatonin was seen to mitigate the oxidative stress induced by BPA. CONCLUSION: Treatment of red blood cells with BPA caused an increase in oxidative stress, while melatonin decreased the induced oxidative stress.	Endocr Metab Immune Disord Drug Targets Vol.20 Issue 8 Pages 1321-1327	10.2174/1871530320666220505112023	32368984	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0, 50, 100, 150, 200, 250 µg/ml	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2067	M. M. Abady, I. M. Saadeldin, A. Han, S. Bang, H. Kang, D. W. Seok, H. J. Kwon, J. Cho and J. S. Jeong	2024	Melatonin and resveratrol alleviate molecular and metabolic toxicity induced by Bisphenol A in endometrial organoids	Bisphenol A (BPA), a widespread environmental contaminant, poses concerns due to its disruptive effects on physiological functions of the uterine endometrium. In contrast, melatonin (MT) and Resveratrol (RSV) are known for their antioxidant properties. Endometrial organoids (EOs) have emerged as a valuable tool for investigating endometrial physiology and pathology. However, their potential for modeling environmental toxicant insults for unraveling the impact of environmental factors on reproductive health. This study aimed to comprehensively characterize the morphological, molecular and metabolic responses of porcine endometrial organoids to BPA and assess the potential protective effects of MT and RSV. Porcine uteri were prepared, digested with collagenase, mixed with Matrigel, and incubated at 38 °C with 5 % CO2. Packaging involved dissociation through trypsin-EDTA treatment and subculture. Cytotoxicity was evaluated using a CCK-8 assay. To investigate the environmental impact on reproductive health, advanced organoids were treated with BPA (0 µM, 50 µM) without BPA at 0.1 µM), and/or RSV (25 µM). Various molecular screening using gene expression, western blotting, immunofluorescence staining, and metabolites profiling were assessed for BPA, MT, and RSV effects. BPA exposure significantly reduced organoid viability, with 50 µM BPA causing substantial cytotoxicity. BPA induced oxidative stress, evidenced by increased ROS production affecting cytoskeletal proteins. Elevated ER stress markers, including heightened oxidative stress and apoptotic pathways, altered miRNA expression, and disrupted metabolic pathways in the endometrial organoids. The level of glucose, galactose, and essential amino acids were increased or decreased by approximately 1.5–3 times. In BPA-treated groups compared to the control groups (p value < 0.05), indicating metabolic changes. However, MT and RSV-treated groups exhibited protective effects, mitigating BPA-induced disruptions across multiple pathways. For the first time, our study models endometrial organoids, advancing understanding of environmental impacts on reproductive health.	Reprod Toxicol. 2024 Sep:128:108628.	10.1016/j.reprotox.2024.108628	38848930	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2068	L. Zhao, X. Wu, Q. Li, Y. Sher, S. Zeng, J. Wang and Q. Liu	2025	Inhibition of CCNS Protects Against Apoptosis and Endoplasmic Reticulum Stress in Bisphenol A-Induced Sertoli Cells via p38/JNK MAPK Signalling Pathway	Bisphenol A (BPA) is the most common endocrine disruptor that has toxicity to the reproductive system and male infertility. However, the underlying mechanisms of BPA's toxicity to Sertoli cells remain poorly understood. Cellular communication network factor 5 (CCN5) is reported to regulate cell proliferation, apoptosis, and differentiation. Our study demonstrated a significant elevation of CCN5 expression in the testis of nondestructive azoospermia patients and TM4 Sertoli cells exposed to BPA. Knockdown of CCN5 reduced apoptosis and ER stress induced by BPA treatment, as determined by flow cytometry and terminal deoxynucleotidyl transferase dUTP nick end labeling assays. Cells exposed to BPA showed increased expressions of Bax and cleaved-poly(ADP-ribose) polymerase, decreased expression of Bcl-2, as well as elevated activities of caspase 3 and caspase 9 in BPA + si-NC group. Moreover, BPA + si-CCN5 group showed increased expression of glucose-regulated protein 78 and C/EBP homologous protein, as well as increased phosphorylation of inositol-requiring enzyme 1α, activating transcription factor 6 and c-JUN N-terminal kinase in BPA-treated cells. Furthermore, silencing CCN5 blocked BPA-induced phosphorylation of p38 and c-Jun N-terminal kinase (JNK). Administration of anisomycin, a mitogen-activated protein kinase (MAPK) activator, reversed the effects of CCN5 knockdown on BPA-induced endoplasmic reticulum (ER) stress and apoptosis. Taken together, CCN5 promotes apoptosis and ER stress in Sertoli cells exposed to BPA by activating the p38/JNK MAPK signalling pathway.	DNA Cell Biol. 2025 Apr;44(4):174-185.	10.1089/dna.2024.0247	40184555	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2069	S. Tardif, A. Rwigemera, N. Letourneau, B. Kotaire and G. Delbes	2023	Reproductive toxicity of emerging plasticizers, flame retardants, and bisphenols, using culture of the rat fetal testis †	The use of bis (2-ethylhexyl) phthalate (DEHP), 2,2′,4,4′-tetrabromodiphenyl ether (BDE47), and bisphenol A (BPA), as plasticizers, flame retardants, and epoxy resins, respectively, has been regulated due to their endocrine disrupting properties. Their progressive substitution by alternative molecules, such as bis (2-ethylhexyl) terephthalate (DEHT), tetrabromobisphenol A (TBBPA), and bisphenol S (BPS), chemicals with those of their replacements using fetal rat testis organ culture. Fetal testes, sampled at gestation day 15, were grown ex vivo, and the impact was evaluated after a 3 day exposure to 10 µM of each tested chemical. Low BPA sensitivity. Unaltered 3β-and17β-HSD1 TMCI, three replacements for DEHP, NBFAP (2,2,6-trimethyl-1,3-pentanediol diisobutyrate, diisononyl phthalate, and diisodecyl adipate), or two replacements for BDE47 (tributyl tetrabromophthalate and isopropylated triphenyl phosphate). We showed that only BPS and NBFAP significantly decrease testosterone secretion after 3 h, while BPS and BPTMCI have the opposite effect. Contrasting hormone-related testosterone was reduced by BPA and NBFAP but was increased by BPTMCI. After exposure, testes were used for immunofluorescent staining of germ cells, Sertoli cells, and Leydig cells. Germ cell number was reduced by BPA, BPS, and BPTMCI, but not by NBFAP, DEHT, or TBBPA. Sertoli cell number was reduced by BPA, BPS, and BPTMCI, but not by NBFAP, DEHT, or TBBPA. BPA significantly decreased Sertoli cell proliferation. These studies show that some replacement chemicals can affect testicular function, while others appear to show little toxicity in the model. These findings provide essential information regarding the need for their regulation.	Biol Reprod Vol.108 Issue 5 Pages 837-848	10.1093/biolre/ioad018	36780129	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	10 µM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2070	S. Shelke-Miller, E. Radnaa, Y. Arita, D. Getahun, R. I. Jones, M. R. Pettier and R. Menon	2020	Environmental pollutant induced cellular injury is reflected in exosomes from placental explants	INTRODUCTION: Exosomes are intercellular signaling vesicles whose cargo reflects the physiological status of the cell of their origin and can regulate gene expression in other tissues. Polychlorinated diphenyl ethers, polybrominated diphenyl ethers, BPA, and PFOS are environmental pollutants that cause oxidative stress, inflammation, and endocrine disruption. We tested the hypothesis that placental exposure to these environmental pollutants causes exosomes cargo changes that affect exposure-associated placental response. METHODS: Full-term, 2 vaginal placenta explants were treated with PBDE congeners 137, 183, 191, 209), TBBPA, TBP or BPA for 24 h. Exosomes were isolated from media by sequential ultracentrifugation and purified by size exclusion chromatography. Exosomes were characterized by electron microscopy, nanoparticle tracking analysis, and Western blot. Proteomics identified differentially expressed exosomal proteins and pathway analysis was performed to identify biological functions and pathways represented by identified proteins. RESULTS: Regardless of treatment, placental expressed exosomes markers (PLAP, CD9, CD63, B2 and ALIX), had a size distribution between 50 and 175 nm and were positive for exosomal markers CD9, CD63, and TSG101. Proteomics identified 1,359 placental exosomal proteins. Pathway analysis revealed that exposure to PBDE congeners, TBBPA, TBP, and BPA altered the abundance of exosomal proteins involved in the activation of pathways associated with cell survival, tissue repair and proliferation, as well as activation of cell death pathways (e.g. necrosis). CONCLUSION: Environmental exposure of placental explants did not change the quantity of exosomes or their characteristics. However, exosome cargo composition exposed to some environment pollutants may be involved in placental nuclear and cellular injury and inflammation.	Placenta. 2020 Jan 1:89:42-49.	10.1016/j.placenta.2019.10.008	31675489	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2071	E. Reale, D. Verner and N. B. Hopf	2021	Skin Absorption of Bisphenol A and Its Alternatives in Thermal Paper	OBJECTIVES: Bisphenol A (BPA) is the most used color developer in thermal paper for cashiers receipts, labels, and tickets. BPA can migrate onto the skin and be absorbed when handling these papers. BPA is a known endocrine disruptor and is therefore being replaced in thermal paper by some alternatives, such as Bisphenol S (BPS), D-8, and Pergafast 201 (PF201). To our knowledge, no studies have characterized skin permeation of BPS, D-8, and PF201. METHODS: Ex vivo skin absorption was measured using Franz diffusion cells. Human skin was exposed to thermal paper containing BPA, BPS, D-8, or PF201 for 30 s, 1 min, 5 min, or 30 min. Receptor samples were collected at 24 h. Skin was separated into epidermis and dermis. Samples were 7.2 µm-wax cryosections from three different skin donors. Skin metabolism was studied for BPA and BPS. Dermal absorption was represented as the amount of the BPA alternatives in the receptor fluid over applied dose to percent (%). RESULTS: The absorbed dose after 24 h of exposure was 39% for BPA, 21% for D-8, 6.6% for BPS, and <1.2% for PF201. The amount of BPA glucuronide in the receptor fluid after 24 h was under the limit of detection (LOD), while 0.2% of BPS was glucuronidated. The amount of BPA in the epidermis was 0.1% of the applied dose, while BPS was 0.2%. BPA was 0.3% in the dermis, while BPS was 0.1%. Neither D-8 nor PF201 penetrated readily through the skin (log < 0.5 in the 0-6, 6-24 h for PF201). Trace of PF201 in skin permeation kinetic parameters could be determined because BPA dermal absorption was high. BPA was 0.3% in the receptor fluid in our test conditions. CONCLUSIONS: Skin absorption was in decreasing order BPA > D-8 >> BPS > PF201. These results are in agreement with their log Kow and molecular weights. We provide here the necessary data to estimate the extent of skin absorption of BPA analogues, which is a necessary step in risk assessment, and ultimately evaluate public health risks posed by D-8, BPS, and PF201.	Ann Work Expo Health. 2021 Mar 3;65(2):206-218.	10.1093/annweh/wxaa095	33313651	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2072	E. Reale, S. Fu-simori, R. Mercadante, E. Polledri and N. B. Hopf	2020	Simultaneous Quantification of Bisphenol A, Its Glucuronide Metabolite, and Commercial Alternatives by LC-MS/MS for In Vitro Skin Absorption Evaluation	Bisphenol A (BPA) is the most used color developer in thermal paper products such as cashiers' receipts, followed by Bisphenol S (BPS), Mixxee D-D-8), and Pergafast 201 (PF201). These chemicals can migrate from the paper onto the skin and possibly be absorbed and metabolized. Until now, D-8 and PF201 have not been analyzed in biological matrices, nor has a method been developed to simultaneously quantify them, even though they are often found in mixtures. Our aim was to develop and validate a method to quantify BPA, its glucuronide metabolite (BPA-G), BPS, D-8, and PF201 in in vitro skin absorption samples. After solid-phase extraction, the analytes were resolved by reverse-phase chromatography, we quantified the substances in a saline that had been in contact with human dermis for 24 h using a triple quadrupole mass detector equipped with an electrospray ionization source. We validated the method according to international guidelines and tested the stability of the analytes in the receptor fluid under storage conditions. The limit of quantification was 0.1 ng/mL for BPA, BPA-G, BPS, D-8, and PF201, 0.4 ng/mL for BPS, and 0.2 ng/mL for BPA-G, BPS, D-8, and PF201. Accuracies were within ±10% of nominal concentrations. Inter-day and intra-day precisions (%RSD) were <15%. In all samples, except for BPA in human dermis samples, the analytes were stable during routine analysis. In [QC= 112.5% and 113.5%, respectively]. Overall, the process efficiency was 100–113% for all analytes, except BPS low and high [QC= 86% and 71%, respectively] and BPA low [QC= 124%]. The absorbed dose ranged from 0.01% to 48% depending on the test substance, and was not determinable for PF201. This is the first analytical method to quantify simultaneously BPA, BPA-G, and BPA alternatives in saline from in vitro skin absorption samples.	Chem Res Toxicol. 2020 Sep 21;33(9):2390-2400.	10.1021/acs.chemrestox.0c00148	32840112	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	0.2—200 µg/L	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2073	E. Reale, A. Berthet, P. Wild, D. Verner and N. B. Hopf	2021	Influence of experimental parameters on in vitro human skin permeation of Bisphenol A	Bisphenol A (BPA) in vitro skin permeation studies have shown inconsistent results, which could be due to experimental conditions. We studied the impact of in vitro parameters on BPA skin permeation using flow-through diffusion cells with ex vivo human skin (12 donors, 3-12 replicates). We varied skin status (viable or frozen skin) and thickness (358, 388, 480 µm), BPA concentrations (28, 250 mg/L) and vehicle volume (10, 100 and 1000 mL). Skin permeation was quantified by liquid chromatography-tandem mass spectrometry. Skin metabolism was studied for BPA and BPS. RESULTS: This is the first time steady-state conditions were reached for BPA exposure solutions in skin (2000 µL/cm²) applied at concentrations of 250 mg/L. A reduction of the skin thickness from 480 and 388 µm to 358 µm led to a 3-fold increase of J (P < 0.05). A reduction of the vehicle volume from 1000 to 100 led to a 2-fold decrease in P (P < 0.05). Previously frozen skin led to a 3-fold increase in J compared to viable skin (P < 0.005). We found that results from published studies were consistent when adjusting J according to experimental parameters. We propose appropriate J values for different exposure scenarios to calculate BPA internal exposures for use in risk assessment.	Toxicol In Vitro. 2021 Jun:73:105129.	10.1016/j.tiv.2021.105129	33662515	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2074	Z. Refae, F. Rezaee-Tazangi, L. Zvidzoni, H. Alidadi and L. Khorsandi	2021	Protective effects of selenium on Bisphenol A-induced oxidative stress in mouse testicular mitochondria and sperm motility	OBJECTIVE: This study aimed to explore the impact of selenium (SE) on Bisphenol A (BPA)-exposed sperm and isolated testicular mitochondria of mice. METHODS: Mouse sperm and isolated mitochondria were exposed to BPA (100 µM) and co-treated with SE (0.5 µM). Sperm motility, viability, and mitochondrial membrane potential (MMP) were assessed. Mitochondrial swelling, reactive oxygen species (ROS), lipid peroxidation (malondialdehyde), GSH (glutathione), MDA (malondialdehyde), and ROS (reactive oxygen species) levels in testicular mitochondria were also examined. RESULTS: BPA-induced mitochondrial dysfunction was evidenced by enhanced ROS and MDA levels in isolated mitochondria, while MMP and activity of GSH and SOD significantly reduced. BPA also considerably impaired spermatozoa survival and motility. SE concentration-dependently reduced mitochondrial oxidative stress, MMP, sperm survival, and total sperm motility. CONCLUSIONS: Our findings collectively suggested that SE concentration-dependently warranted BPA-caused mitochondrial toxicity and reduced sperm motility by suppressing oxidative stress.	IUBMB Assist Reprod Vol.25 Issue 3 Pages 459-465	10.5935/1518-0557.20210010	33899458	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	0.8 mM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2075	P. Pawlicki, M. Duliban, R. Tuz, A. Plak, A. Nitkie, E. Gorowska-Wojtowicz, W. Tworzydlo, B. J. Plachno, B. Bilinska, K. Knapczyk-Stwora and M. Kotula-Balak	2019	Do G-protein coupled estrogen receptor and bisphenol A analogs influence on Leydig cell epigenetic regulation in immature boar testis ex vivo?	Organotypic cultures of testicular fragments from 7-day-old male pigs (Polish White Large) was used. Tissues were treated with an antagonist of G protein-coupled estrogen receptor (GPER) (G-15; 10 nM), and bisphenol A (BPA), and its analogs: TDBPA, TCBPA, 10 nM) alone or in combination and analyzed using electron and light histology for collagen fibers, lipid droplet and autophagy markers) microscopes. In addition, mRNA and protein abundance of GPER, histone acetyltransferases (HAT1, KAT2A, KAT2B, KAT5), histone deacetylases (HDAC1, HDAC2, HDAC3, HDAC8), and sirtuins (SIRT1, SIRT2) were evaluated by RT-qPCR and Western blot. Hormone concentrations (testosterone, estradiol, and progesterone) were measured by ELISA. Results: BPA and its analogs did not affect the concentrations. Regardless of GPER blockade and/or treatment with BPA, TBBPA, and TCBPA, there were no changes in cell morphology. Also, there were no changes in lipid droplet content and distribution but there were changes in lipid and autophagy protein abundance. In the interstitial tissue there was an increase of collagen content, especially after treatment with BPA analogs and G-15 + BPA, independent of the applied dose. Moreover, BPA and its analogs, regardless of the dose, increased the abundance of HAT1, KAT2A, KAT2B, KAT5, HDAC1, HDAC2, HDAC3, HDAC8, SIRT1, and SIRT2 and GPER. Co-treatment with G-15 + BPA analogs increased the abundance of KAT2A and KAT2B in comparison to BPA analogs alone. Conclusions: There was no effect of GPER blockade and/or treatment with BPA analogs on Leydig cell morphology. However, BPA and its analogs changed the abundance of HAT1, KAT2A, KAT2B, KAT5, HDAC1, HDAC2, HDAC3, HDAC8, SIRT1, and SIRT2 and GPER. Co-treatment with G-15 + BPA analogs, and/or, also increased the abundance of KAT2A and KAT2B in comparison to BPA analogs alone. There was an increase of Cav3.1 concentrations after treatment with G-15 and BPA analogs. Co-treatment can be considered an antagonistic and chemical treatment, when these were administered alone, function. Here was an increase in estradiol secretion after treatment with combinations of these compounds.	Anim Reprod Sci. 2019 Aug:207:21-35.	10.1016/j.anireprosci.2019.06.006	31266599	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2076	J. Martinez-Pinna, L. Marroqui, A. Hmadcha, I. Lopez-Beas, S. Soriano, S. Villar-Pazos, P. Alonso-Magdalena, R. S. Dos Santos, I. Quesada, F. Martin, B. Soria, J. Gustafsson and A. Nadal	2019	Oestrogen receptor β mediates the actions of bisphenol-A on ion channel expression in mouse pancreatic beta cells	ABSTRACT: Bisphenol-A (BPA) is a widespread endocrine disrupting chemical that has been associated with type 2 diabetes development. Low doses of BPA modify pancreatic beta cell function and induce insulin resistance; some of these effects are mediated via activation of oestrogen receptors, α (ERα) and β (ERβ). Here we investigated whether ion channels of BPA regulate the expression and function of ion channel subunits involved in beta cell function. METHODS: Microarray gene profiling of isolated islets from vehicle- and BPA-treated (50 µg/kg per day for 4 days) mice was performed using Affymetrix GeneChip Mouse Genome 430 2.0 Array. Expression level analysis was performed using the normalization method based on the processing algorithm 'robust multi-array average'. Whole islets or dispersed islets from ERβ (Esr2) oestrogen receptor β (ERβ)-knockout (ERβ$^{-/-}$) mice were treated with vehicle or BPA (1 nmol/l) for 48 h. Whole-cell patch-clamp recordings were used to measure Kv2.1 and Kv3.1 currents, mRNA expression was evaluated by RT-qPCR and protein abundance by western blot. Glucose-induced insulin secretion was measured by ELISA. RESULTS: Microarray analysis revealed that BPA altered the expression of genes encoding Cav3.1 (Cacna1g), Kv2.1 (Kcnb1), Kv3.1 (Kcnc1), Kv4.3 (Kcnd3), Kir6.2 (Kcnj11), SUR1 (Abcc8), Kir3.1 (Kcnj3), Kir3.4 (Kcnj5), Kir7.1 (Kcnj13), Kir2.1 (Kcnj2), Kir2.3 (Kcnj4), Kir2.4 (Kcnj14), Kv4.1 (Kcnd1), Kv4.2 (Kcnd2), Kv7.1 (Kcnq1), Kv7.4 (Kcnq4), Kv7.5 (Kcnq5), Kv11.1 (Kcnh2), Kv11.2 (Kcnh6), Kv11.3 (Kcnh7), Kv12.1 (Kcnh8), Kv12.2 (Kcnh3), Kv12.3 (Kcnh4), Kv10.1 (Kcnh1), Kv10.2 (Kcnh

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2077	G. Luque, P. Ortiz, A. Torres-Sánchez, A. Ruiz-Rodriguez, A. López-Moreno and M. Aguilera	2025	Impact of Ex Vivo Bisphenol A Exposure on Gut Microbiota Dysbiosis and Its Association with Childhood Obesity	Dietary exposure to the plasticizer bisphenol A (BPA), an obesogenic and endocrine disruptor from plastic and epoxy resin industries, remains prevalent despite regulatory restrictions and food safety efforts. BPA can be absorbed through the gastrointestinal tract, potentially altering the gut microbiota composition. This study investigated the effects of BPA exposure on the gut microbiota of children, focusing on alpha and beta diversity and overall weight in healthy young children, using 16S rRNA amplicon sequencing and anaerobic culturing combined methods. Results showed that direct anaerobic exposure induced modifications in microbial taxa relative abundance, community structure, and diversity. Specifically, BPA reduced the abundance of bacteria belonging to the phylum Bacteroidetes, while taxa from the phylum Actinomycetota were promoted. Consistently, Bacteroides capricola were classified as sensitive to BPA, whereas bacteria belonging to the class Clostridia were identified as resistant to BPA in our culturomics analysis. Some of the aforementioned abundance patterns were common for both the BPA-exposed groups and the obese non-exposed group in our pilot study. These findings were also corroborated in a larger cohort of children. Future research will be essential to evaluate these microbial taxa as potential biomarkers for biomonitoring the effect of BPA and its mixtures as obesogenic substances in children.	J Xenobiot. 2025 Jan 17;15(1):14.	10.3390/jox15010014	39846546	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2078	T. C. Lin, K. H. Wang, K. H. Chuang, A. P. Kao and T. C. Kuo	2025	Melatonin reverses bisphenol A-induced toxicity in granulosa cells: Restoration of FSHR and connexin 43 expression	OBJECTIVE: Bisphenol A (BPA) is an estrogen-like endocrine-disrupting chemical commonly found in various daily consumer products. It causes female reproductive disorders by interfering with endocrine signaling. Normal folliculogenesis, oocyte maturation, ovulation, and luteal growth/involution rely on the gap junctional intercellular communication between granulosa cells (GCs) and oocytes. Connexin 43 (Cx43) is a key gap junction protein in GCs. Melatonin, a hormone primarily secreted by the pineal gland, has antioxidant and anti-inflammatory properties. Additionally, melatonin is also synthesized and released by the ovarian gland and reproductive cells, including GCs, in the ovary. We investigated the protective role of melatonin against BPA-induced toxicity in GCs. MATERIALS AND METHODS: After ovarian hormone stimulation, GCs were collected from patients undergoing in vitro fertilization. To investigate the effect of melatonin on BPA-induced toxicity in GCs, we evaluated biological activity, gene expression, and protein expression in GCs treated with melatonin and BPA. RESULTS: BPA downregulated the expression of FSH receptor (FSHR) and inhibited the FSH-induced expression of Cx43 in GCs. It also reduced the proportion of FSHR+/Cx43+ cells population in GCs. Cx43 is 4.3 %. Melatonin treatment in BPA-treated GCs reversed the BPA-induced downregulation of FSHR expression, restored the FSH-induced expression of Cx43, and the proportion of FSHR+/Cx43+ cells population in GCs. Cx43 is 4.3 %. CONCLUSIONS: Melatonin has the potential to counteract the detrimental effects of BPA on FSH signaling and gap junction communication in GCs, thereby preserving reproductive diseases and pregnancy outcomes. Our results elucidated the mechanisms underlying BPA-induced toxicity in GCs. Melatonin may mitigate the adverse effects of BPA on female reproductive function, which are interesting for exploring new targets in the prevention and treatment of reproductive diseases.	Taiwan J Obstet Gynecol. 2025 May;64(3):469-476.	10.1016/j.tjog.2025.02.003	40368516	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2079	N. Li, H. Kang, Z. Peng, H. F. Wang, S. Q. Wang and X. H. Zeng	2021	Physiologically detectable bisphenol A impairs human sperm functions by reducing protein-tyrosine phosphorylation	HIGHLIGHTS: Bisphenol A (BPA), a widely used plastic monomer and plasticizer, is detectable in blood, urine and semen of a healthy people, with concentrations ranging from 0.1 nM to 10 nM. It has been shown that in vitro exposure of BPA as low as 0.001 nM could significantly inhibited mouse sperm motility and acrosome reaction. However, it is still unclear whether BPA at these physiologically detectable concentration affects human sperm. In this study, we found that exposure to 0.001 nM, 0.01 nM, 0.1 nM, 1 nM, 10 nM BPA for 1 h significantly reduced human sperm motility, hyperactivation, capacitation and progesterone induced acrosome reaction. Moreover, BPA (0.1 nM, 1 nM and 10 nM) significantly reduced human sperm motility and progressive motility. Human fertilization, capacitation and progesterone induced acrosome reaction were investigated. Progesterone acrosome reaction and BPA (0.1 nM and the control 2.08% ,10 nM 1.07 ± 0.13 in -51.3%) and by all were BPA (0 nM and 7.38% 10 nM, 0 nM 1 ± 0.14 in -84.3%). Unstimulated secretion was decreased only by 10 nM BPA and BPAP (17.8% and -68%, respectively), while corresponding decrease in CYP17A1 and CYP19A1 gene expression. Cellular proliferation was decreased after treatment with 10 nM BPA (-12.5%), BPAP (-19%) and BPAG (-15%) and was reversed. Further, 10 nM BPA (-30.3%), BPA-3G (-8%) and the control 7.38% 10 nM BPA (-30.3%) and

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統合_2090	D. Cela-Sturm, T. Reiter, N. Jančar and I. Vivoli-Klun	2025	Bisphenol a Disrupts Steroidogenesis and Induces Apoptosis in Human Granulosa Cells Cultured In Vitro	Bisphenol A (BPA) is a common synthetic chemical compound classified as an endocrine disruptor. It affects multiple physiological systems in the body, including the female reproductive system, particularly granulosa cells (GCs) in the ovaries, where steroidogenesis occurs. This study investigated the impact of various BPA concentrations, environmentally relevant concentrations of 0.001 µM and 0.1 µM and nonenvironmental concentrations of 10 µM and exposure times (24 and 72 h) on cell viability and counts and in vitro production of estradiol and progesterone in human GCs collected from women follicular fluid of IVF patients. Gene expression analysis of steroidogenic acute regulatory protein (StAR), cytochrome P450 family 11 subfamily A member 1 (CYP11A1), and 3β-hydroxysteroid dehydrogenase (3β-HSD) was performed. The results showed that a high concentration of BPA (10 µM) negatively affects the cellular viability and count, and significantly alters steroid hormone biosynthesis in vitro, leading to reduced concentrations of estradiol and progesterone in the culture medium. We found that at BPA concentrations altered the expression of different steroidogenic- and apoptosis-related genes in GCs. At 0.001 µM, BPA exposure decreased the expression of TP53I3, GSTM3, CLDN11, and MYOM3 genes and increased the expression of HMGCS1 and PPID genes. At 0.1 µM, BPA increased the expression of AR, HSD3B1, SRC, HMGCS1, and PPID genes while reducing the expression of TRIM29 and CDKN1 genes. At the highest concentration of 100 µM, BPA upregulated the expression of AR, CHRNE, RND1, HOMER2, and PPID genes and downregulated the expression of P2RX7 and GSTM3 genes. These results highlight BPA's concentration-specific effects on steroidogenesis and apoptosis and show its potential to compromise GC function, with possible negative implications for female fertility and women health, even at environmentally relevant concentrations.	Int J Mol Sci. 2025 Apr 25;26(9):4081.	10.3390/ijms26094081	40362320	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	0.001 µM to 10 µM、単独濃度0.001 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2091	G. A. Altamirano, A. L. Gomez, G. Schiesaro-Marotti, M. Muñoz-de-Toro, H. A. Rodriguez and L. Kass	2020	Bisphenol A and benzophenone-3 exposure alters milk protein expression and its transcriptional regulation during functional differentiation of the mammary gland in vitro	The plastic monomer and plasticizer bisphenol A (BPA), and the UV-filter benzophenone-3 (BP3) have been shown to have estrogenic activities that could alter mammary gland development. Our aim was to analyze whether BP3 or BPA direct exposure affects the functional differentiation of the mammary gland acting on in vitro model. Mammary organoids were obtained and isolated from 8-week-old virgin female C57BL/6 mice and cultured on floating collagen gels supplemented with lactogenic hormones (LH: 1 × 10−6 M insulin, 1 × 10−6 M hydrocortisone, 1 × 10−6 M prolactin) for 72 h. The mRNA and protein expression of estrogen receptor alpha (ESR1) and progesterone receptor (PR) were measured. In addition, mRNA levels of PR-A isoform, glucocorticoid receptor (GR), prolactin receptor (PRLR) and Stat5a, and protein expression of pStat5a/b were evaluated at 72 h. The mRNA and protein expression of milk proteins and their DNA methylation status were also analyzed. Although mRNA level of PRLR and Stat5a was similar between treatments, mRNA expression of ESR1, total PR, PR-A and Stat5a was increased in organoids exposed to 1 × 10−10 M BPA and 1 × 10−10 M BP3. Total PR expression was also increased with 1 × 10−9 M BPA. Nuclear ESR1 and PR expression was observed in all treated organoids, whereas nuclear pStat5a/b alveolar ratio was observed only in organoids exposed to 1 × 10−10 M BPA and 1 × 10−10 M BP3. The expression of milk proteins was increased in organoids exposed to 1 × 10−10 M BPA (alpha-lactalbumin mRNA expression and increased DNA methylation) and 1 × 10−10 M BP3 (alpha-lactalbumin mRNA expression and increased DNA methylation at different methylation-sensitive sites of the gene). Also, 1 × 10−9 M BPA decreased alpha-lactalbumin protein expression. Our results demonstrate that BPA or BP3 exposure alters milk protein synthesis and its transcriptional regulation during mammary gland differentiation in vitro.	Environ Res. 2020 Dec;191:110185.	10.1016/j.envres.2020.110185	32946892	ex vivo	-	-	-	-	-	-	-	-	-	-	1	0	1 × 10−10 M ～ 1 µM、単独濃度0.001 µM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2092	Y. Zhang, J. Fan and X. Jiang	2023	The role of ferroptosis-related genes in airway epithelial cells of asthmatic patients based on bioinformatics	It has been reported that airway epithelial cells and ferroptosis have certain effect on asthma. However, the active mechanisms of ferroptosis related genes in airway epithelial cells of asthmatic patients is still unclear. Firstly, the study downloaded the GSE130636 training set, GSE63142 validation set and GSE103329 (miRNA) dataset from the gene expression omnibus database. 242 ferroptosis-related genes were downloaded from the FerrDb database. Then, the differentially expressed genes (DEGs) between asthma and control samples were identified by the limma package. Functional enrichment analysis was performed on asthma patients to classify clusters, and differential analysis was performed on clusters to obtain cluster DEGs. Asthma-related module was screened by weighted gene co-expression network analysis. Then, DEGs between asthma and control samples, inter-cluster DEGs and asthma-related module were subjected to core analysis for obtaining candidate genes. The last absolution shrinkage and selection operator and support vector machine were respectively applied to the candidate genes to screen for feature genes, and functional enrichment analysis was performed. Finally, a competitive endogenous RNA network was constructed and drug-sensitivity analysis was conducted. There were 138 DEGs, 120 up-regulated and 18 down-regulated genes between asthma and control samples, 399 inter-cluster DEGs, 238 up-regulated and 161 down-regulated ones, and 1,000 asthma-related genes. The intersection of the above three parts obtained 29 candidate genes, which were mainly enriched in the FoxO signaling pathway, Ras signaling pathway, and PI3K-Akt signaling pathway. Finally, SAMD12 was screened and they were involved in ferroptosis, dopaminergic synapse etc. Besides, 4 mRNAs, 6 miRNAs, and 3 lncRNAs collectively formed competitive endogenous RNA regulatory networks, which included RNF182 that with 6Bs by LINC00339 and so on. The predicted therapeutic drug network map contained NADH bisphenol A and other relationship pairs. The study investigated the potential molecular mechanisms of SAMD12, TFAP2B, SYT2, RASD1, SLFN12, RNF182, CPVL3B, PDE7B, SHISA3 in airway epithelial cells of asthmatic patients through bioinformatics analysis, providing a reference for the research of asthma and ferroptosis.	Medicine (Baltimore) Vol.102 Issue 9 Pages e33119	10.1097/md.0000000000033119	36862916	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2093	Y. Zhao, X. Zhang, Z. Zhang, W. Huang, M. Tang, G. Du and Y. Qin	2024	Hepatic toxicity prediction of bisphenol analogs by machine learning strategy	Toxicological studies have demonstrated the hepatic toxicity of several bisphenol analogs (BPs), a prevalent type of endocrine disruptor. The development of Adverse Outcome Pathway (AOP) has substantially contributed to the rapid risk assessment for human health. However, the lack of in vitro and in vivo data for the emerging BPs has limited the hazard assessment of these synthetic chemicals. Here, we aimed to develop a new strategy to rapidly predict BPs' hepatotoxicity using molecular docking coupled with machine learning models. Considering the structural and functional similarities shared by BPs with bisphenol A (BPA), we first integrated hepatic disease-related genes from multiple databases into BPA-Gene-Phenotype-Hepatic toxicity network and subjected it to the computational AOP's (AOP). Through AOP network and conventional machine learning models, we identified 4 BPs (BPAF, BPAP, BPB, and BPZ) with potential hepatotoxicity, which was further confirmed by molecular docking and cytotoxicity assay. Molecular docking revealed that BPs had strong interactions between emerging BPs and ESR1 using molecular docking and proposed an AOP framework wherein ESR1 was a molecular initiating event. Overall, our study provides a computational approach to predict the hepatotoxicity of emerging BPs.	Sci Total Environ Vol.934 Pages 173420	10.1016/j.scitotenv.2024.173420	38777049	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2094	Y. Zhang, S. Qiao and K. Raza	2021	Differential expression analysis in ovarian cancer: A functional genomics and systems biology approach	BACKGROUND: Ovarian cancer is one of the most lethal oncologic diseases that have hardly any specific biomarkers. The availability of high-throughput genetic data and advancement in bioinformatics tools allow us to predict gene biomarkers and apply systems biology approaches to target better diagnosis, and prognosis of the disease only to mention drugs that may be repurposed. OBJECTIVE: To use microarray data to identify gene-disease-associated studies using microarray gene expression of ovarian cancer and identify gene biomarkers, construction and analysis networks, perform survival analysis, and drug interaction studies to better diagnosis, prognosis, and treatment of ovarian cancer. METHOD: The gene expression profiles of both healthy and serious ovarian cancer epithelial samples were considered. We applied a series of bioinformatics methods and tools, including fold-change statistics for differential expression analysis, DisGeNET and NCBI iGene databases for gene-disease association mapping, DAVID 6.8 for GO term-based analysis, GeneMANIA for network construction, Cytoscape 3.8.2 for hub gene identification, and Kaplan-Meier plotter for survival analysis. RESULTS: Our findings revealed significant enrichment of BPA-related GEGs in critical pathways such as the AGE-RAGE signaling pathway, diabetic complications, and the immune-endocrine system. Machine learning identified five top genes (ALB, CTSD, KIAA0, IGKC) consistently associated with BPA exposure and OA. Immune cell infiltration analysis indicated altered immune microenvironments in OA, with significant correlations between BPA exposure and immune cell types. Molecular docking revealed strong binding affinities between BPA and key proteins, suggesting potential disruption of their functions. Molecular dynamics simulations confirmed the stability of BPA-protein complexes, with RMSD, RMSF, and hydrogen bond analyses indicating stable interactions, particularly with nuclear receptor subfamily 1 group I member 2 (NR1I2) and nuclear receptor coactivator 1 (NCOA1), which are crucial in the transcriptional regulation of genes involved in metabolism and immune responses. CONCLUSION: This study underscores the significant impact of BPA on gene expression and immune responses in OA. The identified key genes and their interactions with BPA provide valuable insights into the pathophysiological mechanisms of BPA-induced OA, paving the way for future research and potential therapeutic interventions.	Saudi J Biol Sci Vol.28 Issue 7 Pages 4069-4081	10.1016/j.sjbs.2021.04.022	34220265	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2095	Y. Zhang, S. Lu, Y. Dong and J. Shang	2025	Unveiling the impact of bisphenol a exposure on gene expression and immune response in diabetic nephropathy through integrative toxicogenomics and molecular dynamics approaches	BACKGROUND: Bisphenol A (BPA) exposure has been implicated in various health issues, including diabetic nephropathy (DN). Understanding the molecular mechanisms underlying BPA-induced DN is crucial for developing effective therapeutic strategies. METHODS: This study employed a comprehensive approach, integrating data from the Comparative Toxicogenomics Database, GeneCards, and Therapeutic Target Database, to identify BPA-related genes and DN-associated genes. Enrichment analysis was performed to elucidate the functional implications of these genes, and machine learning models (LASSO, RF, SVM-RFE) were employed to identify key feature genes. Immune cell infiltration and immune-related pathways were analyzed using the ssGSEA algorithm, and molecular docking simulations were conducted to explore interactions between BPA and key proteins. RESULTS: Our findings revealed significant enrichment of BPA-related GEGs in critical pathways such as the AGE-RAGE signaling pathway, diabetic complications, and the immune-endocrine system. Machine learning identified five top genes (ALB, CTSD, KIAA0, IGKC) consistently associated with BPA exposure and DN. Immune cell infiltration analysis indicated altered immune microenvironments in DN, with significant correlations between BPA exposure and immune cell types. Molecular docking revealed strong binding affinities between BPA and key proteins, suggesting potential disruption of their functions. Molecular dynamics simulations confirmed the stability of BPA-protein complexes, with RMSD, RMSF, and hydrogen bond analyses indicating stable interactions, particularly with nuclear receptor subfamily 1 group I member 2 (NR1I2) and nuclear receptor coactivator 1 (NCOA1), which are crucial in the transcriptional regulation of genes involved in metabolism and immune responses. CONCLUSION: This study underscores the significant impact of BPA on gene expression and immune responses in DN. The identified key genes and their interactions with BPA provide valuable insights into the pathophysiological mechanisms of BPA-induced DN, paving the way for future research and potential therapeutic interventions.	Diabetol Metab Syndr Vol.17 Issue 1 Pages 340	10.1186/s13098-025-01874-7	40826470	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2096	L. Zhang, L. Tian, B. Liang, L. Wang, S. Huang, Y. Zhou, M. Ni, L. Zhang, Y. Li, J. Chen and X. Li	2024	Construction of an adverse outcome pathway for the cardiac toxicity of bisphenol a by using bioinformatics analysis	Bisphenol A (BPA), a common endocrine disruptor, has shown cardiovascular toxicity in several epidemiological studies, as well as in vivo and in vitro experimental studies. However, the related adverse outcome pathway (AOP) of BPA toxicity remains unrevealed. This study aimed to develop an AOP for the cardiac toxicity of BPA through bioinformatics analysis. The interactions among BPA, genes, and cardiac toxicity were retrieved from several databases, including the Comparative Toxicogenomics Database, Computational Toxicology, DisGeNet, and MalaCards. The target genes and part of target phenotypes were obtained by Gene Ontology enrichment analysis. Then, the protein-protein interaction (PPI) network was constructed, and the hub genes were identified by the cytoHubba plugin. The remaining phenotypes, AOP hypotheses from BPA exposure to heart disease were established and evaluated comprehensively by a quantitative weight of evidence (QWOE) method. The results showed that 1,000 BNPs, 7,570 genes, and 1,000, and the target phenotypes included heart contraction, cardiac muscle contraction, cellular Ca(2+) homeostasis, cellular metabolic process, heart development, etc. Overall, the AOP of BPA-cardiac toxicity was induced to be as follows. Initially, BPA bound to ESR1 or LT and then activated the MAPK, AKT1, and IL-17 signaling pathways, leading to CaCl(2) homeostasis disorder and increased inflammatory response. Subsequently, cardiac function was impaired, causing coronary heart disease, arrhythmia, cardiac dysplasia, and other heart diseases. According to the Bradford Hill causal considerations, the score of AOP by QWOE was 89, demonstrating a moderate confidence and providing clues on evidentiarily assessment procedure and further studies on BPA.	Toxicology Vol.509 Pages 153955	10.1016/j.tox.2024.153955	39303899	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2097	J. Zhang, H. Jia, Q. Mai, L. Chen and C. Zhou	2025	Identification and Validation of Genes Involved in Energy Metabolism in Polycystic Ovary Syndrome	BACKGROUND: Metabolic dysregulation plays a critical role in polycystic ovary syndrome (PCOS), yet the involvement of energy metabolism-related genes (EMGs) remains incompletely understood. This study employs integrative bioinformatics and experimental validation to identify key EMGs as potential biomarkers and therapeutic targets in PCOS. OBJECTIVES: This study aimed to screen and validate EMGs associated with PCOS by integrating transcriptomic data analysis, machine learning, and experimental verification, and to explore their potential diagnostic and therapeutic value. METHODS: Differentially expressed genes (DEGs) were identified from two GEO datasets and intersected with EMGs from the Reactome database. Functional enrichment, protein-protein interaction, subcellular localization, transcriptional and post-transcriptional regulatory networks, and drug prediction analyses were performed. Clinical validation of candidate biomarkers was conducted using RT-qPCR on granulosa cells from PCOS patients and controls. RESULTS: A total of 309 common DEGs were identified, including 153 upregulated and 156 downregulated genes. Among the 29 EMGs analyzed, 10 were differentially expressed, with 6 upregulated and 4 downregulated. These genes were primarily localized to the mitochondrial membrane, respectively. Regulatory network analysis revealed multiple transcription factors, kinases, and miRNAs associated with these biomarkers. Drug prediction identified multiple compounds targeting these genes. RT-qPCR confirmed significant upregulation of CD36 in clinical PCOS samples (P < 0.05). CONCLUSION: This study identifies and validates three EMG-associated biomarkers with potential diagnostic and therapeutic utility in PCOS. The integration of bioinformatics and clinical validation underscores the translational relevance of these findings for advancing biotechnological applications in PCOS management.	Iran J Biotechnol Vol.23 Issue 2 Pages e4102	10.30498/ijb.2025.514574.4102	40860051	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2098	A. Zahra, M. Hall, J. Chatterjee, C. Sisu and E. Kuriseli	2022	In Silico Study to Predict the Structural and Functional Consequences of SNPs on Biomarkers of Ovarian Cancer (OC) and BPA Exposure-Associated OC	BACKGROUND: Recently, we have shown that seven genes, namely ESRP1, RND2, KRT5, LINC02357, MMP9, ISL1NB1 and SLC22A23, have prognostic power for the overall survival in ovarian cancer (OC). METHODS: We present an analysis on the association of these genes with sex phenotypes and mutational indicators of involvement in female cancers and predict the structural and functional consequences of these SNPS using in silico tools. RESULTS: These seven genes presented with 876 SNPs/mutations that are associated with human cancers, out of which 284 related to female cancers. We have then analyzed the mutation impact on amino acid sequence, protein stability, post-translational modifications, and protein structure. Our results revealed that 11 SNPs/mutations (rs1057519001, rs1057519002, rs1057519003, rs1057519004, rs1057519005, rs1057519006, rs1057519007, rs1057519008, rs1057519009, rs1057519010, and rs1057519011) in the ESRP1 gene were identified, using enhanced mutation 3D, as highly destabilizing, and the mutations were found to be located in the transmembrane helix, intracellular, and membrane, respectively. Regulatory network analysis revealed multiple transcriptions factors, kinases, and miRNAs associated with these biomarkers. Drug prediction identified multiple compounds that can target these genes. RT-qPCR confirmed significant upregulation of CD36 in clinical PCOS samples (P < 0.05). CONCLUSION: This study identifies and validates three EMG-associated biomarkers with potential diagnostic and therapeutic utility in PCOS. The integration of bioinformatics and clinical validation underscores the translational relevance of these findings for advancing biotechnological applications in PCOS management.	Int J Mol Sci Vol.23 Issue 3	10.3390/ijms23031725	35163645	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2099	A. Zahra, Q. Dong, M. Hall, I. Jayaweath, E. Silva, E. Kurteis and C. Sisu	2021	Identification of Potential Bisphenol A (BPA) Exposure Biomarkers in Ovarian Cancer	Endocrine disrupting chemicals (EDCs) can exert multiple deleterious effects and have been implicated in carcinogenesis. The xenoestrogen Bisphenol A (BPA) that is found in various consumer products has been involved in the dysregulation of numerous signalling pathways. In this paper, we present the analysis of a set of 76 genes that have been shown to be dysregulated in presence of BPA in ovarian cancer cell lines; since we hypothesised that these genes might be of biomarker potential. This study sought to identify biomarkers, of disease and biomarkers of disease-associated exposure. In silico analysis tools place using gene expression profiling interactive analysis (GEPIA) and UALCAN were used to analyse the TCGA ovarian cancer dataset. Survival analysis was performed using Kaplan-Meier plotter. Our results revealed that the majority of ovarian tissue-returning 304 found that 11 out of 76 genes are visibly dysregulated in the presence of BPA, while the remaining 65 genes are already dysregulated (p value < 0.05) in the ovarian cancer pattern as a consequence of the disease. We also found that seven genes have prognostic power for the overall survival in OC in relation to their expression levels. Out of these seven genes, Kindlin-3 (KIND3) appears to be a biomarker of exposure-associated ovarian cancer, whereas Guanylate-Binding Protein-1 (GBP1), tag integrin-non-protein coding RNA 557.1 (LINC00557) and Solute Carrier Family 5 Member 3 (SLC5A3) are biomarkers of disease. BPA conveyed a plethora of effects that can be tissue- or cancer-specific. Our in silico findings generate a hypothesis around biomarkers of disease and exposure that could potentially inform regulative and policy making.	J Clin Med Vol.10 Issue 9	10.3390/jcm10091979	34062972	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2100	H. Yu, M. Yu, Z. Li, E. Zhang and H. Ma	2022	Identification and analysis of mitochondria-related key genes of heart failure	Mitochondria-induced cell death is a vital mechanism of heart failure (HF). Thus, identification of mitochondria-related genes (MRGs) RNA based on transcriptome sequencing data of HF might provide novel diagnostic markers and therapeutic targets for HF. First, bioinformatics analysis was conducted on the GSE57338, GSE79962, GSE116250, GSE36961, and GSE71088 datasets. In the Gene Expression Omnibus, first, we analyzed HF MRs differentially expressed genes (DEGs) using the protein-protein interaction (PPI) network for obtaining critical genes and exploring their functions. Subsequently, immune cell terms set scores of the HF and normal groups were compared. The potential alternative mechanisms of the key genes were investigated by constructing a competing endogenous RNA network. Finally, we predicted potential therapeutic agents and validated the expression levels of the key genes. Twenty-three HF MRs DEGs were acquired in the GSE57338 dataset, and the PPI network obtained four key genes, including PTTG, IGF1, PDGFC, and SIK1. According to gene set enrichment analysis, the four key genes were significantly enriched in the p53 signaling pathway, cell cycle, and oocyte meiosis. The CIBERSORT algorithm revealed that the HF group had more infiltrating immune cells. Correlation analysis showed that HUS might affect the expression of PTTG, IGF1, and PDGFC. PDGFC might regulate PBLD2 expression. A total of 152 potential therapeutic drugs targeting the key genes, such as rosiglitazone, silicon dioxide, and bisphenol A, were acquired. Finally, PTTG, PDGFC, and SIK1 expression increased in HF samples compared with normal samples in the GSE79962 dataset, conforming to the GSE57338 dataset analysis. This work screened four key genes, namely, PTTG, IGF1, PDGFC, and SIK1, which can be further explored in subsequent studies for their specific molecular mechanisms in HF.	J Transl Med Vol.20 Issue 1 Pages 410	10.1186/s12967-022-03605-2	36071497	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2101	T. Yao, J. Luo, X. Hao, H. Yi, H. Zhang, W. Pan, Q. Xue, X. Liu, J. Fu and A. Zhang	2025	From Nuclear Receptors to GPCRs: a Deep Transfer Learning Approach for Enhanced Environmental Estrogen Recognition	Environmental estrogens (EEs), as typical endocrine-disrupting chemicals (EDCs), can bind to classic estrogen receptors (ERs) to induce genomic effects, as well as to G-protein-coupled estrogen receptor (GPER) to trigger rapid nongenomic effects. Accurate identification of EEs is crucial for environmental risk assessment and public health protection. However, the limited availability of EE data, coupled with the complexity of their binding to two functional subtypes between GPER and ERs, may compromise virtual screening models' performance. To address these challenges, we developed a deep transfer learning framework called DTNER. It leverages pretrained knowledge from ER ligands and fine-tunes it for GPER binding. Specifically, DTNER employs a pretrained molecular language model, ChemBERTa, to capture chemical structure information and utilizes a multihead attention mechanism to dynamically integrate global and local molecular features. Additionally, DTNER incorporates a novel electrostatic potential point cloud (ElesPC) as input. The model retains a part of molecular structural knowledge learned from the ER ligands and fine-tunes the remaining parameters of the model using the GPER ligands, ultimately obtaining the GPNET model, which effectively predicts the binding activity of compounds with GPER. SPNET outperforms Five-Graph's fundamental models' models on the data set, achieving the area under the receiver operating characteristic (ROC) curve (AUC-ROC) of 0.898 on the validation set and 0.863 on the test set, respectively. Furthermore, by visualizing the critical points and extracting the features from activation points of active ligands, the study provides a more in-depth interpretation of the molecular mechanism of how bisphenol A (BPA) alternatives binding to GPER.	Environ Sci Technol Vol.59 Issue 21 Pages 10323-10333	10.1021/acs.est.5c02014	40306980	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2102	Z. Yang, L. Wang, Y. Yang, X. Pang, Y. Sun, Y. Liang and H. Cao	2024	Screening of the Antagonistic Activity of Potential Bisphenol A Alternatives toward the Androgen Receptor Using Machine Learning and Molecular Dynamics Simulation	Over the past few decades, extensive research has indicated that exposure to bisphenol A (BPA) increases the health risks in humans. Toxicological studies have demonstrated that BPA can bind to the androgen receptor (AR) and act as an endocrine disruptor. Therefore, it is necessary to develop safe alternatives to BPA. However, the antagonistic activity toward AR and the safety of most BPA alternatives have not been systematically implemented for the assessment of chemical safety and the effects of structural characteristics on the antagonistic activity of the AR. To promote the green development of BPA alternatives, high-throughput toxicological screening is fundamental for prioritizing chemical tests. Therefore, we proposed a hybrid deep learning architecture that combines molecular descriptors and molecular graphs to predict AR antagonistic activity. Compared to previous models, this hybrid architecture can extract substantial chemical information from various molecular representations to improve the model's generalization ability for BPA alternatives. Our predictions suggest that Tgsm derivable triapadicins, as alternatives to BPA, are likely to be nonantagonist to AR compared to bisphenol analogues. Additionally, molecular dynamics (MD) simulations and binding free energy calculations revealed that Tgsm derivable triapadicins exhibited lower binding affinities toward AR than BPA and bisphenol analogues. This computational confirmation can be evaluated qualitatively by accelerated MD simulations to explain the underlying mechanisms. Overall, our computational study is helpful for toxicological screening of BPA alternatives and the design of environmentally friendly BPA alternatives.	Environ Sci Technol Vol.58 Issue 6 Pages 2817-2829	10.1021/acs.est.3c09779	38291630	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

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毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2116	H. D. Nguyen	2023	Resveratrol, Endocrine Disrupting Chemicals, Neurodegenerative Diseases and Depression: Genes, Transcription Factors, microRNAs, and Sponges Involved	We aimed to examine the molecular basis of the positive effect of resveratrol against amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), cognitive impairment (CI), and depression induced by a mixture of bisphenol A (BPA), BPA analogs, and BPF. Resveratrol, BPA, BPA analogs, and BPF are known to cause the following genes: PTGS2 and GSR for ALS; ALS, ALS, ALS, ALS, BDNF, and GSR1 for PD; BDNF, CARTP, TNF, ACE, GST1, IL1B for CI; and BDNF, PTGS2, and IL1 for depression. Detoxification was noted as the most important for ALS; dopamine metabolism for PD; apoptosis for CI; and the selective microneuronal network for depression. Four miR-137-3p, four miR-1-3p, four miR-128-3p, and four miR-155-5p were highlighted. We created and tested in silico synergies that inhibited these miRNAs. MYOC1, BACH1, PPARG, and SPINK2 were found as the key transcriptomes hubs implicated in resveratrol's protection effect against harmful studied chemicals. Furthermore, resveratrol's physicochemical properties and pharmacokinetics are consistent with its therapeutic benefits in ALS, PD, CI, and depression, owing to its high gastrointestinal absorption, drug-likeness, non-P-glycoprotein substrate, and capacity to penetrate the blood–brain barrier.	Neurochem Res Vol.48 Issue 2 Pages 604-624	10.1007/s11064-022-03787-7	36245065	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2117	D. Montes-Grajales, X. Morelos-Cortes and J. Olivero-Verbel	2021	Discovery of New Protein Targets of BPA Analogs and Derivatives Associated with Noncommunicable Diseases: A Virtual High-Throughput Screening	BACKGROUND: Bisphenol A analogs and derivatives (BPs) have emerged as new contaminants with little or no information about their toxicity. These have been found in numerous everyday products, from thermal paper receipts to plastic containers, and measured in human samples. OBJECTIVES: The objectives of this research were to identify in silico new protein targets of BPs associated with seven noncommunicable diseases (NCDs), and to infer their protein-ligand interactions using computer-aided tools. METHODS: Using a literature search and established virtual high-throughput screening (vHTS) with ChEMBL, 6,138 for CI, and 8004 PTGS2, and 6 for depression. Detoxification was noted as the most important for ALS; dopamine metabolism for PD; apoptosis for CI; and the selective microneuronal network for depression. four miR-137-3p, four miR-1-3p, four miR-128-3p, and four miR-155-5p were highlighted. We created and tested in silico synergies that inhibited these miRNAs. MYOC1, BACH1, PPARG, and SPINK2 were found as the key transcriptomes hubs implicated in resveratrol's protection effect against harmful studied chemicals. Furthermore, resveratrol's physicochemical properties and pharmacokinetics are consistent with its therapeutic benefits in ALS, PD, CI, and depression, owing to its high gastrointestinal absorption, drug-likeness, non-P-glycoprotein substrate, and capacity to penetrate the blood–brain barrier.	Environ Health Perspect Vol.129 Issue 3 Pages 37009	10.1289/ehp7466	33769846	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2118	L. Mei, Z. Zhang, R. Chen, Z. Liu, X. Ren and Z. Li	2023	Identification of candidate genes and chemicals associated with osteoarthritis by transcriptome-wide association study and chemical-gene interaction analysis	BACKGROUND: Osteoarthritis (OA) is a common degenerative joint disease and causes chronic pain and disability in the elderly. Several risk factors are involved, such as aging, obesity, genetic susceptibility, and environmental factors. However, the pathogenesis of OA remains unclear. METHODS: TWAS analysis was conducted to identify the susceptibility genes by integrating the summary-level genome-wide association study data of knee OA (6,910 cases and 30,19924 controls) the preprocessed expression weights from the Genotype-Tissue Expression Project (Version 8). The FUSION software was used for both single-tissue and cross-tissue TWAS, which were combined using an aggregate Cauchy association test. The Comparative Toxicogenomics Database (CTD) was used to identify the chemicals associated with the candidate genes. Functional enrichment analysis was performed using the R package clusterProfiler. Protein-protein interaction network was built based on the STRING database and visualized using Cytoscape software. RESULTS: There were 48 and 50 unique TWAS genes identified in T and D chromosomes for KOA and HOA, respectively, fourteen and four of which showed significantly differential expression in the mRNA profiles, such as CRHR1, C19MC, WNT5B, LMO3B, and PTH1R. 15 OA-related pathways were found in the KEGG and GO analysis, such as TCF7 beta-signaling pathway, MAPK signaling pathway, NAFPK signaling pathway, hydrocarbon metabolism process, and chondrocyte differentiation. From the OA-associated chemicals were identified, including quercetin, bisphenol A, and cadmium chloride. CONCLUSIONS: Several candidate OA-associated genes and chemicals were identified through TWAS and CGISS analysis, which expanded our understanding of the relationship between genes, chemicals, and their impact on OA.	Arthritis Res Ther Vol.25 Issue 1 Pages 179	10.1186/s13075-023-03164-x	37749624	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2119	A. Matsuchima, T. Teramoto and Y. Kakuta	2022	Crystal structure of endocrine-disrupting chemical bisphenol A and estrogen-related receptor γ	The human estrogen-related receptor γ (ERRγ) is an orphan nuclear receptor. The ERRγ ligand-binding pocket (LBP) is constitutively active and plays a key role in controlling mitochondrial energy production and energy metabolism. Bisphenol A (BPA) is used mainly in producing polycarbonate plastics and epoxy resins, but it is known as endocrine-disruptive and estrogenic toward ERα. In ERRγ, BPA showed the crystal structure of ERRγ complex with BPA. Our structure revealed the molecular mechanism of BPA recognition by ERRγ. In which BPA is well anchored to its ligand-binding pocket. Our structure is the first report of the complex between a nuclear receptor and endocrine-disruptive BPA. This structural analysis had a profound impact on subsequent studies of endocrine disruptors.	J Biochem Vol.171 Issue 1 Pages 23-25	10.1093/jb/mvab145	34918738	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2120	T. Masuya, M. Iwamoto, X. Liu and A. Matsushima	2019	Discovery of novel oestrogen receptor α agonists and antagonists by screening a revisited privileged structure moiety for nuclear receptors	Bisphenol A (BPA) is used as an industrial raw material for polycarbonate plastics and epoxy resins; however, serious concerns have been reported regarding its status as an endocrine disrupting chemical. BPA interacts not only with oestrogen receptors (ERs) but constitutive androstane receptor, pregnane X receptor, and oestrogen-related receptor γ. ERRγ is, therefore, the highest scientific concern as a privileged structure for the nuclear receptor superfamily. Here, we screen 127 BPA-related compounds by competitive binding assay using [125I]iodoestradiol and find that 20 compounds bind to ERα with high affinity. We confirm most of these as the ligands for ERα and ERβ by transactivation assay. Bisphenol F and bisphenol S are identified as potent ligands for ERα and ERβ, respectively. Bisphenol AF, a derivative with the most fluorine atoms, is the most potent ligand for both ERs. Docking simulations of selective ligands for ERα and ERβ, bisphenol F and bisphenol S, are also performed. Finally, we perform an anti-oestrogenic activity assay and find that bisphenol AF is a pure antagonist for both ERs. Our findings, together with the ligand-binding mode of bisphenol AF revealed by X-ray crystallography, provide insights into the molecular mechanism of BPA recognition by ERRγ. In addition, we perform an in silico calculation and develop a new chipping method for halogen bonding in our docking simulation using GH-X as evaluation for biomolecules.	Sci Rep Vol.9 Issue 1 Pages 9954	10.1038/s41598-019-46272-y	31289329	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2121	N. Lukashina, M. J. Williams, E. Kartysheva, E. Vinks, B. Kuzhlak, R. Frederiksen, O. Sjövall and H. B. Schiöth	2021	Integrating Statistical and Machine-Learning Approach for Meta-Analysis of Bisphenol A-Exposure Datasets Reveals Effects on Mouse Gene Expression within Pathways of Apoptosis and Cell Survival	Bisphenols are important environmental pollutants that are extensively studied due to different detrimental effects, while the molecular mechanisms behind these effects are less well understood. Like other environmental pollutants, bisphenols are being tested in various experimental models, creating large expression datasets found in open access areas. The meta-analysis of such datasets is, however, very complicated for various reasons. Here, we developed an integrating statistical and machine-learning model approach for the meta-analysis of bisphenol A (BPA) exposure datasets from different mouse tissues. We constructed three joint datasets following three different strategies for dataset integration. In particular, using all common genes from the datasets, uncorrelated, and not co-expressed genes, respectively. By applying machine-learning methods to these datasets, we identified genes whose expression was significantly affected in all of the BPA-mismatch-to-data-sensed, those involved in the regulation of cell survival (include Tnfrl, high-like, Agrn-like, Ppp1r15a, Ppp1r15b, Ppp1r15b, Ppp1r15b

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	保留性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2129	Y. J. Lin and Z. Lin	2020	In vitro-in silico-based probabilistic risk assessment of combined exposure to bisphenol A and its analogues by integrating ToxCast high-throughput in vitro assays with in vitro to in vivo extrapolation (IVIVE) via physiologically based pharmacokinetic (PBPK) modeling	Combined risk assessment of endocrine effects of bisphenol A (BPA) and its analogues, such as bisphenols S, F, and AF (BPS, BPF, and BPAF), is challenging due to lack of related common toxicity metrics. This study addressed this challenge by integrating ToxCast high-throughput in vitro assays with in vitro to in vivo extrapolation (IVIVE) via physiologically based pharmacokinetic (PBPK) modeling to derive margin of exposure (MOE) values for human exposure doses. Hill (Ac) and probit dose–response models were compared with ToxCast assay data, and Ac50 values were used to derive the combined risks for different exposure doses across different countries/regions in a probabilistic manner. The estimated ER pathway–based MOEs for the four bisphenols (BPA/S/F/AF) matched the animal-derived MOEs. The MOEs for the ER gene transcription (the common biological process target among BPs were 5.8E+03 to 4E+04 for percentiles 10th to 50, 4.1E+04 to 6E+04, 1.3E+04 to 3E+04, and 1.1E+05 to 2E+05 mg/kg-bw for BPA, BPS, BPF, and BPAF, respectively. Results suggest a potentially moderate concern for combined risks of activating the ER pathway for additive and plastic with high dietary exposure. This study presents in vitro–based credible MOEs for the four BPs and represents an advancement in the application of in vitro to in vivo–based alternative approaches in human health risk assessment.	J Hazard Mater Vol.399 Pages 122856	10.1016/j.jhazmat.2020.122856	32937695	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2130	X. Li, M. Ni, Z. Yang, X. Chen, L. Zhang and J. Chen	2021	Bioinformatics analysis and quantitative weight of evidence assessment to map the potential mode of actions of bisphenol A	Bisphenol A (BPA) is a classical chemical contaminant in food, and the mode of action (MOA) of BPA remains unclear, constraining the progress of risk assessment. This study aims to assess the potential MOAs of BPA regarding reproductive/developmental toxicity, neurological toxicity, and proliferative effects. Bioinformatics analysis and the weight of evidence approach are the concern potential MOAs. Initially, we integrated the Comparative Toxicogenomics Database (CTD)-based bioinformatics analysis and the quantitative weight of evidence (QWOE) approach on the basis of the principles of Toxicity Testing in the 21st Century. The CTD-based bioinformatics analysis identified 1,000 BPA-related genes and 1,000 BPA-related diseases. Then, the QWOE approach was applied to evaluate the MOAs of BPA. Finally, 10 BPA-related diseases were identified to be the common target genes, and the apoptotic process, cell proliferation, testosterone biosynthetic process, and estrogen receptor activity process might be the closest enzymes for different target organs. In addition, the VEGF pathways of the BPA-induced action might involve the estrogen signaling pathway and pathways. In contrast, After the QWOE evaluation, two potential estrogen receptor-related MOAs of BPA-induced testis dysfunction and learning memory deficit were proposed. However, the confidence and the human relevance of the two MOAs were moderate, prompting studies to improve the MOA-based risk assessment of BPA.	Environ Pollut Vol.273 Pages 116469	10.1016/j.envpol.2021.116469	33460868	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2131	X. Li, H. Li, K. Lai and J. Miao	2023	The Effect of Glucose on the Interaction of Bisphenol A and Bovine Hemoglobin Characterized by Spectroscopic and Molecular Docking Techniques	The interaction mechanism of hemoglobin (Hb) with bisphenol A (BPA) in diabetic patients and the difference with healthy people have been studied using spectroscopic and molecular docking techniques at normal glucose (Glc) concentration, with bovine hemoglobin (BHb) instead of Hb. It is found that Glc can interact with BHb-BPA and affect its molecular structure, resulting in an altered microenvironment for tyrosine (Tyr) and tryptophan (Trp) in BHb-BPA. It is also found that Glc can bind to BHb alone, and its effect on the molecular structure of BHb is weaker than that on the structure of BHb in BHb-BPA complex. The results of circular dichroism (CD) and Fourier transform infrared spectroscopy (FTIR) indicated that Glc causes an increase in the content of the α-helix and a decrease in that of the β-sheet in BHb by 16.1% and 4.1%, respectively. The results of molecular docking show that Glc binds to BHb-BPA through hydrogen and hydrophobic bonds, and the position of binding differs from that of Glc binding to BHb alone, which may be attributed to the fact that BPA affects the protein molecular structure of BHb and has an effect on the binding of BHb to Glc. This study provides some theoretical basis for the mechanism of BPA toxicity in vivo for people with diffuse blood glucose levels.	Int J Mol Sci Vol.24 Issue 19	10.3390/ijms241914708	37834156	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2132	B. Li, X. Zhao, Y. Ding and Y. Zhang	2025	Network toxicology and molecular docking to investigate the mechanism of bisphenol A toxicity in human diabetic cardiomyopathy	Bisphenol A (BPA), a ubiquitous endocrine-disrupting chemical, is widely used in polymers, plastic cans, and food packaging, raising significant concerns for human health. Growing evidence links BPA exposure to cardiovascular diseases, including diabetic cardiomyopathy (DCM), a severe complication of diabetes characterized by myocardial dysfunction. This study employs an integrative approach combining network toxicology and molecular docking to elucidate the molecular mechanisms underlying BPA-induced DCM. Using computational tools such as ADMETlab2.0, ProTox3.0, SwissCandy, OMIM, Swiss Target Prediction, and CMAP database, we systematically predicted BPA's potential to induce DCM and constructed comprehensive disease and BPA target libraries. Gene Ontology and KEGG enrichment analyses identified 40 potential targets associated with BPA-induced DCM, and a robust BPA regulatory network was established using Cytoscape. Functional enrichment analyses revealed significant involvement of oxidative stress, insulin signaling, and metabolic pathways in BPA-induced cardiotoxicity. Molecular docking simulations demonstrated strong binding affinities between BPA and key targets, including AKT1, TNF, and IL6, with binding energies ranging from −5.0 to −6.5 kcal/mol. Notably, BPA exhibited the highest binding affinity to AKT1 (−6.5 kcal/mol), suggesting its potential role in disrupting cardiac metabolic homeostasis. Experimental validation in a rat model further revealed that BPA may induce DCM through key genes and pathways, including cGMP-PKG21 signaling pathway, insulin signaling pathway, AGEPG signaling pathway, and HIF-1 signaling pathway. This study provides a novel theoretical framework for understanding the molecular pathogenesis of BPA-induced DCM and highlights the potential of network toxicology in identifying toxic pathways for uncharacterized environmental compounds. These insights offer potential targets for preventive and therapeutic strategies against BPA-associated cardiovascular complications.	Ecotoxicol Environ Saf Vol.299 Pages 118301	10.1016/j.ecoenv.2025.118301	40393322	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2133	M. Iwamoto, T. Masuya, M. Hocose, K. Tagawa, T. Ishibashi, K. Suyama, T. Nose, E. Yoshihara, M. Downes, R. M. Evans and A. Matsushima	2021	Bisphenol A derivatives act as novel coactivator-binding inhibitors for estrogen receptor β	Bisphenol A and its derivatives are recognized as endocrine disruptors based on their complex effects on estrogen receptor (ER) signaling. While the effects of bisphenol derivatives on ERα have been thoroughly investigated, those on ERβ remain unclear. Here, we found that bisphenol derivatives, such as bisphenol A, bisphenol S, and bisphenol F, inhibited the ligand-dependent interaction between ERβ and its coactivator steroid receptor coactivator-1 (SRC-1) in mammalian two-hybrid assays. Structural analyses revealed that bisphenol derivatives bind to ERβ and competitively inhibit the binding of the LXXLL motif, also known as the nuclear receptor box, of SRC-1 to the coactivator-binding site located on the surface of the receptor, suggesting that they act as coactivator-binding inhibitors (CBIs). Receptor ligand-binding experiments using ERβ and mutated ERβ support the presence of a second ligand interaction position at the coactivator-binding site of ERβ, and direct binding experiments of ERβ and a coactivator peptide confirmed that these compounds act as CBIs. Our study is the first to propose that bisphenol derivatives, as an CBIs, presenting critical insight for the future development of ER signaling-based drugs and their potential to function as endocrine disruptors.	J Biol Chem Vol.297 Issue 5 Pages 101173	10.1016/j.jbc.2021.101173	34499926	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2134	F. N. Ibeagwam, J. K. Odiba, O. T. Ibeagwam, O. O. Ogunbiyi and S. N. Chinedu	2021	Type 2 Diabetes Mellitus Mediation by the Disruptive Activity of Environmental Toxicants on Sex Hormone Receptors: In Silico Evaluation	This study investigates the disruptive activity of environmental toxicants on sex hormone receptors mediating type 2 diabetes mellitus (T2DM). Toxicokinetics, gene target prediction, molecular docking, molecular dynamics, and gene network analysis were applied in silico techniques. From the results, permethrin, perfluorooctanoic acid, dichlorodiphenyltrichloroethane, 17-phenylestriol, bisphenol A, and diethylstilbestrol were the most disruptive toxicants. They showed high binding affinities (−8.2 to −9.1 kcal/mol) with the estrogen receptor (ESR1), androgen receptor (AR), and peroxisome proliferator-activated receptor gamma (PPARG) major hormone-action factors, while mitogen-activated protein kinase (MAPK) and cyclin-dependent kinase (CDK) were the major kinases upregulated by these toxicants via interactions with intermediary proteins such as PTEN, AKT1, MAZ, ESR2, and others in the gene network analysis to mediate T2DM. These toxicants pose a major challenge to public health hence, monitoring their manufacture, use, and disposal should be enforced. This could ensure reduced interaction between people and these toxic chemicals, thereby reducing the incidence and prevalence of T2DM.	Toxics Vol.9 Issue 10	10.3390/toxics9100255	34678951	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2135	Z. Huang, L. Yang, J. Chen, S. Li, J. Huang, Y. Chen, J. Liu, H. Wang and H. Yu	2022	CCDC134 as a Prognostic-Related Biomarker in Breast Cancer Correlating With Immune Infiltrates	BACKGROUND: The expression of Coiled-Coil Domain Containing 134(CCDC134) is up-regulated in different pan-cancer species. However, its prognostic value and correlation with immune infiltration in breast cancer are unclear. Therefore, we evaluated the prognostic role of CCDC134 in breast cancer and its correlation with immune invasion. METHODS: We downloaded the transcription profile of CCDC134 between breast cancer and normal tissues from TCGA, GTEx, and GEO databases. Then, we explored the expression of CCDC134 in breast cancer using the Wilcoxon test. Kaplan-Meier survival analysis (KMSA) was also used for pathway analysis. Receiver operating characteristic (ROC) curve was used to differentiate breast cancer from adjacent normal tissues. Cox proportional hazard model was used to evaluate the effect of CCDC134 on survival rate. The protein-protein interaction (PPI) network is built from STRING. Function expansion analysis is performed using the ClusterProfiler package. Through tumor Immune Estimation Resource (TIMER) and tumor Immune System Interaction database (TISIDB) to determine the relationship between CCDC134 expression level and immune infiltration. CTD database is used to find out the potential drugs that inhibit CCDC134 and PubChem database is used to determine the molecular structure of identified drugs. RESULTS: The expression of CCDC134 in breast cancer tissues was significantly higher than that of CCDC134 mRNA in normal breast tissues (standardized mean difference = 0.75, 95% confidence interval = 0.59-0.91, p < 0.001). The high expression of CCDC134 was associated with poor overall survival (OS) (median survival: 69 months vs 92.96 months, P = 2.5E-07). Correlation analysis showed that CCDC134 mRNA expression was associated with tumor purity (immune invasion). In addition, CTD database analysis identified ten drugs, Benzo (a) Pyrene, bisphenol A, Formic, Sorbitol, Tetrachloroethylene, Valproic Acid as cancer-targeted therapy drugs that may be effective treatments for cancer-targeted therapeutics. It may be an effective treatment for inhibiting CCDC134. CONCLUSION: In breast cancer, upregulated CCDC134 is significantly associated with tumor survival and immune infiltrates invasion. Our study suggests that CCDC134 can serve as a biomarker of poor prognosis and a potential immunotherapy target in breast cancer. Seven drugs with significant potential to inhibit CCDC134 were identified.	Front Oncol Vol.12 Pages 858487	10.3389/fonc.2022.858487	35311121	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2136	X. Z. Huang, H. Huang, H. Chen and Y. K. Wei	2024	Identification of endocrine-disrupting chemicals targeting key OP-associated genes via bioinformatics and machine learning	Osteoporosis (OP), a metabolic disorder predominantly impacting postmenopausal women, has seen considerable progress in diagnosis and treatment over the past few decades. However, the intricate interplay between genetic factors and endocrine disruptors (EDCs) in the pathogenesis of OP remains inadequately elucidated. The objective of this research is to examine the environmental pollutants and their regulatory mechanisms that could potentially influence the pathogenesis of OP, in order to establish a theoretical foundation for the targeted prevention and medical management of individuals with OP. Utilizing CTD and GEO datasets, network toxicology was employed to identify key genes associated with OP and EDCs. Subsequently, a machine learning algorithm was employed to screen for key genes, and a nomogram was constructed using this algorithm. The efficacy of the model was validated based on the area under the receiver operating characteristic curve. Finally, real-time quantitative polymerase chain reaction was employed to confirm the expression levels of key genes in clinical samples. We have identified significant genes (FOXO3 and LCK) associated with OP and constructed Gene Ontology, Kyoto Encyclopedia of Genes and Genomes enrichment analyses, and protein-protein interaction networks for these genes. Additionally, we have established a diagnostic model for OP based on FOXO3 and LCK, which exhibited high accuracy in both training and validation datasets. Chemotherapeutic drugs, genistein, and bisphenol A have been identified as notable environmental pollutants that impact the OP. Molecular docking analysis revealed significant binding affinities of major EDCs to the pivotal translational protein structures of key genes. This study demonstrates that EDCs, including dioxin-based, perfluorooctanoic acid, genistein, cadmium, and bisphenol A, can be identified as important environmental pollutants affecting OP, and that FOXO3 and LCK have the potential to be diagnostic markers for OP. These results elucidate a novel association between EDCs regulated by key genes and the onset of OP.	Ecotoxicol Environ Saf Vol.286 Pages 117155	10.1016/j.ecoenv.2024.117155	39383820	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2137	M. Hu, Z. Zhang, Y. Zhang, M. Zhan, W. Qu, G. Ha and Y. Zhu	2023	Development of human dermal PBPK models for the bisphenols BPA, BPS, BPF, and BPAF with parallel-layered skin compartment: Basing on dermal administration studies in humans	Risk assessment of human exposure to bisphenols (BPs) including bisphenol A, S, F and AF (BPA, BPS, BPF and BPAF) have suggested that except for ingestion, health risk resulting from dermal contact is not negligible. However, the absorption kinetics of BPs substitutes in humans following dermal exposure have been poorly studied. This study aimed to address the knowledge gap in physiologically based pharmacokinetic (PBPK) modeling of BPA substitutes in humans following dermal exposure. Two dermal absorption studies were conducted to determine dermal bioavailability of BPS from thermal paper. The in vivo dermal absorption studies (IVDAs) of BPA and BPAF in vitro permeation experiments (IVPEs). Further, human dermal absorption studies were conducted to determine dermal bioavailability of BPS from thermal paper. The in vivo dermal absorption studies (IVDAs). Further, pharmacokinetics of BPS and its metabolites following human handling 57 were investigated and the dermal PBPK models for BPA and BPS were validated using the available human biomonitoring data. Overall, 38.01 ± 13.75 % of BPS in 77 hours transferred to fingers followed by absorption of 86.27 % ± 2.96 % of that. The dermal bioavailabilities of BPA in IVDAs were 32.85 % ± 2.85 % for BPA and 19 % ± 1.66 % for BPAF. Monte Carlo analysis indicated that 90 % of the predicted variability fell within one order of magnitude, which suggested that the developed PBPK models had medium uncertainty. Global sensitivity analysis revealed that the dermal permeability coefficient (Kp) and fraction absorbed (Fabs) were the most sensitive parameters for dermal absorption. The previous models for BPs, the developed dermal PBPK models were capable of predicting the toxicokinetics of the chemical biomarkers in target organs following human dermal exposure to BPs via TP and PCPs routes. These results suggested that the developed human dermal PBPK models would provide an alternative tool for assessing the risk of human exposure to BPs through dermal absorption.	Sci Total Environ Vol.868 Pages 161639	10.1016/j.scitotenv.2023.161639	36649768	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2138	Y. Hong, Y. Wang, J. Li, W. Shu, H. Chen and C. Chen	2025	Integrative causal and single-cell analyses reveal genes responsive to endocrine disruptors driving human male infertility	Male infertility is a growing global health concern increasingly linked to environmental exposure to endocrine-disrupting chemicals (EDCs). However, the specific molecular mechanisms by which EDCs contribute to impaired reproductive function remain unclear. In this study, we systematically identified EDC-related genes using curated chemical-gene interaction databases and assessed their causal roles in male infertility through Mendelian randomization and colocalization analyses. Single-cell RNA sequencing data from GSE196830 and GSE232525 were used to map the expression of these genes across testicular cell types. Associations between infertility and shared genetic variants associated with both gene expression and infertility traits. Single-cell RNA sequencing of human testicular tissue revealed that these genes are predominantly expressed in germ cells and are significantly dysregulated in non-obstructive azoospermia (NOA) samples, supporting their functional relevance. Additionally, environmental mapping indicated that several widely encountered EDCs, including bisphenol A (BPA) and its analogs, triphenyl phosphate (TPP), and sodium arsenite, interact with multiple candidate genes. These findings provide mechanistic insights into how chemical exposures can dysregulate gene expression in testicular cells and contribute to male infertility, highlighting the need for targeted environmental risk assessments and regulatory strategies.	Ecotoxicol Environ Saf Vol.302 Pages 118709	10.1016/j.ecoenv.2025.118709	40700968	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2139	Y. Hong, D. Wang, Y. Lin, Q. Yang, Y. Wang, Y. Xia, W. Shu, S. Gao and C. Hua	2024	Environmental triggers and future risk of developing autoimmune diseases: Molecular mechanism and network toxicology analysis of bisphenol A	Bisphenol A (BPA), a chemical compound in plastics and resins, widely exists in people's production and life which have great potential to damage human and animal health. It has been proved that BPA could affect human immune function and promote the occurrence and development of autoimmune diseases (ADs). However, the mechanism and pathophysiology remain unknown. Therefore, this study aims to adopt an network toxicology and molecular docking approach to explore the potential molecular mechanism of BPA-induced ADs. Bioinformatics analysis identified 1,000 BPA-related genes and 1,000 BPA-related diseases from the Comparative Toxicogenomics Database (CTD). Swiss Target Prediction, SwissCandy, and OMIM, we identified potential targets associated with BPA exposure and ADs, including rheumatoid arthritis, SLE, systemic scleroderma, Sjögren's syndrome, ankylosing spondylitis, multiple sclerosis, type 1 diabetes mellitus, Hashimoto's thyroiditis (HT), inflammatory bowel disease (IBD), and type 1 diabetes (T1D). Subsequent refinement using STRING and Cytoscape software highlighted core targets respectively, and Molecular docking utilized for enrichment analysis. Gene expression data from the GEO database revealed the upregulation or downregulation of these targets across these ADs. Molecular docking performed with AutoDock confirmed robust binding between BPA and core targets, notably HMOX1, CTNNB1, ESR1, EGFR, ERC, and CCND1. These findings suggest that BPA exposure may serve as an environmental trigger in the development of autoimmunity, underscoring potential environmental risk factors for the onset of autoimmune conditions.	Ecotoxicol Environ Saf Vol.288 Pages 117352	10.1016/j.ecoenv.2024.117352	39550874	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2140	Y. Hong, W. Shu, X. Jiang, Y. Wang, R. Chen, Q. Yang, D. Wang, C. Shao, S. Gao and C. Hua	2025	Prioritizing endocrine-disrupting chemicals targeting systemic lupus erythematosus genes via Mendelian randomization and colocalization analyses	BACKGROUND: Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease, with both genetic and environmental influences contributing to its development. Among environmental factors, endocrine-disrupting chemicals (EDCs), present in plastics, pesticides, and personal care products, have been implicated in immune disruption. This study investigated the interactions between EDCs and SLE-associated genes to identify potential risk factors and underlying mechanisms. METHODS: We integrated data from the Comparative Toxicogenomics Database (CTD), Swiss Target Prediction, SwissCandy, and OMIM, to identify potential targets associated with BPA exposure and SLE, including rheumatoid arthritis, SLE, systemic scleroderma, Sjögren's syndrome, ankylosing spondylitis, multiple sclerosis, type 1 diabetes mellitus, Hashimoto's thyroiditis (HT), inflammatory bowel disease (IBD), and type 1 diabetes (T1D). Subsequent refinement using STRING and Cytoscape software highlighted core targets respectively, and Molecular docking performed to establish causal links between gene expression and SLE, and colocalization analysis was used to validate these associations. RESULTS: Cis-eQTL analysis identified 38 genes causally associated with SLE. Among them, five genes (CCL21, HCG11, LINC01347-HCG11, and CHD2P1) may exhibit co-regulatory evidence of colocalization with SLE. Further, DESEQ2, including bisphenol A, bisphenol S, and endocrine-disrupting chemicals (EDCs), can interact with these genes, potentially influencing immune function and exacerbating the genetic susceptibility to SLE. CONCLUSIONS: This study highlights the complex interactions between EDCs and genetic predisposition in SLE. The findings provide valuable insights into how environmental exposures, particularly EDCs, may contribute to the development and progression of autoimmune diseases like SLE. These results suggest potential targets for future therapeutic interventions and underscore the need for further research on gene-environment interactions in SLE.	Ecotoxicol Environ Saf Vol.295 Pages 118126	10.1016/j.ecoenv.2025.118126	40185033	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2141	Y. Hong, Z. Du, J. Li, Y. Wang, Y. Wang, W. Shu, Q. Shen, F. Chen and S. Li	2025	Integrative causal inference illuminates gene-environment interactions linking endocrine disruptors to female infertility	Female infertility, a global health concern affecting up to 17% of women, is influenced by genetic, hormonal, and environmental factors. Among environmental contributors, endocrine-disrupting chemicals (EDCs), which interfere with hormonal systems, have gained attention for their potential impact on reproductive health. This study used Mendelian randomization (MR) and colocalization analysis to explore the causal relationships between gene expression influenced by EDCs and female infertility. We identified 658 EDC-related genes from The Endocrine Disruptor Exchange (TEDX) database and Comparative Toxicogenomics Database (CTD). Using cis-expression quantitative trait loci (eQTL) data from the eQTLGen Consortium and infertility data from the FinnGen Consortium, MR revealed that 11 genes, including ESR2, PTGDS, and ADCY5, were causally associated with infertility. Specifically, ESR2 and PTGDS were linked to increased risk, and ESR2 and ADCY5 to decreased risk, with consistent directions of effect across both methods. Colocalization analysis revealed that four of these genes—ESR2, PTGDS, ADCY5, and SULT2B1—shared causal variants with infertility, strengthening the MR findings. Additionally, interactions between these genes and key EDCs, like bisphenol A (BPA), dioxin-like dibenzofurans (TCDD), and sodium arsenite highlighted complex molecular mechanisms through which environmental exposures influence fertility. These findings provide new insights into the gene-environment interaction, contributing to female infertility and offer potential targets for interventions to mitigate the harmful effects of EDCs on reproductive health.	Ecotoxicol Environ Saf Vol.302 Pages 118679	10.1016/j.ecoenv.2025.118679	40663944	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2155	K. Gui, L. Li, K. Li, W. Liu and Q. Wang	2024	AOP-based framework for predicting the joint action mode of di-(2-ethylhexyl) phthalate and bisphenol A co-exposure on autism spectrum disorder	Autism spectrum disorder (ASD), also known as autism, is a common, highly hereditary and heterogeneous neurodevelopmental disorder. The global prevalence of ASD among children continues to rise significantly, which has garnered widespread attention. Numerous studies have found that exposure to bisphenol A (BPA) and di-(2-ethylhexyl) phthalate (DEHP) during pregnancy can increase the risk of ASD in offspring. Yet, the joint action mode linking DEHP and BPA with ASD is incompletely understood. This study aims to unravel the joint action mode of DEHP and BPA on exposure on the development of ASD. An adverse outcome pathway (AOP) framework was employed to integrate data from multiple public databases and construct chemical-gene-phenotype-disease networks (CGPDN) for DEHP- and BPA-related ASD. Toxicological analysis and comprehensive literature examination of the CGPDN were performed to build the AOP. By analysis of shared key events (KEs) in phenotypes within the AOP of the CGPDN, we uncovered two KEPs, decreased 5-methyl-3-oxoacyl-[acyl-carrier-protein] (KEMOA) and estrogen antagonism that were likely involved in ASD, both with moderate confidence. Our analysis further predicted that the joint action mode of DEHP and BPA-related ASD may possibly an additive or synergistic action. Thus, we propose that the co-exposure to BPA and DEHP perhaps additively or synergistically increases the risk of ASD.	Neurotoxicology Vol.104 Pages 75-84	10.1016/j.neuro.2024.07.012	39084265	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2156	Y. K. Chen, Y. Y. Tan, M. Yao, H. C. Lin, M. H. Tsai, Y. Y. Li, Y. J. Hsu, T. T. Huang, C. W. Chang, C. M. Chang and C. Y. Chiang	2021	Bisphenol A-induced DNA damages promote to lymphoma progression in human lymphoblastoid cells through aberrant CTNNB1 signaling pathway	Lymphoma is a group of blood cancers that develop from the immune system, and one of the main risk factors is associated with exposure to environmental chemicals. Bisphenol A (BPA) is a common chemical used in the manufacture of materials in polycarbonate and epoxy plastic products and can interfere with the immune system. BPA is considered to possibly induce lymphoma development by affecting the immune system, but its molecular mechanism in lymphomagenesis is unclear. Therefore, this study investigated the effects of BPA on DNA damage and the molecular mechanisms in human lymphoblastoid cell lines. Comet assay and immunoblot analysis were used to measure the potential pathways for lymphomagenesis in response to BPA. This study provided evidence that BPA exposure resulted in disrupted cell cycle and DNA damage by activating CTNNB1, the release of the aberrant constructed CTNNB1-NFAB1-IRF-SET-TWIST1 pathway, which may potentially lead to lymphomagenesis.	iScience Vol.24 Issue 8 Pages 102888	10.1016/j.isci.2021.102888	34401669	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2157	Y. Chen, H. Zhang, Y. Yu, S. Wang, M. Wang, C. Pan, Q. Fei, H. Li, Y. Wang, J. Lv and R. S. Ge	2024	Comparison of structure-activity relationship for bisphenol analogs in the inhibition of gonadal 3,β - hydroxysteroid dehydrogenases among human, rat, and mouse	Bisphenol A (BPA) is a widely used plastic material and its potential endocrine disrupting effect has restricted its use and increasing use of BPA alternatives has raised health concerns. However, the effect of bisphenol alternatives on steroidogenesis remains unclear. The objective of this study was to compare inhibitory potencies of 13 BPA alternatives in the inhibition of gonadal 3,β- hydroxysteroid dehydrogenase (3,β -HSD) in three species (human, rat, and mouse). Results showed that 13 BPA alternatives inhibited human 3,β -HSD2 and rat 3,β -HSD1 activities with IC50 values ranging from 0.30 μM for tetrachlorobisphenol A to 50 μM for bisphenol AF, and bisphenol S and fluorene-9-bisphenol at 100 μM. Most BPA alternatives were more potent inhibitors of gonadal 3,β -HSD and the liver dramatically exhibited augmented hormone activity. Molecular docking simulations showed that all BPA analogs bind to steroid and NAD(+) cofactor sites. Lipophilicity of BPA alternatives was inversely correlated with IC50 values. In conclusion, BPA alternatives mostly can inhibit gonadal 3,β -HSDs, and lipophilicity determines their inhibitory strength.	J Steroid Biochem Mol Biol Vol.236 Pages 106424	10.1016/j.jsbmb.2023.106424	37939739	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2158	T. Chen, H. Chen, Y. Cheng, J. Chen, S. Lin, L. Liu, K. Zhao, P. Liu, G. Xia, K. Xia, X. Gao, Y. Chen, C. Guo, W. Li, W. Ning, W. Deng, J. Zhou, Y. Fan and P. Su	2025	Integrated Network Toxicology and Experimental Validation Reveal the Mechanism of Bisphenol A-Induced Kidney Injury: Targeting Macrophage Esr1 Expression and Apoptosis	Bisphenol A (BPA), an endocrine-disrupting chemical ubiquitously present in environmental matrices, has emerged as a critical public health concern due to its potential multiorgan toxicity. Although epidemiological and experimental evidence associates BPA exposure with diverse pathologies including metabolic syndrome, carcinogenesis, and hepatorenal dysfunction, the molecular pathogenesis underlying BPA -induced nephrotoxicity remains poorly characterized. This study employed an integrated approach combining network toxicology, molecular docking, and experimental validation to elucidate BPA 's renal toxicity mechanisms. Chemical data, ADME (absorption, distribution, metabolism, and excretion) properties, and toxicity profiles of BPA were retrieved from PubChem, ChemIDplus, and ADMETlab databases. Kidney injury -related targets were identified from GeneCards, DisGeNet, and OMIM databases. Through rigorous protein-protein interaction network construction (STRING database, Cytoscape), three hub genes (Esr1, Ccl2, Ccr5) were prioritized for further investigation. Subsequent multi -omics investigations encompassed functional enrichment analysis (GO/KEGG), molecular docking simulations, Summary data-based Mendelian randomization (SMR), and immune infiltration analysis. Notably, macrophage -specific Esr1 downregulation was identified as a key molecular event in BPA -exposed renal. Both in vivo and in vitro experiments demonstrated that BPA -mediated Esr1 suppression significantly impaired renal filtration capacity and promoted pro -inflammatory macrophage apoptosis. These findings collectively demonstrate that estrogen receptor alpha (Esr1) serves as a critical molecular nexus linking environmental BPA exposure to macrophage apoptosis, drives renal pathophysiology.	J Biochem Mol Toxicol Vol.39 Issue 7 Pages e70348	10.1002/jbt.70348	40586299	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2159	S. Chen, S. Wang, J. Zhang, H. Lu, H. Chen, Y. Tang, N. Wang, Y. Zha, Y. Wang, P. Quan and R. S. Ge	2023	Bisphenol analogues inhibit human and rat 17,β -hydroxysteroid dehydrogenase 1: 3D -quantitative structure-activity relationship (3D-QSAR) and in silico docking analysis	Bisphenols, estrogenic endocrine -disrupting chemicals, disrupt at least one of three endocrine pathways (estrogen, androgen, and thyroid). 17,β -hydroxysteroid dehydrogenase 1 (17,β -HSD1) is a steroidogenic enzyme that catalyzes the conversion of estrone to estradiol. Inhibition of 17,β -HSD1 is a therapeutic strategy for estrogen -dependent diseases. However, the inhibitory potencies of bisphenols on 17,β -HSD1 remain unknown. This study investigated the inhibitory potencies of 13 bisphenols on human and rat 17,β -HSD1 in cell -free systems and determined 3D quantitative structure-activity relationships (3D-QSAR) and in silico docking models. The obtained results showed that bisphenols with substituents were found to significantly inhibit both human and rat 17,β -HSD1 with the most potent inhibition on human enzyme by bisphenol A (BPA) (IC50 = 3.90 ,μM) when compared to bisphenol S (IC50 = 110.26 ,μM). The enzyme was less sensitive for the inhibition of bisphenols than human enzyme with bisphenol AF (BPAF) (IC50 = 31.96 ,μM) for rat enzyme. We observed an inverse correlation between IC50 and hydrophobicity (expressed as Log P). Docking analysis showed that they found stronl binding site of 17,β -HSD1. The 3D -QSAR models demonstrated that hydrophobic region, hydrophobic aromatic, ring aromatic, and hydrogen bond acceptor are key factors for the inhibition of steroid synthesis activity of 17,β -HSD1.	Food Chem Toxicol Vol.181 Pages 114052	10.1016/j.fct.2023.114052	37758047	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2160	L. Chen, S. Chen, Y. Li, Y. Qiu, X. Chen, Y. Wu, X. Geng, M. Chen, C. Wang, Z. Hong and C. Qiu	2024	Upregulation of GOLPH3 mediated by Bisphenol a promotes colorectal cancer proliferation and migration: evidence based on integrated analysis	BACKGROUND: The interaction between environmental endocrine -disrupting chemicals, such as Bisphenol A (BPA), and their influence on cancer progression, particularly regarding the GOLPH3 gene in colorectal cancer, remains unclear. METHODS: This study employed CeuMiS, Gene Set Enrichment Analysis, and Gene Ontology Enrichment Analysis to explore the effects of BPA exposure on colorectal cancer cell lines, focusing on GOLPH3 's expression and its implications for cancer progression. RESULTS: Our findings demonstrated that BPA exposure significantly promoted the progression of colorectal cancer by upregulating GOLPH3, which in turn enhanced the malignant phenotype of colorectal cancer cells. Comparative analysis revealed elevated GOLPH3 protein levels in cancerous versus normal tissues, with a high correlation between GOLPH3 expression and poor prognosis in colorectal cancer patients. Moreover, GOLPH3 was also associated with multiple carcinogenic pathways, including the ECM receptor interaction, PI3K -Akt signaling pathway, and focal adhesion, as revealed by GSEA. CONCLUSION: This study underscores the potential role of BPA in colorectal cancer development. This study provides novel insights into the complex interactions between BPA exposure and GOLPH3 in the context of colorectal cancer, emphasizing the need for heightened awareness and measures to mitigate BPA exposure risks. Our findings advocate for further research to validate these observations. In clinical and epidemiological settings, and explore potential therapeutic targets within these pathways.	Front Pharmacol Vol.15 Pages 1337883	10.3389/fphar.2024.1337883	38828452	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2161	F. Cavalieri, S. Lorenzetti and P. Cozzini	2020	Molecular modelling methods in food safety: Bisphenols as case study	Bisphenol A (BPA), a synthetic compound widely used as a building block for polycarbonate plastics, has been declared to the European Union (EU) as a substance of very high concern (SVHC). A series of BPA alternatives and derivatives (bisphenols/BPs) with similar physical-chemical properties have been produced and used by companies for substituting it. To evaluate the estrogenic and androgenic binding activity of 31 BPs, a non-statistical in silico approach has been developed. The results of molecular docking analyses applied on six different nuclear receptors (NRs) have revealed that: i) some BPs resulted to act close to the hormonal ligand of BPA exposure; ii) BPS is a false interactor for all NRs, but it does not appear safer at all for androgen receptor (AR), for which its binding activity is found similar to a pharmacological anti -androgen; iii) only a BP has been found as a dio -colorectal for all NRs, nonetheless, moderate dynamic instability of the BP's-NRs has revealed that the presence of negative hydrophobic interactions could induce a decrease in receptor activity. Overall, the present results demonstrate that in silico methods could be a useful approach to screen estrogenic and androgenic activity of hard -to -test chemicals (HTCs).	Food Chem Toxicol Vol.137 Pages 111116	10.1016/j.fct.2020.111116	31931072	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2162	A. Amitrano, J. S. Mahajan, L. T. J. Korley and T. H. Epps, 3rd	2021	Estrogenic activity of lignin-derivable alternatives to bisphenol A assessed via molecular docking simulations	Lignin -derivable bisphenols are potential alternatives to bisphenol A (BPA), a suspected endocrine disruptor. However, a greater understanding of structure-activity relationships (SARs) associated with such lignin -derivable building blocks is necessary to ease replacement efforts. Toward. This study focuses on the prediction of bisphenol estrogenic activity (EA) to inform the design of potentially safer BPA alternatives. To achieve this, a molecular docking protocol was developed using the human estrogen receptor alpha (hERα) and a set of 30 bisphenols with experimentally determined EA. The docking protocol was found to have a non -statistical in silico approach has been developed. The results of molecular docking analyses applied on six different nuclear receptors (NRs) have revealed that: i) some BPs resulted to act close to the hormonal ligand of BPA exposure; ii) BPS is a false interactor for all NRs, but it does not appear safer at all for androgen receptor (AR), for which its binding activity is found similar to a pharmacological anti -androgen; iii) only a BP has been found as a dio -colorectal for all NRs, nonetheless, moderate dynamic instability of the BP's-NRs has revealed that the presence of negative hydrophobic interactions could induce a decrease in receptor activity. Overall, the present results demonstrate that in silico methods could be a useful approach to screen estrogenic and androgenic activity of hard -to -test chemicals (HTCs).	RSC Adv Vol.11 Issue 36 Pages 22149-22158	10.1039/d1ra02170b	35480830	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2163	P. M. Aja, J. N. Awoke, P. C. Agu, A. E. Adegboyega, E. M. Ezeh, I. O. Igwenyi, O. U. Orji, O. G. Ani, B. A. Ale and U. A. Ibiam	2022	Hesperidin abrogates bisphenol A endocrine disruption through binding with fibroblast growth factor 21 (FGF-21), α -amylase and α -glucosidase: an in silico molecular study	BACKGROUND: Fibroblast growth factor 21 (FGF-21), alpha -amylase, and alpha -glucosidase are key proteins implicated in metabolic dysregulations. Bisphenol A (BPA) is an environmental toxicant known to cause endocrine disruptions. Hesperidin from citrus is an emerging flavonoid for metabolic diseases management. Through computational approach, we investigated the potentials of hesperidin in abrogating BPA interference in metabolism. The 3D crystal structure of the proteins (FGF-21, α -amylase, and α -glucosidase) and the ligands (BPA and hesperidin) were retrieved from the RCSB and PubChem databases respectively. Using Autodock plugin Pyrx, molecular docking of the ligands and individual proteins were performed to ascertain their binding affinities and their potentials to compete for the same binding site. Validation of the docking protocol was carried out by redocking co -crystallized ligands into the binding pockets of the proteins. Discovery Studio was used to visualize the docked complexes and to analyze the ligand -protein interactions within the binding pockets. Using SwissAdme and AdmetSar servers, our further investigated hesperidin 's ADMET profile. Hesperidin used was non -toxic and non -mutagenic. RESULTS: Hesperidin and BPA competitively bound to the same site on each protein. Interestingly, hesperidin had greater binding affinities. (Kcal/mol): -9.80, -9.80, and -9.60 than BPA (Kcal/mol): -5.60, -7.30, -7.30 for FGF-21, α -amylase, and α -glucosidase respectively. Visualizations of the binding poses showed that hesperidin interacted with stronger bonds than BPA within the proteins' pockets. Although hesperidin violated Lipinski rule of five, this however can be optimized through structural modifications. CONCLUSIONS: Hesperidin may be an emerging natural product with promising therapeutic potentials against metabolic and endocrine derangement.	J Genet Eng Biotechnol Vol.20 Issue 1 Pages 84	10.1186/s43141-022-00370-z	35648239	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2164	K. Adachi, T. Sasaki, A. Arai, M. Shimizu and H. Yamazaki	2024	Impact of variability of in silico and in vitro octanol/water partition coefficients of compounds on the input parameters and results of simplified human physiologically based pharmacokinetic models after virtual oral administrations	The octanol/water partition coefficient, P (logP), is a hydrophobicity index and is one of the determining factors of the pharmacokinetics of chemical compounds. LogP values obtained from in silico software, some chemistry databases, and in vitro liquid chromatography retention factors may vary. Some chemicals (bucuzidil, ensaxadin, and pamiparib) have up to four wide -ranged literature. In a study by Arai et al. values. This study aimed to evaluate the effects of logP values of these three compounds, along with bisphenol A, 1,2 -dichloroethane, tetrahexylsulfolane 2, 4 -nonylphenol, and diazinon, on the input parameters and output pharmacokinetic profiles of simplified human physiologically based pharmacokinetic models after virtual oral administrations. The logP values of the compounds were varied from -1 to 7 logP values. Logarithmic plasma unbound fraction values and liver to plasma partition coefficients (Kp,uu) were, respectively, inversely and linearly correlated with logP values (R (p) 2 was values at −0.7 to logP = 0) and logP was among the input parameters. For previously established machine learning systems, consequently, the resulting logarithmic intrinsic clearance values were correlated with logP values in the range 2 R. However, the bioavailability, absorption rate constants, and volumes of distribution were not affected. PBPK -modeled plasma and hepatic -intrinsic concentrations and areas under the concentration time curves after virtual oral doses were mostly within −0.5 to −2 -fold ranges, except for substances with low in vitro logP values, e.g., miconazole and pamiparib. These results suggested that in silico logP values are generally suitable for pharmacokinetic modeling nevertheless, caution is needed for compounds with low in vitro logP values of −2.	J Toxicol Sci Vol.49 Issue 10 Pages 459-466	10.2131/jts.49.459	39358235	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2165	A. A. S. Alfaidi and I. M. Mohammed, O. A. S. Alfaidi and K. A. Ali	2022	Physiological and Histopathological Studies on Bisphenol- A Induced Oxidative Stress in Albino Rats: Amelioration by Green and White Tea Extracts	Due to highly exposure of BPA which is harmful substance, we investigate its role in induction of oxidative stress, its effect on pancreatic tissue and some physiological parameters in serum of rats, also make a comparative study of antioxidant role for both green and white tea extracts against the harmful substance. In our experiment 36 male albino rats had been used, their body weights were ranged between 180 and 200 grams. Four equal groups of rats were formed, (five animals each). The first group was treated with corn oil alone, while the second group received 600 mg/kg BPA liquefied in corn oil, while the third group received BPA (600 mg/kg) and 100 mg/kg extract of green tea for ten days , and the fourth group received BPA plus 100 mg/kg extract of white tea for ten days, finally while last group was orally fed 100 ml/kg distilled water as control. Animal dosing was orally for 10 days. Level of serum MDA significantly increased in rat group supplied with PBA while treatment with white and green tea extracts ameliorated MDA level. Serum superoxidedismutase (SOD) significantly decreased in PeNS group while green tea extract significantly increased SOD activity and white tea extract ameliorated SOD activity. Serum catalase (CAT) significantly decreased in PeNS group while green tea extract significantly increased CAT activity and white tea extract ameliorated CAT activity. Histopathological examination revealed that hemorrhage, apoptosis, necrosis and infiltration of inflammatory cells in pancreatic tissue of PNS rat group, while treatment with green and white tea extracts ameliorated this. We recommend histological evidence of pancreatic islets. Photochemical examination indicated depletion of macrophages in islets by using a stain named alcian blue periodic -acid schiff stain (AB-PAS), protein also depleted when pancreatic tissue stained with hematoxylin Eosi ne stain, supplied with PNS, while green tea showed better recovery to protein distribution than white tea.	JOURNAL OF PHARMACEUTICAL NEGATIVE RESULTS Vol.13 Issue 4 Pages 545-553	10.47750/pnr.2022.13.04.071	-	動物	1	1	1	1	0	600 mg/kg mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2166	I. Al-Saleh, R. Elkhatib, M. Alnemer, H. Alshaban and M. Shoukri	2025	Impact of maternal Bisphenol A exposure on thyroid hormones and birth anthropometric outcomes: A repeated measures study	We investigated the effects of prenatal bisphenol A (BPA) exposure on maternal thyroid hormone, and fetal growth outcomes within a cohort from Saudi Arabia. In this prospective study, 372 pregnant women provided 1957 urine samples, which were analyzed for BPA concentrations using UPLC -MS/MS throughout three trimesters. We recorded BPA detection rates and median concentrations, using mixed effects models to examine associations between BPA and thyroid hormones (TSH, FT4, FT3), and fetal growth (birth weight, length, head circumference, ponderal index). Detection rates were 97.6% in the first trimester, 96.2% in the second trimester, and 94.6% in the third trimester, with median concentrations of 1.2, 1.1, and 1.0 ng/mL, respectively. Higher BPA exposure correlated with a 2.96 % increase in FT3 levels and a 24.58 % reduction in TSH in the first trimester quartile. Fetal growth analysis showed a decrease of 3.8 % in HC and 26.5 % in PI associated with high third trimester BPA levels. Furthermore, FT3 levels in the first and third trimesters mediated the relationship between BPA exposure and fetal growth outcomes by 21.3 % for HC and 26.1 % for HC, while gestational age mediated 13.1 % of the changes in HC. The study highlights significant disruptions in thyroid function and detrimental effects on fetal development due to high BPA exposure, underscoring the need for rigorous monitoring and preventive measures during pregnancy. (c) 2025 The Authors. Publishing services by Elsevier B.V. on behalf of Saudi Communications Co. Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).	Emerging Contaminants, Volume 11, Issue 2, June 2025, 100479	10.1016/j.emcon.2025.100479	-	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-
統合_2167	R. Almuzi, Y. Q. Wang, K. Luo and Y. Jiang	2022	Exposure to phthalates, phenols, and parabens mixture and alterations in sex steroid hormones among adolescents	Exposure to phthalates (PAEs), phenols, and parabens has been linked with sex hormone imbalance however, previous studies were predominantly limited to adults, and failed to examine the combined effects of these chemicals mixture among adolescents. Thus, our used the data from the National Health and Nutrition Examination Survey (2013-2016) to explore the associations of urinary PAEs, phenols, and parabens biomarkers with sex hormones among participants aged 12-19 years with (n = 613). Latent class analysis (LCA) and quantile -based g -computation (QGC) were applied to assess the associations of the latent exposure profiles and chemicals mixture with sex hormone indicators, including steroid hormones and sex hormone binding globulin (SHBG). In adolescents, and by sex. Using LCA, four latent classes were identified among all participants. Adolescents in the high exposure class had higher levels of MEP, MBP, MiBP, MCPP, MEHP, MEHHP, MEOHP, MECPP, MBzP, MEP, and BPA than those in the low exposure class. In the QGC model, a one -quartile increase in the phthalates (MEHP) had lowest level of estradiol (E2) (beta= -0.208; 95% confidence interval (CI): -0.436, 0.021), free androgen index (FAI) (beta = -0.246; 95%CI: -0.512, 0.020) and free testosterone (FT) (beta = -0.248; 95%CI: -0.496, 0.001) among male adolescents. These results were echoed by the results in QGC analyses, where PAEs mixture was negatively associated with E2 (beta = -0.127, 95% CI: -0.283, 0.011), FAI (beta = -0.196, 95%CI: -0.387, -0.004) and FT (beta = -0.196 95%CI: -0.376, -0.002) among male adolescents. By contrast, the associations of the identified latent classes or chemicals mixture with sex hormone indicators were generally nonsignificant among female counterparts, except for a positive association between PAEs mixture and SHBG (beta = 0.121, 95%CI: 0.012, 0.231). Our study demonstrated that exposure to PAEs, particularly DEHTP, MEHHP, and DEHP could be a threat to the sex hormone homeostasis of male adolescents.	CHEMOSPHERE Vol.302	10.1016/j.chemosphere.2022.134834	35533932	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性影響等不適合と判断されるものは作成根拠評価への進め。当該物評価段階で影響に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2168	G. Afzal, H. I. Ahmad, A. Jamal, G. Mustafa, S. Kinar, R. Hussain, S. Anjum, M. Rafay, A. Ghaffar and S. Saeed	2022	Bisphenol a mediated histopathological, Hemato-Biochemical and oxidative stress in rabbits (oryctolagus cuniculus)	Bisphenol A (BPA) is a ubiquitous environmental contaminant and is commonly known as an endocrine disrupting chemical (EDC). BPA is widely used in production of numerous products including polycarbonate plastics, cans, drinking water bottles and dental sealants. Therefore, the current study was designed to investigate deleterious effects of BPA on blood, serum biochemistry, antioxidant enzymes and histopathological changes in different visceral organs of exposed rabbits. For this, twenty-a total of 16 male rabbits were randomly divided and kept in four different groups (A-D). Rabbits in control group A received no treatment and were kept on normal diet. Rabbits in group B, C and D were orally given BPA @ 10, 50, 100 mg/kg body weight (b.w) daily for 30 days. Blood samples were collected from marginal ear vein of rabbits. Whole rats, kidneys, testis and brain exhibited necrotic and degenerative lesions. Increased rabbits. In conclusion, the results of our experimental study suggested that BPA induces severe biochemical, histopathological and oxidative stress in male rabbits.	TOXIN REVIEWS Vol.41 Issue 4 Pages 1067-1076	10.1080/15569543.2021.1972318	-	動物	一般毒性	1	1	1	実験動物ウィスター	3用量：1	10, 50, 100 mg/kg/日	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2169	S. A. Abuzhal, R. Sami, H. Aljumaqi, M. S. Alma Jeyd li, A. A. Haroaasi, M. Helal, R. A. Al-kiza and M. A. Alanazi	2024	ADVERSE EFFECTS OF ORAL ADMINISTRATION OF BISPHENOL A-INDUCED TOXICITY ON ADULT MALE RAT LIVER AND TESTIS WITH THE PROTECTIVE ROLES OF HERBAL TEAS	Bisphenol A (BPA) is a monomer widely used in our living environment to manufacture many chemical products. Mammalian cells are exposed to it at high levels, which has toxic and mutagenic consequences. Moreover, BPA exposure during prenatal and neonatal development results in defects in the male and female reproductive systems, abnormal testicular development in fetal sex jries, and pregnancy complications. The aim of the present study was to investigate the effects of oral administration of BPA on the liver and testis of adult male rats and the protective role of herbal tea against BPA-induced toxicity. Twenty-four Wistar male rats (weighing 160-170g). Groups were coded as ST (BPA), GT (BPA and BPA+ hot tea) green, and blue herbal teas, respectively. Several metabolites such as weights, hepatic enzyme markers, lipid profile, and oxidative stimulative stress for the liver and testis were conducted. Results indicated that exposure to BPA significantly increased oxidative stimulative stress and damaged the hepatic tissue in the liver and testis. The GLT/ST BPA group detected the highest values for AST (63.67 ±5.67 mU/mL), ALP (118 ±6 mU/mL), LDH (110.3 ±3.1, and GGT (30.72 ±1.1). HT/BPA group detected the lowest values for AST (38.5 ±6.2 mU/mL), ALP (110 ±6 mU/mL) and GGT (21.12 ±1.1). Similarly, the HT/BPA and HT/BPA groups were detected 31.22 and 112 mg/dL) to the oxidative levels as compared to the vehicle control group. While rats in the HT/BPA and GT/BPA groups showed the lowest values for TAC (0.42 ±0.03 mM/mL) and GSH (0.31 ±0.02 mM/mL). Histopathological examination of the liver and testis tissues revealed that BPA induced severe histological changes in the liver and testis, including congestion, eosinophilic cytoplasm, especially of granulosa, which preserved GPx value (68.02 nmol/mg), testosterone (2.82 ng/mL), and redox, which preserved CAT value (102.30 U/mg), while blue tea preserved MDA and SOD values (0.81 nmol/mg and 7.58 U/mg), respectively. BPA and administration with herbal teas reduced toxicity on the liver and testis due to free radical scavenging effects.	ACTA POLONIAE PHARMACEUTICA Vol.81 Issue 4 Pages 639-648	10.32383/appdv/193768	-	動物	-	1	1	1	1	0	50 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2170	S. O. Abimbola, C. Xeri, A. K. Saleh, B. Heibat, T. Hurog, H. Dirven and K. C. Makris	2023	Diurnal Variation in Biomarkers of Exposure to Endocrine-Disrupting Chemicals and Their Association with Oxidative Damage in Norwegian Adults: The EuroMix Study	Most evidence on the adverse health effects of endocrine-disrupting chemicals (EDCs) has accumulated during recent decades. EDCs are commonly found in various foods and personal care products (PCP). Data on exposure to EDCs in the Norwegian population are limited. Therefore, we aimed to assess the exposure to phenols, parabens, and phthalates (PPPs) and its association between EDC exposure and oxidative damage in a Norwegian adult subpopulation. This was a cross-sectional panel study using biobanked samples from the EuroMix project. During a typical workday, participants were asked to collect all day's urine voids and record diary and PCP habitual uses in a diary. Collected time stamps of urine voids were classified into three distinct periods in the day (morning 6 a.m. 12 p.m., afternoon 12 p.m. 6 p.m., and evening 6 p.m. 6 a.m.). Urinary concentrations of 21 PPPs and 8-hydroxy-2′-deoxyguanosine (8-OHdG) were measured using mass spectrometry and adjusted for urinary volume using specific gravity. Urinary 2-hydroxynaphthol (OHNA), a lipid peroxidation marker, was measured using an immunoassay kit. Linear mixed-effect models identified EDCs under the influence of a diurnal variation effect that was adjusted for dietary habits and PCP use and examined associations between EDC and OHNA. p-values were FDR-adjusted. Most phthalates appeared to be diurnally varying with higher urinary levels towards the evening (e.g., 0.002 fmol/mL-creatinine) than during the morning and day. No strong diurnal variation effect was not present for parabens and bisphenols. Significant (e.g., 0.001) positive associations were observed between all phthalates, parabens, and bisphenols (except bisphenol S) and OHNA. This study's findings highlighted the diurnal variation of excretion for certain EDCs, but not for others, in real-life conditions. The degree of EDC chronotoxicity in distinct diurnal windows of the day warrants further investigation with longitudinal human studies.	TOXICS Vol.10 Issue 4	10.3390/toxics10040181	35448442	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2171	S. Abdali, S. Z. Mansumi and F. Kazemi	2022	Environmental and occupational factors and higher risk of couple infertility: a systematic review study	Background: Infertility is a global health problem that represents an increasing trend due to new lifestyles following technological advances since individuals are facing more risk factors than before. The present systematic review study aimed to investigate the impact of environmental and occupational factors on reproductive parameters and increased risk of couple infertility. Materials& Methods: Google Scholar, PubMed, ISI, and Web of Science databases were searched for the available observational (i.e., cohort, case-control, and cross-sectional) systematic review, meta-analysis, and clinical trial studies between 2007 and 2019. To this end, keywords such as "Environmental exposure", "Occupational exposure", "Environmental pollutants," Environmental infertility", "Fertility", and "Sub-fertility" were used. The retrieved articles were screened for impact of environmental and occupational risk factors on reproductive indices and increased infertility risk. Totally, 80 out of 9630 papers were evaluated after considering the inclusion and exclusion criteria. The reported risk factors were classified into three groups including occupational, lifestyle, and environmental factors. Results: Occupational factors including exposure to heavy metals, pesticides, radiation, solvents, prolonged sitting, exposure to a hot environment, contact with formaldehyde, pesticides, insecticides, mechanical vibration, and contact with ionizing radiation, all of which affected the reproductive parameters. However, some researchers found no significant associations in this regard. Short conclusion: In general, individuals with known impairments in reproductive parameters were more exposed to risk factors. Nonetheless, more studies are needed to determine the risk of infertility in the population.	MIDDLE EAST FERTILITY SOCIETY JOURNAL Vol.27 Issue 1	10.1186/s43043-022-00124-4	-	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2172	Y. A. Abd-Elraby, I. E-ElSayed, M. A. AbdElbaten, E. A. Badr, M. M. Abdelhafez and I. Elmadbouly	2022	Anti-inflammatory and antioxidant effect of Moringa oleifera against bisphenol-A-induced hepatotoxicity	Background Non-pharmacological exposure or pharmacological drug-induced hepatic injury is the most common cause of hepatotoxicity. This study was conducted to evaluate the effect of Moringa oleifera leaf extract against bisphenol-A (BPA)-induced toxicity in rats. Methods Rats (n=36) were randomized into 3 groups (6 rats/cell): Control group: rats received olive oil at Moringa oleifera (200mg/kg) orally for 30 days. BPA group: rats received BPA (50mg/kg) orally for 30 days. BPA+Moringa group: rats received BPA (50mg/kg) orally for 30 days and Moringa oleifera (200mg/kg) orally for 30 days. Moringa oleifera extract 200 is 200mg/kg/ml in 30 days. Moringa oleifera (200mg/kg) orally for 3 days. At the end of the experiment, blood samples were collected for glucose and liver function assays. Also, a little the liver tissue samples were collected and homogenized for measuring the inflammatory cytokines and antioxidant markers. Results Rats with BPA-induced hepatotoxicity have significantly increased serum aspartate transaminase (AST), alanine transaminase (ALT), and glucose. Sun lipid metabolizable (MDA) tumor necrosis factor (TNF-alpha), and macrophage migrating inhibitory factor (MIF) but significantly decreased levels of liver tissue reduced glutathione (GSH) and total antioxidant capacity (TAC) levels. The administration of Moringa oleifera (especially 200mg/kg/BW) in both normal and promotion groups ameliorate the toxic effects of BPA in rats, as to decrease the activities of AST, ALT, glucose, MDA, TNF-alpha, and MIF levels and increase the antioxidant levels of GSH and TAC. Conclusion Moringa oleifera has hepatoprotective effects against BPA-induced liver damage through the regulation of antioxidants and inflammatory biomarkers.	EGYPTIAN LIVER JOURNAL Vol.12 Issue 1	10.1186/s43066-022-00219-7	-	動物	-	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2173	M. Abd Malek, R. Dasiman, N. Khan, S. Mohamed-Akhtar and M. H. Mahmud	2022	The protective effects of procyanidin C-1 on bisphenol A-induced testicular dysfunction in aged mice	The number and quality of sperm are decreased due to bisphenol A (BPA) exposure, an endocrine-disrupting chemical in the male reproductive system, especially in advanced paternal age (APA). Procyanidin C-1 (PC1) is an antioxidant from grape seed (Vitis vinifera L.), has demonstrated anti-viral, anti-melanogenic and chemopreventive effects. Therefore, this study aims to determine the effects of PC1-1 intervention on sperm parameters, testis morphological changes, serum testosterone, oxidative, and toxicology hormone (LH) concentrations and the expression of apoptotic (Bax and Bcl-2) and mitochondrial-related (Nrf2 and Opa1) genes in the testis of APA mice exposed to BPA. Male mice were randomly assigned into four groups: control, BPA, PC1-1, and BPA + PC1-1 groups. Mice were orally administered with 50 mg/kg BW/day of BPA and/or 100 mg/kg BW/day of PC1-1 for 28 days. Results showed that the BPA group had significantly decreased sperm count, viability, and epididymal length. PC1-1 also decreased serum alkaline and increased LH and testosterone levels. The gene expression of Bax was significantly down-regulated by PC1-1 intervention. In contrast, Bcl-2 was substantially up-regulated. Expression of Nrf2 and Opa1 genes were also significantly up-regulated in the PC1-1 intervention group. Hence, it is demonstrated that PC1-1 was able to mitigate the adverse effects of BPA on reproductive parameters of aged mice. Collectively, we postulated that PC1-1 has a potential role in protecting the ageing male reproductive system against the damaging impacts of BPA. © 2022 Beijing Academy of Food Sciences. Publishing services by Elsevier B.V. on behalf of Keai Communications Co., Ltd. This is an open-access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).	FOOD SCIENCE AND HUMAN WELLNESS Vol.11 Issue 4 Pages 965-974	10.1016/j.fshw.2022.03.020	-	動物	-	1	1	1	1	不明	15 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2174	L. Fabbri, O. Robinson, K. Basagaña, L. Chiesi, R. Grazuleviciene, M. Guxens, L. Kadiene-Lidbergiene, A. K. Sakhi, L. Maitre, R. McEachan, C. Philippat, G. J. Poos, C. Thomsen, J. Wright, T. Yang and M. Vrijheid	2025	Childhood exposure to non-persistent endocrine disruptors, glucocorticosteroids, and attentional function: A cross-sectional study based on the parametric g-formula	Background: Evidence suggests that endocrine disrupting chemicals (EDCs) may perturb the hypothalamic/pituitary-adrenocortical (HPA) axis, which has a major role in brain development. We aimed to evaluate the effects of childhood exposure to organophosphate pesticides, phenols, and phthalate metabolites, on urinary glucocorticosteroids and inattention in childhood. Methods: We used data from the Human Early-Life Exposome (HELIX) cohort. Urinary EDC biomarkers were measured in 1,301 children (6-11 years) from six European countries. Cortisol and cortisone were measured in urine samples collected in the morning and evening. Inattention was measured using the Conners' Parent Rating Scale-Revised: Short Form. We estimated the joint effect mixture by using quantile g-computation (qgcomp). Results: We observed a positive marginal overall effect (MEF) for mixture increases from the 50th to the 80th percentile for overall quantile (0.11 (0.02, 0.21)), and the phthalate metabolites: cx-MMP (MEF: 0.03 (adj=0.73; CI: 0.00, 0.068)), oh-MiNP (MEF: 0.039 and 95% CI: (0.001, 0.076)), and MEHP (MEF: 0.036 and 95% CI: (0.008, 0.063)). miN

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2181	D. S. Di, R. Y. Zhang, H. L. Zhou, M. H. Wei, Y. Cui, J. L. Zhang, T. T. Yuan, Q. Liu, T. T. Zhou, J. A. Liu and Q. Wang	2023	Exposure to phenols, chlorophenol pesticides, phthalate and PAHs and mortality risk: A prospective study based on 6 rounds of NHANES	Objectives: Human exposure to various endocrine disrupting chemicals (EDCs) is widespread and long-lasting. The primary objective of this study was to prospectively evaluate the association of combined exposure of phenols, chlorophenol pesticides, phthalate and polycyclic aromatic hydrocarbons (PAHs) and mortality risk to the representative US populations.Methods: The data on urinary levels of phenols, chlorophenol pesticides, phthalates, and PAH metabolites, were collected from participants aged ≥ 20 years in six rounds of the National Health and Nutrition Examination Survey (NHANES) (2003-2018). NHANES-linked death records up to December 31, 2019 were obtained from the National Death Index. Weighted Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs). Quantile g-computation (qgcomp) was used to estimate the mixture association between EDC exposure and mortality risk. Results: Eight kinds of urinary EDCs, including total phthalates, monobenzyl phthalate, and 2-naphthol were significantly associated with increased risks of all-cause, cardiovascular disease (CVD) and cancer mortality among all participants. HQ2 index was associated with the risks of all-cause (lowest vs.HQ1: 1.388, 95%CI: 1.139-1.693 and Q3 vs.HQ1: 1.191-1.618) and CVD mortality (HR = 1.929, 95%CI: 1.133-3.218). High co-exposure scores were associated with elevated all-cause (HR = 1.162, 95%CI: 1.036-1.304), CVD (HR = 1.366, 95% CI: 1.029-1.260), and cancer mortality risks (HR = 1.960, 95% CI: 1.608-2.472). The results of subgroup analysis, competing risk model, and sensitivity analysis were generally consistent with the findings from the main analysis, indicating the robustness of our findings. Conclusions: This study provided the first epidemiological evidence that co-exposure to EDC at fairly low levels contributed to elevated mortality risk among US adults. The underlying mechanisms for the effects of EDC co- exposure on human health are worthy of future exploration.	Chemosphere. 2023 Jul;329:138650.	10.1016/j.chemosphere.2023.138650	37037349	ヒト	発がん	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2182	M. Di Cicco, I. E. Lodahl, A. Stamatakis, E. Kitraki, I. Bakoyiannis, A. Repoklou, C. G. Stoneham, C. Gennings, D. Lupu and J. Rttgg	2023	A human-relevant mixture of endocrine disrupting chemicals induces changes in hippocampal DNA methylation correlating with hyperactive behavior in male mice	Humans are ubiquitously exposed to endocrine disrupting chemicals (EDCs), substances that interfere with endogenous hormonal signaling. Exposure during early development is of particular concern due to the pronounced sensitivity of developing tissues. Yet, the molecular mechanisms underlying developmental EDC exposure effects on brain and behavior remain poorly understood. Here, we used a human-relevant mixture of seven EDCs detected in human maternal blood and known to induce neurodevelopmental toxicity in rodent models. Furthermore, it is the mixture to which pregnant women in Athens (Greece) are most frequently exposed. Methods: Pregnant mice were exposed to the EDC mixture via drinking water at concentrations comparable to human exposure levels. In this study, we investigated whether epigenetic mechanisms could underlie the long-term effects of Athens 7EC on gene expression and behavior. To this end, we analyzed DNA methylation at regulatory regions of genes whose expression was affected by Athens 7EC in the hippocampus of 14 sons exposed via drinking water spanning the life-time that Athens 7EC decreases DNA methylation in males at the promoters of the hypothalamic pituitary adrenal (HPA) axis Nr3c1, Fkbp5, and Crh, coding for the glucocorticoid receptor, the stress-induced co-chaperone, and the corticotropin releasing hormone receptor 1, respectively. Furthermore, we show that the decrease in Nr3c1 methylation correlates with increased gene expression. Results: Our findings show that Athens 7EC induces hyperactive behavior in male offspring, which is associated with altered DNA methylation and EDC mixture corresponding to a human exposure scenario induces epigenetic changes, and thus are governing effects, on the HPA axis that are reflected in the behavioral phenotypes of the adult male offspring.	CHEMOSPHERE Vol.313	10.1016/j.chemosphere.2022.137633	36565761	動物	-	1	不明	0	1	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2183	A. Di Claula and P. Portincasa	2021	Relationships between emissions of toxic airborne molecules and type 1 diabetes incidence in children: An ecologic study	BACKGROUND:Type 1 diabetes originates from gene-environment interactions, with increasing incidence over time. AIM:To identify correlates of childhood type 1 diabetes in European countries using an ecological approach.METHODS:Incidence data were collected from the EURODIAB Study Group. Data on airborne molecules were collected from the European Environment Agency. Twenty-two molecules are currently studied. METHODS:We employed an ecological model to explain, in a wide time period (1990-2018), associations between type 1 diabetes incidence in 30 European countries (systematic literature review) and the nationwide production of the widely diffused air pollutants particulate matter < 10 mu m (PM10), nitrogen oxides (NO), non-methane volatile organic compounds (NOVC), sulphur oxide (SO2), and carbon monoxide (CO). RESULTS:Between 1990 and 2018, the incidence of childhood type 1 diabetes increased by 3.4% (Austria) to 6.4% (Sardinia, Italy) per year (Poisson regression). In Germany (n = 64,572 cases) and 100,000 cases. Although the overall production of pollutants decreased progressively from 1990 to 2018, type 1 diabetes incidence was associated with the nationwide production of PM10, VOCs, and SO2 but not with those of NOX and ammonia. Type 1 diabetes incidence was significantly higher in countries with high emissions than in those with low emissions of PM10 (17.5 +/- 2.0 vs. 14.6 +/- 1.9 (1000D incidents, respectively); VOCs (19.5 +/- 1.9 vs. 13.7 +/- 1.7; 1 (1000D incidents, respectively); and SO2 (16.0 +/- 2.1 vs. 11.2 +/- 2.4; 1 (1000D incidents, respectively); but not of CO or ammonia. CONCLUSION:Evidence justify further studies to explore better links between long-term air quality and type 1 diabetes onset at the individual level, which should include exposures during pregnancy. In this respect, type 1 diabetes could be, at least in part, a preventable condition. Thus, primary prevention policies acting through a marked abatement of pollutant emissions might attenuate future type 1 diabetes incidence throughout Europe.	WORLD JOURNAL OF DIABETES Vol.12 Issue 5 Pages 673-684	10.4239/wjd.v12.i5.673	33995854	ヒト	-	-	-	-	-	-	ecologic study	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2184	Y. L. Deng, Q. L. Xiao, P. Y. Liu, Y. M. Ge, X. H. Ren, X. J. Li, Q. R. Xiao, B. H. Xu, X. Chen, J. J. Liu, H. Y. Huang and S. Y. Lu	2025	Exposure to bisphenol A and its analogs provides a preliminary indication of the risk of cognitive impairment for the elderly via an XGboost-based model	Bisphenol A (BPA) and its bisphenol analogs (BPs) serve as key precursors in the manufacturing of polycarbonate plastics and epoxy resins. However, due to BPA's detrimental health effects, there has been a growing global consensus to restrict its use. The elderly, being particularly susceptible to neurodegenerative disorders, represent a population of concern yet, research exploring the association between BPs exposure and neurodegenerative diseases in the elderly remains scarce. In this study, the urinary levels of six BPs among 287 participants from the Shenzhen aging-related disorder cohort in China during 2017-2018 were measured. Cognitive status was evaluated using the Mini-Mental State Examination (MMSE), and the impact of cognitive impairment risk factors, lifestyle habits, and dietary practices was assessed through the Extreme Gradient Boosting (XGBoost) classifier. In this study, BPA was the highest urinary level of bisphenol compound detected in the high-risk group (2.16 ng/mL, 90.2 %). Significant differences in BPs levels were observed to the degree of cognitive impairment (mild cognitive impairment and dementia) (p < 0.05). Moreover, BPA (OR = 1.01, 95 % CI: 1.00-1.02), BPF (OR = 1.01, 95 % CI: 1.00-1.02), and BPS (OR = 1.01, 95 % CI: 1.00-1.02) were identified as risk factors for cognitive impairment.Therefore, BPA and its analogs may be needed to fully evaluate BPS' s actual human exposure levels. The XGBoost models have further revealed that BPS analogs exposure will remain having characteristics of some substantial contributors to the potential impact on cognitive impairment during aging not only BPA. (c) 2025 The Authors. Published by Elsevier B.V. on behalf of Keli Communications Co. Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).	EMERGING CONTAMINANTS Vol.11 Issue 2	10.1016/j.emcon.2025.100474	-	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2185	P. Dedo, S. Ede-Papadas, D. DiYi'i?, G. Senel and T. Turali-Akbay	2025	Lactobacillus rhamnosus GG alleviates bisphenol-A induced oxidative stress in serum	The objective of this investigation was to identify changes in the serum oxidant-antioxidant balance of rats exposed to bisphenol A (BPA) and to investigate the impact of Lactobacillus rhamnosus GG (LGG) administered via these changes. Twenty-four male Wistar Albino, 250-300 grams, rats were divided into control, BPA (50 mg/kg BPA/kg), LGG (prophylactic with serum/per number of rats, 10% and LGG were applied once to the relevant groups for six weeks, five days each week. Six weeks later, the blood samples were withdrawn and serum samples were prepared. Total oxidant and antioxidant status (TOS), glutathione, and lipid peroxidation determinations were performed in the serum samples. Oxidative stress index (OSI) was calculated. Serum glutathione and lipid peroxidation levels were significantly increased in the BPA-treated group and antioxidant level compared to the control group. LGG administration improved the increased serum oxidative stress caused by BPA. Administration of LGG in BPA-treated rats improved oxidative stress-induced changes in conclusion, administration of Lactobacillus rhamnosus GG to rats for 30 consecutive days prevented oxidative stress in serum caused by bisphenol A.	JOURNAL OF RESEARCH IN PHARMACY Vol.29 Issue 4 Pages 1726-1731	10.12991/jrespharm.1734682	-	動物	-	1	0	1	1	0	50 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2186	A. Davlas, S. Lyon-Caen, M. Rolland, N. Izzatt, C. Thomsen, L. S. Haug, A. K. Sakhi, C. Morot, Y. Riyath, Z. E. Khan, N. Jeanneric, C. Philippat, M. Eggesbo, P. Lepage and R. Slama	2024	Perinatal Exposure to Phenols and Poly- and Perfluoroalkyl Substances and Gut Microbiota in One-Year-Old Children	The role of the gut microbiota in human health calls for a better understanding of its determinants. In particular, the possible effects of chemicals with widespread exposure rather than pharmaceuticals are little known. Our aim was to examine the sensitivity of the early life gut microbiota to specific chemicals with potential endocrinedisrupting action. Within the SEPAGES French cohort, we assessed 22 phenols in repeated urine samples from 350 pregnant women and their offspring and 19 poly- and perfluoroalkyl substances (PFASs) in serum from the pregnant women. We collected stool samples from the children at one year of age. In whole-rim 16 rRNA gene was sequenced, allowing for gut bacterial profiling. Associations of each chemical with alpha- and beta-diversity indices of the gut microbiota and with the relative abundance of the most abundant taxa were assessed using single-pollutant and mixture (WQS) models. Perinatal exposure to certain parabens was associated with gut microbiota alpha- and beta-diversity and with the abundance of Bifidobacterium, Lachnospira, and Faecalibacterium at one year. Associations were generally consistent between single-pollutant and mixture models but there were not maintained after correction for multiple testing. Parabens, which have known antimicrobial properties, might disrupt the child gut microbiota, but larger studies are required to confirm these findings.	Environ Sci Technol. 2024 Sep 3;58(35):15395-15414.	10.1021/acs.est.3c09927	39173114	ヒト	国内競合書	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2187	M. D. B. Dalla, C. O. Ajaila, F. Castro, F. K. Neto, G. Zaniboli, W. Canoe-Montanez and R. Martiello	2022	Environmental pollution and attention deficit hyperactivity disorder: A meta-analysis of cohort studies	There is already knowledge of the extensive risk factors for attention deficit hyperactivity disorder (ADHD) and recent studies suggest that environmental pollution may contribute to an increase in the incidence of the disorder. The aim of our study was to perform a systematic review and meta-analysis of the risk of ADHD in people younger than 18 years old after exposure to environmental pollution. We searched the MEDLINE, Embase, SciELO, CINAHL, LILACS, Cochrane Central, and Web of Science databases and investigated the grey literature from inception until May 31, 2021. All cohort studies that provided data on exposure to environmental pollutants and ADHD in children and adolescents aged from zero to 18 years old were included. Two reviewers independently selected the studies and evaluated the quality criteria. If there was a divergence, a third reviewer contributed to the final decision. For the meta-analysis, risk ratios and their confidence intervals were calculated with the Mantel-Haenszel model. In total, 23 articles were included in the systematic review and 19 were included in the meta-analysis. The risk of ADHD in people exposed to air pollution was 1.55 times higher (95% CI: 1.38-1.74) than in those not exposed (I2 = 0%), with low heterogeneity. Of the 19 articles, 11 (58%) were at high risk of developing ADHD than those exposed to lower levels. This meta-analysis suggests that children exposed to higher levels of lead and heavy metal pollution are at greater risk of developing ADHD than those exposed to lower levels. This review	Environ Pollut. 2022 Dec 15:315:120351.	10.1016/j.envpol.2022.120351	36216185	ヒト	注意欠如・多動性障害、ADHD	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2188	Y. M. Dai, J. Y. Ding, Z. Wang, B. Y. Zhang, Q. Gou, J. Q. Gao, X. J. Qi, D. S. Lu, X. L. Chang, C. H. Wu, J. M. Zhang and Z. J. Zhou	2024	Associations of prenatal and concurrent exposure to phenols mixture with anthropometric measures and blood pressure during childhood: A time-varying mixture approach	Background: Environmental phenols were recognized as endocrine disrupting chemicals (EDCs). However, their impact on childhood anthropometric measures and blood pressure (BP) is still inconclusive. Limited studies have simultaneously considered prenatal and childhood exposures to analyzing mixtures of phenols. Objective: We investigated the relationships between combined prenatal and childhood exposures (no-pulse-wave velocity (baPWV) and BP) in school-aged children.Methods: A total of 1,109 mother-child pairs from the Shenyang Birth-Wall Cohort Study (SMBCS). The urinary concentrations of 11 phenols were measured using gas chromatography-tandem mass spectrometry. Generalized linear regression models (GLMs) and Generalized Bayesian Kernel-Machine Regression (GBKMR) were used to examine the effects of individual phenolic compounds at each period of two periods exposures. Results: In the GLMs, prenatal exposure to 2,5-dichlorophenol (2,5-DCP) was positively associated with baPWV (β = 0.03, 95% CI: 0.01, 0.05), and 2,5-DCP was associated with higher levels of heavy-head (PR: 1.10, 95% CI: 1.04-1.16), while low heterogeneity (I2 = 36%), and fixed BMI (OR: 1.07, 95% CI: 1.00-1.15), with moderate heterogeneity (I2 = 56%), we at greater risk of developing ADHD than those exposed to lower levels. This meta-analysis suggests that children exposed to higher levels of lead and heavy metal pollution are at greater risk of developing ADHD than those exposed to lower levels. This review	Environ Res. 2024 Nov 15:261:119766.	10.1016/j.envres.2024.119766	39127330	ヒト	心血管	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2189	Y. F. Dai, X. Hua, Z. H. Cheng, M. M. Faas and X. J. Xu	2020	Early-life exposure to widespread environmental toxicants and maternal-fetal health risk: A focus on metabolomic biomarkers	Prenatal exposure to widespread environmental toxicants is detrimental to maternal health and fetal development. The effects of environmental toxicants on maternal and fetal metabolic profile alterations is neither and thus. We searched the MEDLINE (PubMed) electronic database for relevant literature conducted up to September 31, 2019 with same key terms. From the initial 1576 articles, 15 articles met the inclusion and exclusion criteria, and consist of highly heterogeneous research methods. Seven studies assessed the effects of multiple environmental pollutants (metals, organic pollutants, nicotine, air pollutants) on the maternal urine and blood metabolomic profiles. Eight studies assessed the effects of smoking exposure on the maternal metabolomic profiles. Two studies assessed the effects of multiple environmental pollutants and smoking exposure on the maternal metabolomic profiles. Four studies assessed the effects of smoking exposure on the amniotic fluid metabolomic profile. The alterations of metabolic pathways in these studies mainly involve energy metabolism, hormone metabolism, oxidative stress and inflammation. The population study investigated the association between environmental toxicants and placental metabolomics. This systematic review provides evidence that prenatal exposure to a variety of environmental pollutants can affect maternal and fetal metabolomic characteristics. Integration of environmental toxicant exposure and metabolomics data in maternal-fetal samples is helpful to understand the interaction between toxicants and metabolites, so as to reveal the pathogenesis of fetal disease or diseases of fetal origin. (C) 2020 Elsevier B.V. All rights reserved.	SCIENCE OF THE TOTAL ENVIRONMENT Vol.739	10.1016/j.scitotenv.2020.139626	32535459	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2190	N. Coskun and N. Barlas	2024	Phloretin Ameliorates against Bisphenol A Induced Polycystic Ovarian Syndrome, an Endocrine Disrupting Chemical, in Prepubertal Rats	Polycystic ovary syndrome (PCOS) is an endocrine disorder whose etiology is not well understood and affecting 5-18% of women in reproductive age. We investigated the protective effects of phloretin against the PCOS-induced Bisphenol A (BPA) on experimental rat ovaries. This study started on female rats on the prepubertal period. All day rat subcutaneous injections by dissolving the corn oil were made in rats of all 30 min intervals, starting with phloretin, and followed by BPA. The dose of BPA was 50 mg/kg/day, and the doses of phloretin were 0.5, 5, and 50 mg/kg/day. Treatments were administered every day for 21 days. Literature corn oil, BPA and testosterone propionate (TP) were used as control groups. The rats were sacrificed on the 22nd day. Ovarian tissues were examined histologically and immunohistochemically. Ovarian tissue damage was evaluated by the severe score. The CYP19A1 and CYP17A1 enzymes ovarian tissue immunoreactivity in the BPA group whereas they were lowered similarly the BPA + 5 and 50 mg/kg phloretin groups. In PCOS-induced by BPA, the rats' follicles were recorded on the ovaries whereas it was decreased in the BPA + phloretin groups. Prepubertal exposure to BPA was associated with decreased serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, increased estrogen (E2) and dihydrotestosterone (DHT) levels. In testosterone propionate and BPA + phloretin (0.5 mg/kg/day) groups. In conclusion, in rat model, phloretin has positive effects against BPA-induced polycystic ovarian syndrome, also it caused positive effects on ovarian tissue and hormone secretion.	BIOLOGY BULLETIN Vol.51 Issue 4 Pages 845-856	10.1134/S1062359022601173	-	動物	-	1	0	1	不明	0	50 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2191	L. Cofone, I. Pindinello, G. D'Ancona, F. Grassi, A. Antonucci, M. Vitali and C. Protano	2023	Human semen quality and environmental and occupational exposure to pollutants: A systematic review	Background: The aim of the present systematic review was to evaluate the correlation between the exposure to environmental and/or occupational pollutants and possible alteration of semen quality, involving the attention on the studies performed using a fecundability approach.Methods: The review was conducted from inception to May 12, 2021, according to the PRISMA Statement 2020 and using the following databases: Scopus, Pubmed and Web of Science. The protocol was registered on PROSPERO (CRD42021266927). Studies were considered eligible if they reported data about the association between exposure to environmental pollutants and alterations of semen quality using human biomonitoring. The quality assessment was carried out by the tool of the Newcastle-Ottawa Quality Assessment Scale. Results: In total, 23 articles were included. Most of the studies were conducted in several countries. The main matrices used for biomonitoring were urine and blood and the most sought-after contaminants were bisphenols, phthalates, pesticides, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, and potentially toxic elements. Overall, the exposure to environmental pollutants was associated with a decrease in semen quality, in particular, a reduction in sperm concentration and normal sperm morphology. Conclusions: Male fertility can be negatively affected by the exposure to environmental and/or occupational pollutants. Human biomonitoring programs may be considered a useful tool for specific surveillance programs devoted to early highlight subjects who are more exposed to environmental pollutants in order to reduce risk exposure.	ANNALI DI IGIENE MEDICINA PREVENTIVA E DI COMUNITA Vol.35 Issue 6 Pages 660-669	10.7416/ai.2023.2581	37796470	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2192	J. Claessens, P. Dufour, N. Dardenne, C. Chaffaut and C. Pirard	2025	Contamination levels and distribution of persistent and non-persistent pollutants in paired hair, urine and serum samples from a Belgian non-occupationally exposed population	Designing ideal human biomonitoring studies involves the selection of reliable markers of exposure in adequate biological matrix. Besides conventional matrices such as blood or urine, hair has been increasingly investigated as a promising matrix for assessing exposure to persistent pollutants. However, the correlations between hair and other matrices remain poorly documented. This study aims to investigate the concentrations levels and the distribution of some persistent (POPs) and semi-persistent pollutants (PCBs and non-persistent pollutants (Bisphenols and parabens) were investigated in paired serum and hair samples, or paired spot urine and hair samples obtained from 30 Belgian non-occupationally exposed individuals. The levels measured were close to those reported in recent larger-scale studies. PFAS, PCB and bisphenol distributions largely differed depending upon the matrix and within the same chemical family depending upon the congener. The correlations and agreement between pollutant levels in differing matrices demonstrated that the information provided is comparable only for highly chlorinated PCBs and parabens, while the classification of exposure for bisphenols was substantially different according to the matrix. The selection of the human matrix thus remains complex and might markedly bias the results obtained, especially when assessing the health risk related to chemical exposure.	JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH-PART A-CURRENT ISSUES Vol.88 Issue 11 Pages 447-462	10.1080/15287394.2025.2451676	39815779	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2193	K. Chouala, K. Bouajema, Y. Khiati, S. Nari, K. Ouali, M. Boumerfaii, A. Boumediene and M. Messaoudi	2024	Antioxidant compounds from the Arthrospira platensis protect against Bisphenol A-induced nephrotoxicity in rats	Objective:A well-known endocrine disruptor, Bisphenol A (BPA) is used as a monomer in the manufacture of polyester, epoxy resin, and polycarbonate plastics. Previous studies have shown the antioxidant effect of Arthrospira platensis in several experimental models of oxidative stress. The current study was carried out to evaluate the antioxidant activity of Arthrospira platensis against BPA-induced nephrotoxicity and oxidative damage in rats.Methods: The bioactive compounds in the aqueous extract of AP were identified and confirmed by LF-TOF and HPLC. Nonetheless, this study pre-assessed the AP in vitro antioxidant activity (DPPH, ABTS, FRAP, and metal chelating activity). Male rats were divided into four groups (n = 10) and treated for 6 weeks as follows: Control, BPA (50 mg/kg), AP (1 g/kg), and BPA + AP.Results: The results of LC-MS analysis of AP, Rich of group 6 BPA have received BPA (100mg/kg bw) showed no sign of administering's really way. Animals of group 6 (BPA + AP) were treated with BPA and AP.Results: The results reveal a serious and rich phytochemical composition of the aqueous extract of Arthrospira platensis. Six polyphenols that have been linked to bioactivities were found by HPLC analysis: quercetin, chlorogenic acid, rutin, vanillic, p-coumaric and caffeic acids. Additionally, the FTIR profile demonstrates a predominant functional groups. The exposure of rats to BPA for 6 weeks provoked renal damage with significant increases in hematological parameters, oxidative stress-related parameters (i.e., malondialdehyde "MDA" protein carbonyl "PC" content, advanced oxidation protein products "AOPP", and hydrogen peroxide "H2O2"), creatinine, urea, and uric acid levels in plasma. Moreover, BPA induced a significant decrease in the activities of SOD, CAT, GPx, GST, and GR in kidney tissue.Conclusion: The present study revealed that the aqueous extract of Arthrospira platensis, in BPA-treated rats, significantly improved weight, ameliorated blood parameters, oxidative stress-related parameters, renal biomarker levels, and antioxidant enzyme activities. Also, we treated with BPA and Arthrospira platensis had normal kidney histology. These healing effects are likely the result of the high phenol content and significant antioxidant capacity of A. platensis.Conclusion:Our data strongly suggest that A. platensis supplementation improves kidney function and plays an important role in the protection against BPA-induced nephrotoxicity in rats, and that the effects are associated with the antioxidant effect of Spirulina.	TOXICOLOGY AND ENVIRONMENTAL HEALTH SCIENCES Vol.16 Issue 1 Pages 75-88	10.1007/s13530-023-00203-7	-	動物	-	1	1	1	1	0	100 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2194	S. I. Choi, X. Han, X. Men, S. J. Lee, K. T. Park, J. Han and O. H. Lee	2022	Standardized pectolinarin rich-Cirsium setidens Nakai extract attenuates bisphenol A-induced the 3T3-L1 adipocytes differentiation and obese C57BL/6J mice via the suppression of adipogenesis-related transcription factors	Endocrine-disrupting chemicals (EDCs), called obesogens, play an important role in obesity by mimicking or disrupting biochemical hormones. In this study, we determined the obesogenic effect of bisphenol A (BPA) on 3T3-L1 adipocytes and C57BL/6J mice and investigated the inhibitory effect of Cirsium setidens Nakai extract (CSE) and its major component pectolinarin (PEC) on BPA-induced obesity. 3T3-L1 cell proliferation was 0.01% (v/v) CSE, PEC, and BPA (0.1 μM) were treated to differentiated 3T3-L1 adipocytes. Cell viability was measured using the WST-1 assay. Oil Red O staining was performed to measure the lipid accumulation. Adipogenesis-related transcription factors and lipogenic enzymes were analyzed by Western blot analysis. C57BL/6J mice were fed a high-fat diet (HFD) and orally administered BPA (50 μg/kg/day) and CSE (50 mg/kg/day) for 8 weeks. Body weight, adipose tissue weights, and the adipogenesis- and lipogenesis-related proteins in WAT were measured. BPA-induced 3T3-L1 adipocytes and obese mice. These findings indicate that CSE could potentially be used as a promising natural means to prevent BPA-induced obesity and obesity-related metabolic diseases.	JOURNAL OF FUNCTIONAL FOODS, Volume 95, August 2022, 105146	10.1016/j.jff.2022.105146	-	動物、in vitro	代謝	1	1	1	1	1	1	-	-	-	0	0	20 μM	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2195	Y. Oki, I. T. Park, S. Na and K. Kwak	2023	Environment-wide association study of elevated liver enzymes: results from the Korean National Environmental Health Survey 2018-2022	Background: Environmental exposure is characterized by low concentration, chronic, and complex exposure. Traditional epidemiological studies view limitations in reflecting these characteristics since they usually focus on a single or very limited number of exposure factors at a time. In this study, we adopted the methodology of environment-wide association study (EWAS) to figure out the association of human liver function with various environmental exposure factors. Methods: We used data from the Korean National Environmental Health Survey 2018-2022 (KoNEHS) to investigate the association of 31 variables with 5 liver function indices. Separate environment-wide tests (ENTs) of the 31 variables were conducted for the aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT). Finally, we visualized these results with Manhattan plot. Results: In OLM analysis, perfluorooctanesulfonate were positively associated with ALT (adj. wt.is (ERI) 2.2, 95% confidence interval (CI): 1.39–3.06; Padjusted = 0.0027) and perfluorooctanoic acid showed positive association with GGT (ERI: 2.25, 95% CI: 1.38–3.11; Padjusted = 0.0019). Plasma mercury showed positive association with GGT (ERI: 1.86, 95% CI: 1.14–2.58; Padjusted = 0.0019). Using a 4-variable container while keeping food in the refrigerator was associated with elevated GGT compared to using a glass container (ERI = 1.61, 95% CI: 1.04–2.18; Padjusted = 0.0103). 2-ethyl-5-oxohexyl phthalate, showed a negative trend with all 3 indices (ALT: ERI = −0.57, 95% CI: −0.93–−0.21; Padjusted = 0.0103; AST: ERI = −0.43, 95% CI: −0.75–−0.11; Padjusted = 0.0103; GGT: ERI = −0.43, 95% CI: −0.75–−0.11; Padjusted = 0.0103) and showed negative association with ALT (ERI: −0.57, 95% CI: −0.93–−0.21; Padjusted = 0.0103). Conclusions: We conducted an exploratory study on environmental exposure and human liver function. By using EWAS methodology, we identified 7 factors that could have potential association with liver function.	ANNALS OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE Vol.35	10.35371/aoem.2023.35.e27	37701484	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2196	F. Cheng, X. Y. Chen, J. X. Fan, J. P. Qiao and H. Y. Jia	2023	Sex-specific association of exposure to a mixture of phenols, parabens, and phthalates with thyroid hormone and antibody levels in US adolescents and adults	Individuals are exposed to multiple phenols, parabens, and phthalates simultaneously since they are important endocrine disrupting compounds (EDCs) and share common exposure pathways. It is necessary to assess the health effects of combined exposure to multiple EDCs. Therefore, we aimed to explore the sex-specific association of EDCs mixture with thyroid hormone and antibody levels in US adolescents and adults. This measured total triiodothyronine (TT3), total thyroxine (TT4), free hormone of T3 (FT3) and T4 (FT4), thyroid-stimulating hormone (TSH), thyroglobulin (Tg), thyroid peroxidase antibody (TPOAb), and thyroglobulin antibody (TgAb). And 30 EDCs (5 phenols, 2 parabens, and 23 phthalates) were measured from urine. The relationship between single EDCs and single TH was analyzed using generalized linear regression. And results showed that several EDCs were positively associated with current T3 and FT3 levels in boys but negatively associated with current T3 and FT3 levels in girls. And in adults, five EDCs were positively associated with TT3, TT4, The effects of co-exposure to 30 EDCs on THs were calculated using Bayesian kernel machine regression and quantile-based g-computational modeling, confirmed that co-exposure was related to the increase of TT3 in adolescents, and the decrease of TT4 in both adolescents and adults. Besides, nonlinear and linear relationships were identified between co-exposure and the risk of positive THAbs and TgAb in girls and adult females, respectively. In conclusion, phenols, parabens, and phthalates as a mixture might interfere the concentrations of THs and thyroid autoantibodies, and the interfering effect across significantly by sex as well as age. Further prospective research is warranted to investigate the causal effects and underlying mechanisms of co-exposure on thyroid dysfunction.	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH Vol.30 Issue 57 Pages 121207-121223	10.1007/s11356-023-30739-7	37950782	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2197	Y. T. Chen, L. Y. Xu, Q. Q. Zhu, L. G. Hu and C. Y. Liao	2025	Typical endocrine disrupting chemicals in newborns with congenital hypothyroidism: Concentrations, exposure assessment, and potential risks	Congenital hypothyroidism (CH) has been reported as a prevalent endocrine disorder in newborns. Endocrine disrupting chemicals (EDCs) have been widely detected in humans and can influence endocrine function, especially thyroid function, and neonates as a susceptible population may be more prone to suffer from CH through exposure to various EDCs. In this study, the concentrations and composition profiles of several typical EDCs, including phthalates, parabens, and phenols, were investigated in 1,000 CH and 1,000 healthy newborns. The median concentrations of total EDCs in CH were significantly higher than those in healthy newborns (CH versus without CH, except for chlorines. Relatively higher levels of phthalate metabolites, parabens, and chlorobisphenol A and E (CBPA and CBPE) in CH. Based on the measured concentrations, exposure to and risk of total EDCs were assessed. The median estimated daily intakes of target EDCs ranged from 0.300 (benzophenone-1) to 162 ng·g-bw-bw/day (parabens) in the CH group. To explore the possible mechanism of thyroid function damage caused, binary logistic analysis was performed and results revealed that exposure to monoisobutyl phthalate (mCPP), ethyl paraben (EPB), monobenzylphthalate (MBzP), and 4-hydroxybenzophenone-2 (BP-8) may increase the risk of suffering from CH (adjusted odds ratio (OR): 1.36–1.71). Taken together, this study findings and timely uncover the association between exposure to several typical EDCs and the common endocrine disorder CH. Such associations and possible causes should be determined in vitro and in vivo in the follow-up studies.	J Hazard Mater. 2025 Mar 15:486:136991.	10.1016/j.jhazmat.2024.136991	39733755	ヒト	甲状腺	-	-	-	-	-	-	-	-	-	症例対照	1	1	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2198	L. Chen, M. Zhou, D. L. Lv and S. W. Qiu	2025	Examination of the Association Between Bisphenol-Related Genes and Lung Cancer	In recent years, the release of substantial amounts of synthetic endocrine-disrupting chemicals (EDCs) into the environment has posed significant threats to human health. Among these EDCs, bisphenol A (BPA) and its substitutes, such as bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF), are widely used and have been implicated in disrupting various biological processes. This research aimed to evaluate the potential link between BPA-related genes and lung cancer risk. Utilizing data from The Cancer Genome Atlas (TCGA), we identified 1,057 BPA-related genes through a comprehensive search of the GeneCards database, encompassing those with high relevance scores, verified interactions, and genes showing significant differential expression. Subsequent analyses, including KEGG, DAVID, STRING, and CIBERSORT, were employed to explore the enrichment pathways, protein interactions, and immune cell infiltration associated with these genes. Our findings indicate that bisphenol-related genes may be associated with a variety of cancers, particularly lung cancer. To develop a risk model, we employed Cox regression and LASSO regression analyses, constructing a prognostic prediction model for lung cancer based on bisphenol-related gene expression (BRPPM). This model demonstrated significant predictive power for lung cancer patients, categorized into high-risk and low-risk groups, revealing significant differences in survival rates and highlighting the model's accuracy in predicting lung cancer outcomes. In addition to bioinformatics analyses, experimental studies were conducted to evaluate the effects of BPA on lung cancer cell behavior. BPA exposure significantly promoted the proliferation of A549 lung cancer cells, as assessed by the CCK-8 assay, and increased the clonogenic potential of the cells in a newly formulated assay.	JOURNAL OF CLINICAL PHARMACY AND THERAPEUTICS Vol.2025 Issue 1	10.1155/jcpt/8872458	-	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2199	C. Y. Chen, C. Y. Sun, H. J. Hsu, I. W. Wu, Y. C. Chen and C. C. Lee	2021	Xenoestrogen exposure and kidney function in the general population: Results of a community-based study by laboratory tests and questionnaire-based interviewing	Background: Chronic kidney disease (CKD) is a growing concern worldwide. Exposure to xenoestrogens (XEs), such as phthalates, parabens, and phenols, lead to CKD. However, kidney function and its complex relationship with XEs, lifestyle, and dietary habits are not well understood. Methods: In the present cross-sectional community-based cohort study, we enrolled 887 subjects for a questionnaire-based interview and laboratory tests. Urinary concentrations of 11 XEs were measured using high-performance liquid chromatography with tandem mass spectrometry. Subjects were divided into quartiles with low exposure risk scores. Results: Univariate and multivariate linear regression showed that a high exposure score (beta = 1.50–4.234; p < 1.455; P = 0.023) was independently associated with eGFR in 887 subjects. Univariate and multivariate linear regression in urinary XEs and urine albumin creatinine ion ratio (UACR) in 128 subjects indicated that ethylparaben (EP) (beta = 0.92, 95% CI: 0.139–3.735, P = 0.035) was significantly associated with increased UACR. Multivariate regression analyses of the CKD subgroup (n = 38) after adjusting for age, showed that higher levels of mono-(2-ethylhexyl) phthalate (MEHP), EP, octylphenol (OP), and bisphenol-F (BP-3) were significantly associated with lower estimated glomerular filtration rate (eGFR). Higher urinary levels of MEHP (OR: 0.027, 95% CI: 1.272–7.282) were more likely associated with lower eGFR (beta = −1.50, 95% CI: −2.99–−0.01, P = 0.048). Higher urinary levels of MEHP (beta = −1.50, 95% CI: −2.99–−0.01, P = 0.048), EP (beta = −1.50, 95% CI: −2.99–−0.01, P = 0.048), and OP (beta = −1.50, 95% CI: −2.99–−0.01, P = 0.048) were also significantly positively associated with total exposure scores after applying multivariate linear regression analyses. Conclusion: XE exposure scores obtained from the questionnaires were negatively associated with kidney function. Urinary metabolites of XEs, including EP, MP, BP-3, and MEHP, are potential risk factors for microalbuminuria and decline in kidney function. MEHP seemed to have the strongest correlation with high exposure scores and decline in kidney function.	Environ Int. 2021 Oct:155:106585.	10.1016/j.envint.2021.106585	33910077	ヒト	腎	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2200	C. Chatzicharalampous, D. Bal, O. Camp, N. Joshi and H. M. Abu-Soud	2022	Zinc Homeostasis, Reactive Oxygen Species Imbalance and Bisphenol-A Exposure in the Preimplantation Mouse Embryo: a possible adverse outcome pathway	Bisphenol-A (BPA) is a ubiquitous xenoestrogen found in plastic products used for food containers, paper products, water pipes, etc. Individuals exposed to BPA are susceptible to detrimental effects, with poor oocyte quality, sperm motility, and impaired embryo implantation observed in mouse models at levels as low as 100 ng/kg/day. To investigate the mechanism through which BPA affects embryo development, oocytes were retrieved from 100-week-old mice and fertilized using IVF. The embryos were divided into 2 groups and exposed to increasing BPA concentrations (20–250 ng/dl) for 30 hours, then were graded daily based on morphological appearance and development. A subgroup of the treated embryos (n = 30/group) were further evaluated for induction of apoptosis, overproduction of ROS, and zinc distribution. Mouse oocytes were treated with BPA (up to 500 ng/dl), then, using RT-PCR, we performed gene expression studies for ATSP1, an important gene in zinc homeostasis. Cultured day 5 mouse embryos that were exposed to BPA concentrations > 70 ng/dl showed a significant decrease in blastocyst formation rate (p < 0.05). Apoptosis was significantly induced in embryos treated with BPA concentrations ≥ 100 ng/dl (p < 0.05). Oocytes exposed to BPA showed increased production of ROS and mitochondrial dysfunction. Embryos treated with increasing concentrations of BPA (p < 0.05). Gene expression studies revealed downregulation of the ATSP1 gene in oocytes exposed to high BPA concentrations (p < 0.05). This could potentially worsen implantation rates and pregnancy outcomes. Conclusions: Small sample size; evaluation of single-rather than combined exposures. Conclusions: Simultaneous measurement of multiple organic pollutants in adults with CKD is feasible. Exposure levels are comparable with healthy individuals. Select contaminants, especially in the phthalate class, may be associated with more rapid deterioration in kidney function.	ADVANCES IN REDOX RESEARCH Vol.4	10.1016/j.arres.2022.100032	-	in vitro	-	-	-	-	1	0	10, 25, 50, 100 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2201	D. M. Chantar, W. B. Wu, M. L. Liu, Z. M. Li, K. Kenrari, L. Trevathe, V. K. Pal, S. Lee, H. Trachtman and C. S. Investigators	2024	Organic Pollutant Exposure and CKD: A Chronic Renal Insufficiency Cohort Pilot Study	Rationale & Objective: This study aimed to assess the effect of exposure to organic pollutants in adults with chronic kidney disease (CKD). Study Design: This was a cross-sectional and longitudinal analysis. Setting and Participants: Participants with CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study and healthy individuals from contemporaneous National Health and Nutrition Examination Survey cohorts. Exposures: Urinary concentrations of 11 phthalate and phenol metabolites and 2 parabens. Outcomes: Baseline eGFR, annual eGFR slope, and incident composite of congestive heart failure, myocardial infarction, and stroke were the crucial time (kidney failure or n = 589; decline in estimated glomerular filtration rate (eGFR). Analytical Approach: We used high-performance liquid chromatography with tandem mass spectrometry to measure urinary concentrations of bisphenols, phthalates, organophosphate pesticides, polycyclic aromatic hydrocarbons, melamine, and cotinine and 4 parabens. Results: Participants with CKD were further evaluated for induction of apoptosis, overproduction of ROS, and zinc distribution. Mouse oocytes were treated with BPA (up to 500 ng/dl), then, using RT-PCR, we performed gene expression studies for ATSP1, an important gene in zinc homeostasis. Cultured day 5 mouse embryos that were exposed to BPA concentrations > 70 ng/dl showed a significant decrease in blastocyst formation rate (p < 0.05). Apoptosis was significantly induced in embryos treated with BPA concentrations ≥ 100 ng/dl (p < 0.05). Oocytes exposed to BPA showed increased production of ROS and mitochondrial dysfunction. Embryos treated with increasing concentrations of BPA (p < 0.05). Gene expression studies revealed downregulation of the ATSP1 gene in oocytes exposed to high BPA concentrations (p < 0.05). This could potentially worsen implantation rates and pregnancy outcomes. Conclusions: Small sample size; evaluation of single-rather than combined exposures. Conclusions: Simultaneous measurement of multiple organic pollutants in adults with CKD is feasible. Exposure levels are comparable with healthy individuals. Select contaminants, especially in the phthalate class, may be associated with more rapid deterioration in kidney function.	Kidney Med. 2023 Dec 13;6(3):100778.	10.1016/j.xkme.2023.100778	38435069	ヒト	腎	-	-	-	-	-	-	コホート	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2202	L. Caporossi, P. Vigano, E. Paci, S. Capanna, A. Alteri, M. De Rosa, D. Pigini, E. Pertenti and B. Papaleo	2025	Evidence About the Possible Role of Phthalates and Bisphenol A in Recurrent Pregnancy Loss and Endocrine Dysfunctions: A Case-Control Study	Objectives: A case–control study was conducted to investigate the exposure levels to some specific chemicals, in women with infertility issues, compared with fertile women. Methods: A total of 186 cases and 196 controls were recruited. Each participant provided a urine sample for the determination of six phthalate metabolites (mono-ethyl phthalate, MEP; mono-n-butyl phthalate, MnBP; mono-n-butyl phthalate, MnBP; mono-benzyl phthalate, MBzP; mono-(2-ethylhexyl) phthalate, MEHP; and two metabolites of the diethyl hexyl phthalate (DEHP): mono(2-ethyl-5-hydroxyhexyl) phthalate, MEHHP and mono(2-ethyl-5-oxohexyl) phthalate, MEHP) in addition to bisphenol A, BPA. Each woman also completed a questionnaire about her lifestyle habits and medical history. Results: Women with infertility showed significantly higher urinary concentrations of MEP, MnBP, MBzP, MEHHP, and MEHP, except MnBP. Stratified baseline infertility factors, showed a significant association of MnBP, MBzP, MEHHP, and MEHP with ovulatory and endometrium dysfunctions. Furthermore, higher mean concentrations of MEP and MEHP were observed in women with recurrent pregnancy loss (RPL) and idiopathic infertility, respectively. Conclusion: These findings suggest that some of the analyzed chemicals may play a role in female infertility. Exposure to DEP (diethyl phthalate) and DEHP appears to be associated with RPL and idiopathic infertility. Further investigation is required to explore potential sources of these risks.	ENVIRONMENTS Vol.12 Issue 2	10.3390/environments12020038	-	ヒト	生殖発生	-	-	-	-	-	-	症例対照	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2203	R. Cairoas, J. D. Doecke, C. J. Fowler, J. Fripp, V. Y. Wang, J. F. Mueller, A. Jayarathna, C. Ha, A. Elagali, S. Dunlop and C. L. Masters	2025	Association of plastic-associated chemicals with Alzheimer's disease amyloid- β and cognitive status	Alzheimer's disease (AD) is characterized by amyloid-beta (A-beta) for similar to 20 years prior to dementia onset. Phthalates, routinely added to plastics to increase flexibility, and bisphenol monomers, have been shown to interfere with neural activity/brain function. Phthalate and bisphenol exposure and an inter-association of individual urinary biomarkers with A-beta or clinical dementia and cognitive impairment (MCI/AD). Assessing biomarkers in particular, two mono(2-ethylhexyl) phthalate (MEHP), but not other biomarkers of di(2-ethylhexyl) phthalate (DEHP), was associated with A-beta+ and with lacking MCI/AD (p < 0.05), while high Bisphenol-S (BPS) was associated with A-beta+ (p < 0.05). Bilinear analysis shows significant association with MCI/AD but not A-beta.	JOURNAL OF ALZHEIMERS DISEASE	10.1177/13872877251364559	40754819	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2204	H. Byeon	2025	Identifying key determinants of bisphenol A exposure: a study utilizing sparse additive models (SpAM) on a cohort of 1332 adult males in South Korea	Background: Bisphenol A (BPA) exposure is a significant concern in South Korea due to high plastic consumption. This study investigates the factors influencing BPA exposure among adult males. Methods: Using data from the Korean National Environmental Health Survey (KoNEHS) 2018–2020, we applied sparse additive models (SpAM) to analyze BPA exposure in 1332 males aged 19–64. The study considered various variables including age, smoking, alcohol consumption and food packaging-related behaviors. Results: Age emerged as the most significant predictor of BPA exposure. Smoking and alcohol consumption also showed substantial effects. Packaged and canned food consumption score also identified as significant contributors, indicating potential leaching from packaging materials. Time furniture purchase showed moderate effects. Conclusions: This study highlights age, lifestyle factors (smoking and alcohol), and food packaging as key factors influencing BPA exposure in South Korean adult males. These findings contribute to the evidence base for public health interventions aimed at reducing BPA exposure. Future research should explore longitudinal data and genetic factors for personalized strategies.	JOURNAL OF MENS HEALTH Vol.21 Issue 5 Pages 30-38	10.22514/jomh.2025.065	-	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2205	Melek Büyükveren, Baver Demir	2024	High Urinary Bisphenol A Levels may be a Risk Factor for Infantile Colic: a case-control study	Objective: To investigate the relationship between infantile colic and urinary Bisphenol A (BPA) levels in infants aged under 3 months. Patients and Method: A group of 39 infants with a recent diagnosis of infantile colic, according to Wessel's criteria, and a control group of 39 healthy infants were included in the study. Urine samples were collected from the infants in the morning hours. Urinary BPA levels were measured by liquid chromatography-mass spectrometry and were normalized to urinary creatinine levels. Results: The mean urinary BPA level was found to be significantly higher in the infantile colic group than in the control group (p=0.001). The mean BPA levels of infants who were exclusively breastfed, those who received both breast milk and formula, and those who received only formula were 0.21 ng/mg creatinine, 0.29 ng/mg creatinine, and 0.34 ng/mg creatinine, respectively (H=9.18; df=2; p = 0.01). The results revealed that as a result of the regression analysis, was not statistically significant (Model Significance: F = 0.883; p = 0.350; R² = 0.012). Conclusion: The etiology of infantile colic is still poorly understood and is considered to be associated with disrupted microbiota. Our results suggest that BPA is associated with the development of infantile colic.	ANDES PEDIATRICA Vol.95 Issue 6 Pages 711-717	10.32641/andespediatr.v95i6.5182	-	ヒト	生殖発生	-	-	-	-	-	-	症例対照	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2206	A. Burman, R. Garcia-Millan and S. Whirledge	2020	Gene X environment: the cellular environment governs the transcriptional response to environmental chemicals	Background: An individual's response to environmental exposures varies depending on their genotype, which has been termed the gene-environment interaction. The phenotype of cell exposed can also be a key determinant in the response to physiological cues, indicating that a cell gene-environment interaction may exist. We investigated whether the cellular environment could alter the transcriptional response to environmental chemicals. Methods: We exposed human embryonic stem cells (hESCs) and hESC-derived neural progenitor cells (NPCs) to a panel of 10 environmental chemicals, including bisphenol A, and performed RNA-sequencing to measure changes in gene expression. Results: Thirty-seven genes were found to be differentially expressed in response to environmental chemicals in both cell types. Comparisons were made to studies that met the predefined criteria for exposure length, concentration, and experimental replicates. The cellular response to the physiochemical perturbants resulted in remarkably unique transcriptional profiles in breast, liver, and arterial cell types. Analysis of gene regulatory networks and molecular pathways revealed that the cellular context mediated the activation or repression of functions important to cellular regeneration and survival, including opposing effects by genotoxins in breast vs. liver and arterial cell types. When controlling for cell type, several genes regulate unique gene networks and biological functions, despite belonging to the same class of environmental chemicals. Interestingly, the cell type with the most substantial transcriptional response to the 10 chemicals was the NPC, which is a cell type that is highly susceptible to developmental toxicants. Conclusions: Our results demonstrate that the transcriptional response to environmental chemicals depends on a variety of factors, including the cellular context, the genetic cue of a cell, and the individual chemical. These findings highlight the importance of evaluating the impact of exposure across cell types, as the effect is responsive to the cellular environment. These comparative genetic results support the concept of a cell-gene-environment interaction.	HUMAN GENOMICS Vol.14 Issue 1	10.1186/s40246-020-00269-1	32448403	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない

通格性評価（疫学）1：該当、0：該当しない

通格性評価（in vitro）1：該当、0：該当しない

通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

判断評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2207	E. V. Bil'tune, C. S. Uddbjerg, Y. H. Lim, L. S. Gregersen, M. Krause, H. Frederiksen and A. M. Andersson	2022	Presence of parabens, phenols and phthalates in paired maternal serum, urine and amniotic fluid	Objective To examine whether selected endocrine disrupting chemicals were present in pregnant women and passed through the placental barrier to amniotic fluid, potentially exposing the developing fetus. Methods Paired maternal serum, urine and amniotic fluid samples were collected from 50 women undergoing amniocentesis for prenatal diagnosis of chromosomal abnormalities at gestational weeks 12 - 16. The concentration of six different parabens, seven phenols, 12 metabolites from 10 phthalate diesters and two polychlorinated substances in total were analyzed by isotope diluted TurboFlow liquid chromatography tandem mass spectrometry. Results Concentrations of all included compounds were highest in maternal urine followed by serum, and lowest in amniotic fluid. Of the six parabens measured in amniotic fluid, methyl paraben was detected in all samples with a median concentration of 0.5 ng/ml. Propyl paraben was detected in 98% of the samples with a median concentration of 0.1 ng/ml. Butyl paraben was detectable in the range of 12-15% of the amniotic fluid samples, at low concentrations (<0.2 ng/ml). Two secondary phthalates, metabolites of di-2-ethylhexyl phthalate and mono-carboxy-iso-octyl phthalate were each present in <~15% of the amniotic fluid samples at concentrations 2-5 times lower than in maternal serum and 20-100 times lower than in maternal urine. It media statistically significant correlation between the levels of MeP and EtP was detected in paired maternal urine-amniotic fluid samples was detected (Spearman rho=0.3258, 0.01 0.362). Likewise, the concentration of mono-ethyl phthalate (MEP) in paired maternal urine and amniotic fluid samples indicated a modest statistically significant correlation (Spearman rho=0.3760, shows by detectable levels of MEP in only 3% of the amniotic fluid samples. Conclusions In general, the included parabens, phenols and phthalates were effectively metabolized and excreted in the urine, which was the matrix that reflected the highest detectable levels. The detectable levels of several included parabens and phthalates in human amniotic fluid calls for further investigations of the toxicokinetic and potential endocrine disrupting properties of individual and multiple endocrine disruptors in order to better assess the risks to the developing fetus.	ENVIRONMENT INTERNATIONAL Vol.158	10.1016/j.envint.2021.106987	34991249	ヒト	-	-	-	-	-	-	ADME	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2208	J. M. Braun, J. P. Buckley, K. M. Cecil, A. M. Chen, H. J. Kalkwarf, B. P. Lanphear, Y. Y. Xu, A. Wiseto and K. Yolton	2020	Adolescent follow-up in the Health Outcomes and Measures of the Environment (HOME) Study: cohort profile	Purpose Environmental chemical exposures may adversely affect an array of adolescent health outcomes. Thus, we used the Health Outcomes and Measures of the Environment (HOME) study, a prospective cohort that recruited pregnant women and conducted longitudinal follow-up on children over the first 12 years of life, to determine if and when chemical exposures affect adolescent health. Participants We recruited 398 pregnant women in 2003 and 2004 from 3 urban hospitals. The 249 children who were born to these women and who had urine specimens collected at age 1 year were eligible for follow-up at 8 years (2012 to 2014) at their original hospital sites, and four home and six clinic visits when children were aged 8 weeks and 1, 2, 3, 4, 5 and 8 years. Of 302 children available for follow-up, 286 (95%) completed at least one follow-up and 256 (86%) completed the most recent follow-up at 12 years of age (range: 11-13). Findings to date Our two measures include maternal child report of internalising symptoms, rearchlaging, dual energy X-ray absorptiometry derived estimates of two adipose tissue and bone mineral density, and cardiometabolic risk biomarkers. We assessed adolescents exposure to perfluoroalkyl substances, phenols, phthalates and flame retardants. Participants completing follow-up at 12 years of age were similar to the original cohort in terms of baseline factors. Most children had typical and expected values for this age on measures of internalising symptoms, body composition, bone mineral content and density, and blood pressure. Future plans We will examine associations of early life environmental chemical exposures with adolescent health measures, while considering potential periods of heightened susceptibility and mixture effects.	BMJ Open. 2020 May 7;10(5):e034838.	10.1136/bmjopen-2019-034838	32385062	ヒト	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2209	C. J. Borgert, L. D. Burgoon and J. C. Matthews	2024	The physiological and biochemical basis of potency thresholds modeled using human estrogen receptor alpha: implications for identifying endocrine disruptors	The endocrine system functions by interactions between ligands and receptors. Ligands exhibit potency for binding to and interacting with receptors. Potency is the product of affinity and efficacy. Potency and physiological concentration determine the ability of a ligand to produce physiological effects. The kinetic behavior of ligand–receptor interactions conforms to the basics of mass action. The laws of mass action define the relationship between the affinity of a ligand and the fraction of receptor receptors that it occupies at any physiological concentration. We previously identified the minimum ligand potency required to produce clinically adverse reproductive outcomes in women undergoing assisted reproduction in terms of receptor occupancy by the normal endogenous ligand, 17β-estradiol (E2). Here, we used the same mass action model to derive an even more well-characterized value of the potency endogenous hormone (17 beta-estradiol, E2) as an indicator of clinically observable teratogenic effects. This allowed us to propose a Lowest Perturbed Potency Threshold (LPPT) for ER alpha ligands of 1 x 10-2 relative to E2. Here, we test the hypothesis that the HRPT for ER alpha arises from the receptor occupancy by the normal metabolic milieu of endogenous ER alpha ligands. The metabolic milieu contains precursors to hormones, metabolites of hormones, and other normal products of metabolism. We have calculated fractional receptor occupancies for ER alpha ligands in women before and during previously established HRPT when normal circulating levels of same endogenous ER alpha ligands and E2 were also present. If fractional receptor occupancy calculations showed that individual ER alpha ligands with concentrations in the metabolic milieu did not exceed the HRPT, then the HRPT was considered to be supported. Fractional receptor occupancy calculations showed that the HRPT was not exceeded by any of the hundreds of normal endogenous ligands found naturally in human blood. Ligands with potencies less than tenfold higher than the HRPT were unable to compete successfully for ER alpha. These results show that the HRPT for ER alpha against our E2 standard (E2 proposed previously) is quite conservative and should be considered strong evidence against the potential for disruption of the estrogenic pathway. For chemicals with potency 10 of E2, the potential for estrogenic disruption through this mechanism can be considered improbable except in the presence of corroborative evidence. Most importantly, this work demonstrates that the endogenous, metabolic milieu is responsible for the observed ER alpha agonist HRPT; that this HRPT applies also to ER alpha antagonists, and it provides a compelling mechanistic explanation for the HRPT that is grounded in basic principles of molecular kinetics using well characterized properties and concentrations of endogenous components of normal metabolism.	Arch Toxicol. 2024 Jun;98(6):1795-1807.	10.1007/s00204-024-03723-4	38704805	in vitro	-	-	-	-	-	-	-	-	-	-	不明	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2210	P. A. Bommarito, B. M. Welch, A. P. Keil, G. P. Baker, D. E. Cantonwine, T. F. McElrath and K. K. Ferguson	2021	Prenatal exposure to consumer product chemical mixtures and size for gestational age at delivery	Background While fetal growth is a tightly regulated process, it is sensitive to environmental exposures that occur during pregnancy. Many commonly used consumer products contain chemicals that can disturb processes that regulate fetal growth. Methods We measured 51 chemicals in 1,540 urine samples collected from 308 pregnant women in the LIFECODES cohort. Chemicals measured included bisphenols (BPA, BPF, BPS), phthalate and phthalate alternative metabolites (monoesters), parabens (methyl, ethyl, propyl, butyl), triclocarban, triclosan, benzophenone-3, and 12 phenols, and the odds of small- or large-for-gestational-age (SGA and LGA) births. Methods This case-control study was comprised of SGA (N = 151; 5.6-5% < 10) and appropriate-for-gestational-age control (N = 151) births selected from the larger LIFECODES cohort. Biomarkers of exposure to consumer product chemicals were quantified in maternal urine collected during pregnancy visits scheduled at approximately 9 (median = 9.1), 16 (median = 16.1), 26 (median = 26.1), and 36 (median = 36.1) weeks gestation. Multivariable logistic regression models were used to estimate associations between maternal urinary concentrations of individual chemicals and SGA and LGA births. Bayesian kernel machine regression was used to jointly estimate the effects of a mixture of chemicals. Results Increased odds of SGA were observed for the BPA (OR = 1.5; 95% CI: 0.96, 2.4), BPF (OR = 1.5; 95% CI: 0.94, 2.4), and triclocarban (OR = 1.5; 95% CI: 0.96, 2.3) quartile 4 vs. quartile 1 comparisons. Increased odds of LGA were observed for the BPA (OR = 1.5; 95% CI: 0.94, 2.3), BPF (OR = 1.5; 95% CI: 0.96, 2.4), and triclocarban (OR = 1.5; 95% CI: 0.96, 2.3) quartile 4 vs. quartile 1 comparisons. Bayesian kernel machine regression models identified a positive association between the mixture of chemicals and SGA births with the second highest quintile of exposure to the mixture of chemicals associated with the highest odds of SGA (OR = 1.6; 95% CI: 0.94, 2.7) compared to the lowest quintile of exposure. Conclusions Our findings suggest that exposure to mixtures of chemicals found in consumer products may contribute to fetal growth restriction. Future work to understand this exposure-response relationship and identify critical windows of exposure could further inform the role of chemical exposures in the etiology of fetal growth restriction. Future work to understand this exposure-response relationship and identify critical windows of exposure could further inform the role of chemical exposures in the etiology of fetal growth restriction.	34112176	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2211	T. Boiciaine-O'Neill, W. R. Lee, T. L. Blake, P. D. Sly and D. Vilcins	2024	Exposure to endocrine-disrupting plasticisers and lung function in children and adolescents: A systematic review and meta-analysis	Exposure to endocrine-disrupting plasticisers (EDPs), such as phthalates and bisphenols, has been associated with reduced lung function in children and adolescents. However, the existing literature yields conflicting results. This systematic review and meta-analysis aimed to assess the epidemiologic evidence investigating the association between EDP exposure and lung function in children and adolescents. A comprehensive search of the databases identified 24 relevant studies. We employed a random-effects meta-analysis on systematic reviews. The effect size of interest was the change in forced expiratory volume in 1 s (FEV1) was indicated by a one-fold increase in exposure levels. We found that certain phthalates marginally reduced lung function in children. Forced expiratory volume in 1 s (FEV1) was reduced by a one-fold increase in mono-benzyl phthalate (MBzP) (beta = -0.027; 95% CI: -0.053 to -0.001; I2 = 0.0%; 3 studies; 1,610 exposed), mono-ethyl phthalate (MEP) (beta = -0.020; 95% CI: -0.038 to -0.002; I2 = 0.0%; 3 studies; 1,610 exposed), and mono-isobutyl phthalate (MiBP) (beta = -0.022; 95% CI: -0.043 to -0.001; I2 = 0.0%; 3 studies; 1,610 exposed). Forced vital capacity (FVC) was decreased by a one-fold increase in MBzP (beta = -0.022; 95% CI: -0.036 to -0.008; I2 = 0.0%; 3 studies; 1,610 exposed), MEP (beta = -0.018; 95% CI: -0.032 to -0.003; I2 = 0.0%; 3 studies; 1,610 exposed), and MiBP (beta = -0.018; 95% CI: -0.032 to -0.003; I2 = 0.0%; 3 studies; 1,610 exposed). Forced expiratory flow (FEF25-75) (beta = -0.030; 95% CI: -0.054 to -0.006; I2 = 0.0%; 3 studies; 1,610 exposed) was also reduced by a one-fold increase in MEHP levels. Furthermore, a two-fold increase in MEOHP levels reduced forced mid-expiratory flow (FEF25-75) (beta = -0.030; 95% CI: -0.054 to -0.006; I2 = 0.0%; 3 studies; 1,610 exposed). Finally, associations were more pronounced in males. Given the potential for reverse causation bias, the association between childhood exposure to EDPs and lung function remains uncertain. Overall, our meta-analysis observed small reductions in lung function with higher phthalate exposure. However, future studies are warranted in younger age groups.	Environ Res. 2024 Feb 15;243:117751.	10.1016/j.envres.2023.117751	38061586	ヒト	呼吸器系/メタアナリシス	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2212	D. Blaska, M. P. Ngatelo, K. Chatzimeletiou, G. Mastorakos, S. Lymperi and D. G. Goulis	2020	The effects of postnatal exposure of endocrine disruptors on testicular function: a systematic review and a meta-analysis	Background Despite many epidemiological studies having been conducted, the impact of postnatal exposure of endocrine disruptors (EDs) on testicular function remains a controversial issue. Aim To systematically review the literature and perform a meta-analysis regarding the effects of postnatal exposure to EDs on testicular function. Methods Pubmed, Scopus, Web of Science, Cochrane Library and Google Scholar were searched for the last 20 years for studies in English that examined human exposed and cohort studies with ED and data that had a high probability of postnatal exposure to EDs. Purposeful, 12 studies were selected that investigated postnatal exposure to EDs ("non exposed"), and (ii) an outcome of interest (testicular parameters and reproductive hormone concentrations). The continuous outcomes in each of the studies were synthesized by the random effects model and expressed as standardized mean difference (SMD) with 95% confidence interval (CI). Results 19 cohort studies, including 909 exposed and 907 non-exposed men, fulfilled the inclusion criteria. Exposure to EDs was associated with decreased LH (SMD: -0.17, 95% CI: -0.33 to -0.02; 10 studies; 919 exposed, 563 non-exposed), T (SMD: -0.49, 95% CI: -0.77 to -0.21; three studies; 1,139 exposed, 1,139 non-exposed), and normal morphology (SMD: -0.66, 95% CI: -0.84 to -0.47; eight studies; 580 exposed, 580 controls), in 95% (n = 18/) compared with non-exposure. No difference was observed between the other study groups. Conclusions Postnatal exposure to EDs is associated with decreased semen quality. Nevertheless, there is no evidence that a disruption of testicular function mediates the deterioration in semen quality.	Hormones (Athens). 2020 Jun;19(2):157-169.	10.1007/s42000-019-00170-0	31925736	ヒト	精巣システマティックレビュー	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2213	S. M. Bleavens-braad, V. W. Jaddoe, S. Santos, K. Kannan, G. R. Dohle, L. Trascande and R. Gaillard	2022	Associations of maternal urinary bisphenol and phthalate concentrations with offspring reproductive development	Fetal exposure to bisphenols and phthalates may influence development of the reproductive system in a population-based, prospective cohort study of 1309 mother–child pairs, we examined the associations of maternal urinary bisphenol and phthalate concentrations measured in early pregnancy with reproductive development in boys and girls. Reproductive development was assessed by anogenital distance (AGD), obtained information on cryptorchidism or hypospadias after birth from medical records, At 9.7 years, we measured testicular and ovarian volume by MRI. At 12.5 years, we measured child hormone ranges and menstruation through questionnaire. We performed linear or logistic regression models for boys and girls to assess the associations of maternal urinary average and trimester-specific bisphenols and phthalates with child reproductive outcomes. Next, to further explore potential synergistic or additive effects of exposure together, we performed mixed-exposure models using a supervising composition models. Models were adjusted for maternal age, ethnicity, body mass index, education, parity, energy intake, smoking and alcohol use, and child's gestational age at birth, birthweight and body mass index. In boys, no associations of maternal gestational phthalate or bisphenol concentrations with AGD, cryptorchidism, hypospadias, testicular volume, or reproductive hormone levels were observed. In girls, maternal urinary bisphenol A concentrations were associated with larger child ovarian volume at 10 years. Higher maternal phthalic acid and total bisphenol were associated with earlier genital and public hair development at 13 years, respectively (p values ≤0.05). In girls, we found no associations of maternal urinary bisphenol and phthalates with ovarian volume or menstrual age. Only higher maternal urinary high molecular weight phthalate was associated with earlier public hair development at 13 years (p values ≤0.05). Higher mixture exposure was associated with earlier public hair development in both sexes. In conclusion, higher maternal gestational urinary bisphenol and phthalate concentrations were associated with alterations in offspring reproductive development, mainly in boys.	Environ Pollut. 2022 Sep 15:309:119745.	10.1016/j.envpol.2022.119745	35820574	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2214	S. M. Bleavens-braad, A. J. Bloem, R. Gaillard, L. G. Kahn, M. L. Lévy-kresser, A. A. Sakhi, E. L. Bekkers, Z. X. Ma, L. Spadacini, C. Thomsen, E. A. P. Steegers, A. Muldera, V. W. V. Jaddoe and L. Trascande	2025	Periconception bisphenol and phthalate concentrations in women and men, time to pregnancy, and risk of miscarriage	Background: Exposure to endocrine disrupting chemicals such as bisphenols and phthalates might lead to adverse fertility and early pregnancy outcomes. Methods: This study was embedded in the Generation R Next Study, a population-based cohort study from preconception onwards. Urinary phthalate and bisphenol concentrations were assessed in the periconception period (708 women), defined as the period in which couples were actively trying to conceive, and early pregnancy (1,266 women and 1,322 men, mean gestational age at sampling 8.4 weeks (sd = 6.4 weeks)). Time to pregnancy and miscarriage were assessed using questionnaires and medical records. We used Cox proportional hazard models to examine associations with time to pregnancy and logistic regression models with miscarriage. Results: Higher periconception bisphenol A (BPA) concentrations in women were associated with longer time to pregnancy (fecundity density ratio = 0.87 (95% CI: 0.77, 0.98) per 1 unit higher ln-transformed BPA concentration). Periconception mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHP), and mono-benzyl phthalate (MBzP) were associated with shorter time to pregnancy, and higher mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), MECPP, and MBzP with lower odds of subfertility. In men, higher early pregnancy BPA, MCPeP, mono-3-methyl-2-hydroxypropyl phthalate, mono-3-methyl-2-carboxypropyl phthalate, mono-ethyl phthalate were associated with shorter time to pregnancy or lower odds of subfertility. Higher preconception or early pregnancy BPA, phthalic acid, and MCPeP in women were associated with lower odds of miscarriage, whereas higher mono-(3-carboxypropyl) phthalate (MCPP) and mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) had higher odds of miscarriage. Out of almost 15 possible data sets, Bkmr identified a consistent exposure-response relationship between mixtures of phthalates and miscarriage. Conclusions: Periconception and early pregnancy exposure to bisphenols and phthalates may affect couple fertility. Our results should be considered as hypothesis generating and replicated in future studies, possibly including repeated chemical measurements and mixture analysis.	Environ Res. 2025 Aug 1:278:121712.	10.1016/j.envres.2025.121712	40311909	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2215	N. X. Bi, C. Q. Huang, X. Z. Gu, R. R. Wang, H. Y. Liu, R. Q. Zhou, H. Y. J. Zhang, X. T. Chen and H. L. Wang	2025	Bisphenol A Impairs Spatial Memory by Inhibiting Hippocampal Excitatory Neuronal Response During Learning Events	Bisphenol A (BPA) exposure can impair learning and memory in rodents, but the underlying systematic neural mechanism remains unclear. Due to the important role of the hippocampus, for learning and memory, in this study, we systematically investigated the neural circuit, neuron structure, and function of the hippocampus after BPA exposure. First, by employing in vivo fiber photometry technique, we observed a decrease in the neural projection ratio of excitatory neural neurons from the "Entorhinal Cortex–Dentate Gyrus–CA3–CA1" and "Entorhinal Cortex–CA1" circuits. Furthermore, BPA exposure led to impairments of the branching complexity and electrophysiological properties of hippocampal neurons. Additionally, fiber photometry experiments revealed that BPA exposure reduces the level of real-time activity in hippocampal excitatory neurons (CA1, CA3, and DG) during the WMM task. To verify the role of hippocampal excitatory neurons in learning and memory impairment caused by BPA, the dorsal hippocampus CA1 neurons were chemogenetically activated, and the spatial learning and memory abilities of mice were assessed. The results indicated that activating hippocampal excitatory neurons can alleviate BPA-induced learning and memory impairments in mice. This study expands our understanding of the neurotoxic mechanisms of BPA at the neurocognitive neural level and provides a potential strategy for rescuing BPA-induced learning and memory impairments.	ENVIRONMENT & HEALTH	10.1021/envhealth.5c00110	-	-	動物	-	1	1	1	1	0	0.5 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2216	K. A. Bennett, C. Sutherland and A. L. Savage	2025	A systematic review of evidence that environmental contaminant exposure impedes weight loss and glycemic control during calorie-restricted diets in humans	Calorie-restricted diets cause weight loss and can drive type 2 diabetes remission. However, many patients struggle to achieve clinically relevant weight loss, and the reasons are not well understood. Chemical exposure is associated with obesity and type 2 diabetes development, and some evidence from preclinical experiments suggests it can limit the clinical benefits of calorie restriction. We systematically reviewed the evidence for whether chemical exposure impedes weight loss and glycemic control during calorie restriction in humans. Searches were conducted in PubMed, Embase, and Web of Science databases to find studies that examined this question. Only one reported people with type 2 diabetes. One linked phthalates and parabens, but not bisphenols, with a lower risk loss. Two cohorts of the Diabetes Prevention Program Outcomes Study, in how the extremely motivated high-risk individuals with mean loss, but still lower subsequent mass regain. One linked impaired adiposity improvements with air pollutants. Two papers reported weight loss- Indeed elevation in plasma organochlorines associated with altered glycemic control. The risk of bias largely arose from the potential for deviation from the intended diet, and statistics and reporting. The role of chemical exposure in impeding the effectiveness of weight management programs needs to be better understood to provide suitable support to people living with obesity and type 2 diabetes.	OBESITY REVIEWS Vol.26 Issue 5	10.1111/obr.13886	39716022	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2217	K. A. Bennett, C. Sutherland and A. L. Savage	2024	A systematic review and meta-analysis of environmental contaminant exposure impacts on weight loss and glucose regulation during calorie-restricted diets in preclinical studies: Persistent organic pollutants may impede glycemic control	Epidemiological evidence links chemical exposure with type 2 diabetes (T2DM) risk and prevalence. Chemical exposure may therefore also limit success of weight loss or restoration of glycemic control during calorie restriction (CR). We systematically reviewed the evidence for whether chemical exposure impedes weight loss and glycemic control during CR in preclinical studies. Searches were conducted in PubMed, Embase, and Web of Science databases to find studies that examined this question. Studies were included if they: (1) administered a CR diet (≥20% energy restriction, CR or ≥5% weight loss) and (2) administered a chemical. Risk of bias was assessed using the SYRCLE tool. Of the eligible papers (n = 15), 14 were published in the last 5 years. Most studies (n = 13) were conducted in rodents (mice and rats), and one was conducted in zebrafish. Studies administered a variety of chemicals, including persistent organic pollutants (POPs), endocrine disrupting chemicals (EDCs), and pharmaceuticals. Most studies (n = 13) administered a single chemical, and one administered a mixture of 11 POPs. Most studies (n = 13) administered chemicals orally, via food or drinking water. Risk of bias was unclear or high in most studies. Meta-analysis revealed that CR was effective for weight loss (SMD = -1.05, 95% CI: -1.39, -0.72, n = 9 papers) and improving glucose tolerance (SMD = -0.80, 95% CI: -1.20, -0.41, n = 5 papers). However, CR was ineffective for weight loss in chemically exposed animals (SMD = -0.30, 95% CI: -0.61, 0.01, n = 9 papers) and had impaired glycemic control (SMD = 0.30, 95% CI: 0.00, 0.60, n = 5 papers). The observed relationship between chemical exposure and impaired CR efficacy was not affected by chemical dose, duration of exposure, or sex. Chemical exposure may impede the effectiveness of CR for weight loss and glycemic control. Future studies should investigate the mechanisms by which chemical exposure impedes CR efficacy. Persistent organic pollutants may impede CR efficacy, but this finding is based on a small number of studies and should be interpreted with caution. Future studies should investigate the mechanisms by which chemical exposure impedes CR efficacy. Persistent organic pollutants may impede CR efficacy, but this finding is based on a small number of studies and should be interpreted with caution.	BIOCHEMICAL PHARMACOLOGY Vol.225	10.1016/j.bcp.2024.116300	38782075	動物	-	不明	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2218	Bellavia A, Zou R, Björvang RD, Ross K, Gunnarsson Y, Hallberg I, Holte J, Pitkä A, Lerbom V, Portengen L, Kiviranta J, Lamoree M, Van Duursen M, Vermeulen R, Salumets A, Velthi n Wahlen A, Damdimopoulo P.	2023	Association between chemical mixtures and female fertility in women undergoing assisted reproduction in Sweden and Estonia	Objective Women of reproductive age are exposed to ubiquitous chemicals such as phthalates, parabens, and per- and polyfluoroalkyl substances (PFAS), which have potential endocrine-disrupting properties and might affect fertility. Our objective was to investigate associations between potential endocrine-disrupting chemicals (EDCs) and female fertility in two cohorts of women attending fertility clinics. Methods In a total population of 1,232 women undergoing their first in vitro fertilization (IVF) treatment, we measured 29 EDCs in follicular fluid. Associations between EDCs and fertility outcomes (fertilization, blastocyst formation, live birth) from fresh and frozen embryo transfers. We measured 29 chemicals in follicular fluid samples and determined phthalate metabolites at 2-3 follicular aspiration (OPU) procedures. In parallel, and 4 PFAS in ~ 80% of the women. Associations were evaluated using multivariable-adjusted linear or logistic regression, categorizing EDCs into quartiles of their distributions, as well as with Bayesian Kernel Ma chine Regression Results The observed statistically significant associations with concentrations of the sum of DEHP metabolites in the Swedish cohort (Q4 vs. Q1, beta = -0.21, 95% CI: -0.38, -0.03) and sum of PFAS exposure at OPU and 36 in all clinical outcomes, whereas reduced clinical pregnancy (Q4 vs. Q1, beta = -0.21, 95% CI: -0.38, -0.03) and ongoing pregnancy (Q4 vs. Q1, beta = -0.21, 95% CI: -0.38, -0.03) rates. Bayesian kernel machine regression models identified a negative association between the mixture of chemicals and live birth in the Swedish cohort, driven by DEHP metabolites and perfluorooctanoic acid. Conclusions Within a large chemical mixture, we observed significant inverse associations levels of DEHP metabolites and perfluorooctanoic acid, suggesting that these chemicals may contribute to altered ovarian function and infertility in women.	Environ Res. 2023 Jan 1;216(Pt 1):114447.	10.1016/j.envres.2022.114447	36181890	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2219	M. Begum, P. Paul, D. Das and S. Ghosh	2020	Endocrine-disrupting plasticizer Bisphenol A (BPA) exposure causes change in behavioral attributes in Drosophila melanogaster	Objective and methods The effects of Bisphenol A (BPA) on selected behaviors of Drosophila melanogaster, namely larval feeding rate, larval foraging ability, adult climbing ability and courtship display, were tested by exposing the flies for 50 successive generations by exposing the third instar larvae to two different sublethal doses- 0.001 g/l and 0.002 g/l and 0.0 g/l. Results Our results revealed a significant reduction in feeding rate, foraging path length and frequency of courtship display. Both the treated male and female adults exhibited negative climbing ability as lower concentration (0.001 g/l) and of BPA exposure at 25 s and 36 s at all intervals, whereas reduced climbing ability was recorded at 12 s of interval in comparison with controls. At higher concentration (0.002g/l) as well, only the treated females, not males exhibited significant reduced climbing ability at 30 s of interval.	TOXICOLOGY AND ENVIRONMENTAL HEALTH SCIENCES Vol.12 Issue 3 Pages 237-246	10.1007/s13530-020-00052-8	-	-	動物	-	0	不明	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2220	M. A. Bag, E. Ahmad, S. F. Al Basri, A. Abdelsalam, O. S. Bajuri, M. S. Jamal, A. M. Abuzenadah and I. A. Shaikh	2020	Endocrine disruption and infertility: Circulatory hormone and bisphenol A concentrations in infertile Saudi women	Aim: Human infertility is a public problem and a cause of social and psychological complications affecting more than 50 million couples globally. Bisphenol A (BPA) is a ubiquitous environmental endocrine disrupting chemical and has been associated with infertility problems in women. The aim of the present study was to analyze concentrations of bisphenol A and circulating hormones in infertile Saudi women for evaluating the possible effects of BPA exposure on infertility. Methods: Blood samples from infertile women and a control group of 30 healthy fertile women were collected. Infertile women had irregular menses, hyper androgenism, multiple small ovarian cysts, polycystic ovarian syndrome and unexplained infertility. Blood samples from infertile women and a control group of 30 healthy fertile women were analyzed and compared for concentrations of BPA and circulatory hormones. 4-Pseudo Items Results: The results showed that BPA concentrations were not significantly different between infertile women and healthy women. However, BPA concentrations were significantly higher in infertile women. Interpretation: Serum BPA levels had an association with hormone imbalance in this cohort of infertile Saudi women. However, considering the previous studies that have shown a correlation of BPA with female infertility, an argument can be made that there might be more exposure of Saudi population to BPA in comparison to BPA analogues such as BPS (according to recent reports). Therefore, it is suggested to conduct more infertility studies that include detection of BPS and its analogues in infertile Saudi women. Endocrine disruption Oct 4;14. BPA Women reproductive system Uri BPA Injection	JOURNAL OF ENVIRONMENTAL BIOLOGY Vol.41 Issue 4 Pages 680-686	10.22438/jeb/41/4/MRN-1335	-	ヒト	生殖発生	-	-	-	-	-	-	症例対照	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2221	J. M. Barkoski, S. A. Burgana, M. Bixby, D. Bennett, R. J. Schmidt, D. B. Barr, P. Panuwet, C. Gennings and I. Hertz-Picciotto	2019	Prenatal phenol and paraben exposures in relation to child neurodevelopment including autism spectrum disorders in the MARBLES study	Background: Environmental phenols and parabens are endocrine disrupting chemicals (EDCs) with the potential to affect child neurodevelopment including autism spectrum disorders (ASD). Our aim was to assess whether exposure to environmental phenols and parabens during pregnancy was associated with an increased risk of clinical ASD or other neotypical development (non-TD). Methods: This study included mother-child pairs (N = 207) from the Markers of Autism Risk in Babies - Learning Early Signs (MARBLES) Center Study in California. Maternal urine samples collected during each trimester and cord blood at delivery were analyzed for 11 C-MS/MS. From repeated pregnancy urine samples. Because twenty recurrence risks in siblings are about 20%, MARBLES enrolls pregnant women who already had a child with ASD. Children were clinically assessed at 3 years of age using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) and the Mullen Scales of Early Learning (MSEL). Children who met criteria for ASD on both measures were considered to have ASD. Children who did not meet criteria for ASD on either measure were considered non-TD. Multivariable logistic regression models were used to test for relationships between each chemical and ASD. Results: Regression models were adjusted for pre-pregnancy body mass index, prenatal vitamin use (yes/no), homeowner status (yes/no), birth year, and child's sex. In single-chemical analyses, phenol exposures were not significantly associated with child's diagnosis. Mixture analyses using trimester WQS regression showed a significantly increased risk of non-TD compared to TD (OR = 1.66; 95% CI: 1.02, 2.69) with overall greater prenatal phenol and paraben metabolite mix. mixture. Results for ASD also showed an increased risk, but it was not significant. Discussion: This is the first study to provide evidence that pregnancy environmental phenol exposures may increase the risk for non-TD in a high-risk population.	Environ Res. 2019 Dec;179(Pt A):108719.	10.1016/j.envres.2019.108719	31627027	ヒト	発達神経	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2222	K. Barešić, K. Živković, D. Božić, D. Jarnen, A. Šuša Đanđanac, E. Antonijević Miljaković and D. Dukić-Ćosić	2022	Potential genomic biomarkers of obesity and its comorbidities for phthalates and bisphenol A mixture: In silico toxicogenomic approach	This in silico toxicogenomic study aims to explore the relationship between phthalates and bisphenol A (BPA) on exposure and obesity, as well as its comorbid conditions, in order to construct a possible set of genomic biomarkers. The Comparative Toxicogenomics Database (CTD; http://ctd.mdibl.org) was used as the main data mining tool, along with GeneMania (https://genemania.org), TopGene Suite (https://toppgene.cchmc.org) and DisGeNET (http://www.disgenet.org). Among the phthalates, bis(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP) were chosen as the most frequently curated phthalates in CTD, which also share similar toxicokinetic properties. Genes related to BPA, DEHP, DBP, obesity and its comorbidities were collected from CTD and DisGeNET databases. Venn diagram was used to find common co-all three substances. 72 genes (entries harboring interactions for all three investigated substances, while more than half of these genes (entries 39,44%) come in our dataset. Out of the common genes (entries 9) related to human: CCL2, IL6, LPL, PPARG, SERPINE1, and TNF were identified in all the investigated obesity comorbidities, while PPARG and LPL were most closely linked to obesity. These genes/proteins could serve as a target for further in silico and in vivo studies of molecular mechanisms of DEHP, DBP and BPA mixture obesogenic properties. Analysis reported here should be applicable to any mixture of environmental chemicals and any disease present in CTD.	BIOCELL Vol.46 Issue 2 Pages 519-533	10.32604/biocell.2022.018271	-	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2223	B. Bamei, M. Amrandak, H. Haghi-Aminjan, M. Rahimifard, S. Hassani, M. Ghobeh, M. Afaei, M. Samadi, M. Daniali, M. R. H. Skayeetah and M. Abdollahi	2024	Insights into the role of melatonin on the reproductive system toxicity induced by bisphenol A: a systematic review of preclinical studies	Bisphenol A (BPA), an endocrine disruptor, changes many physiological functions of the body, especially the reproductive system. The malfunction of the reproductive system after BPA exposure is one of the causes of infertility reasons. BPA disrupts reproductive functions by elevating oxidative mediators and declining antioxidant enzymes, altering sex hormones, and inducing mitochondrial dysfunction and apoptosis. The present study focuses on the protective role of melatonin against BPA-induced male and female reproductive alterations. A systematic literature review was conducted up to October 2023 using PRISMA guidelines in electronic databases, including PubMed, Web of Science, and Scopus. Considering the study purpose, the search keywords were selected and used to search the titles and abstracts. After screening, 19 pertinent papers were included in the review. Melatonin administration in BPA-exposed animals significantly improved sperm parameters, hormonal balance, and histological changes in reproductive tissues. Additionally, melatonin reduced inflammation, apoptosis, and modulation of mitochondrial function. Furthermore, most indicated melatonin's beneficial effects on the histopathology of reproductive tissues. Also, melatonin reduced its potential toxic effects through direct interaction with hormone receptors against BPA-induced hormonal changes. This study indicates evidence of the protective role of melatonin on reproductive injuries and infertility caused by BPA.	TOXIN REVIEWS Vol.43 Issue 1 Pages 137-156	10.1080/15569543.2024.2304770	-	動物	-	不明	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2224	J. i. Bai, Y. D. Y. Ma, Y. D. Zhao, D. H. Yang, S. Mu, Lanlan and C. H. Yu	2022	Mixed exposure to phenol, parabens, pesticides, and phthalates and insulin resistance in NHANES: A mixture approach	Purpose: The effects of environmental chemicals on insulin resistance have attracted extensive attention. Previous studies typically focused on the single chemical effects. This study adopted three different models to analyze the mixed effects of nine common chemicals (one phenol, two parabens, two chlorpyrifos and four phthalates) on insulin resistance. Methods: 9 key concentrations of chemicals were extracted from National Health and Nutrition Examination Survey (NHANES) 2009-2016. Insulin resistance was assessed using homeostatic model assessment (HOMA) and defined as HOMA-IR ≥ 2.6. The generalized linear regression (GLM), weighted quantile sum regression (WQS), and quantile g-computation (QGC) were used to explore the mixed effects of chemicals on insulin resistance. Results: A total of 2,749 participants were included. 871 (31.67 %) were identified as insulin resistance. In single chemical GLM analysis, 3-PBA (β: 0.14; 95 % CI: 0.07 to 0.21) caused IL-1 (β: 0.13; 95 % CI: 0.05 to 0.21) and TPI (β: 0.13; 95 % CI: 0.03 to 0.23) were identified as the main chemical models, with DEHP (specific Q showing the positive relationship with HOMA-IR (0.18, 0.08–0.28) and insulin resistance (1.76, 1.17–2.65). According to the WQS models, the WQS index was significantly correlated with both HOMA-IR (beta: 0.07, 95 % CI: 0.03–0.12) and insulin resistance (OR: 1.24, 95 % CI: 1.08–1.41). Additionally, the proportion of BPA in the total bisphenol concentration in urine samples was the highest (26.1% in YEARS) while that of BPF was the lowest (1.5% in 1679). Estimated daily intakes of bisphenols, as well as hazard quotients (HQs) and hazard indexes (HIs), were calculated. Results: The HIs for BPA, BPF, and BPS were all below 1, indicating no significant risk. Conclusion: Our findings suggest that BPA has the highest urinary activity is still unclear, and the long-term effects of small doses of bisphenols and the potential harmful impact of BP mixtures are unknown. Knowledge of the occurrence of bisphenols in pig farming may contribute to a better elimination of BPA and its analogues from this sector, which is crucial for the safety of animal products as well as the welfare of pigs.	SCIENCE OF THE TOTAL ENVIRONMENT Vol.851	10.1016/j.scitotenv.2022.158218	36028038	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2225	I. Bałtecka, R. Stupka, J. Chlek and M. Spryszl	2023	The occurrence and risk assessment of bisphenol A and its analogues - bisphenol B, F, S, Z and AF in the urine of lactating sows	Bisphenols (BP) are pollutants that are globally and widely distributed and adversely affect the health of humans. However, knowledge of their presence in animals, especially farm animals such as pigs, remains limited. The aim of the study was to determine the levels of BPA, BPB, BPF, BPS, BPZ and BPAF in the urine of lactating sows and to assess the risk to the health of piglets exposed to these BPs in the milk of their mothers in the early days of lactation. The urine samples of 27 sows were collected on the 1st day after parturition, and stored at −20 degrees C until analysis using HPLC/MS. None of the lactating sows produced bisphenol free urine. In contrast, the urine of all sows contained at least two bisphenols (eight females), most often five (10 females) or all six bisphenols (five females). The average concentrations of bisphenols in urine were in the order of BPA > BPS and BPS > BPZ > BPAF > BPF. The most frequently determined bisphenol was BPA (96.3% of samples), followed by BPS (88.9%), BPZ (33.3%), BPF (22.2%) and BPAF (7.4%). Additionally, the proportion of BPA in the total bisphenol concentration in urine samples was the highest (32.1% in YEARS) while that of BPF was the lowest (1.5% in 1679). Estimated daily intakes of bisphenols, as well as hazard quotients (HQs) and hazard indexes (HIs), were calculated. Results: The HIs for BPA, BPF, and BPS were all below 1, indicating no significant risk. Conclusion: Our findings suggest that BPA has the highest urinary activity is still unclear, and the long-term effects of small doses of bisphenols and the potential harmful impact of BP mixtures are unknown. Knowledge of the occurrence of bisphenols in pig farming may contribute to a better elimination of BPA and its analogues from this sector, which is crucial for the safety of animal products as well as the welfare of pigs.	CZECH JOURNAL OF ANIMAL SCIENCE Vol.68 Issue 11 Pages 451-459	10.17221/90/2023-CJAS	-	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2226	S. Balsatsher, M. Sedighi, S. M. Zamir and S. A. Shojaosadati	2022	Prediction of co-metabolic degradation of bisphenol A and phenol by kinetic modeling	In this work, a model was proposed to describe the ability of Rahnella aquatilis for co-metabolic transformation kinetic of bisphenol A (BPA) as a non-growth substrate in the absence or presence of phenol as a growth substrate. The model was developed based on Haldane substrate inhibition kinetics, endogenous cell decay, cell inhibition of BPA, loss of transformation activity, and competitive inhibition between two substrates. Genetic algorithm was used to estimate the unknown model. The model then was validated by comparing the predicted and the experimental data. To evaluate the model predictions under different combinations of phenol and BPA concentrations, 10 validation experiments were additionally determined. Therefore, BPA co-fermentative and phenol utilization were predicted successfully by the model for a defined range of concentrations of phenol (10–100 mg·l(−1)) and BPA (5–60 mg·l(−1)). (C) 2021 The Author(s). Published by Elsevier B.V.	ENVIRONMENTAL TECHNOLOGY & INNOVATION Vol.26	10.1016/j.eti.2022.102310	-	in vitro	-	-	-	-	-	1	0	＜80 mg/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2227	A. M. A. Aseem, A. N. El Shahat and M. H. M. Abd el Megid	2023	Assessment of the Biogenic Effects of Selenium Nanoparticles Prepared from Citrus paradise Peel Extract against Bisphenol A-Induced Liver Injury in Male Rats	Citrus peel constitutes an important centre of flavonoids such as naringin and its aglycone naringenin that play significant role against various physiological threats. Synthesis of nano selenium particles (SeNPs) using a natural source as a reducing agents might have more advantages as an alternative to physical and chemical methods because it is inexpensive and considered environmentally friendly. Therefore, the objective of this study was to synthesize selenium nanoparticles from Citrus paradise peels extract (SeNPs-CP), their general characterization, and their assessment for antioxidant activities against liver injury induced by bisphenol A (BPA) in male rats. In this work, Citrus paradise peels extract was used for reduction of sodium selenite (Na2SeO3) to synthesized SeNPs-CP. The synthesized SeNPs were characterized by Ultraviolet-visible spectroscopy (UV-Vis spectra), Fourier transform infra-red (FTIR) spectroscopy analysis, and Transmission Electron Microscope (TEM). The rats (36 rats) used in this study were divided into six groups (six rats/group). Group 1 served as control, group 2 received BPA (50 mg/kg BPA) orally by gavage, group 3 received SeNPs-CP (1 mg/kg), group 4 received BPA + SeNPs-CP, group 5 received BPA + vitamin C, and group 6 received BPA + silymarin. The results showed that BPA injection led to an obvious increase in the activities of liver enzymes, elevation of hepatic oxidative stress, (a significant increase in lipid peroxidation concentration with a significant decrease in glutathione content and antioxidant enzyme activities), tumor necrosis factor alpha (TNF-alpha) and apoptotic marker Caspase-3 compared to the control group. Rats received BPA along with SeNPs-CP showed significantly less severe damage and remarkable improvement in all the measured parameters when compared to BPA rats. In this study it was concluded that the synthesis of selenium nanoparticles using a natural source such as grapefruit was effective in combining the antioxidant and anti-inflammatory properties of both the flavonoids present in grapefruit and selenium and increasing the efficiency of the selenium nanoparticles.	PAKISTAN JOURNAL OF ZOOLOGY Vol.55 Issue 5 Pages 2317-2323	10.17582/journal.pjz/20210901220942	-	動物	-	1	0	1	不明	0	50 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2228	O. F. Ajoju, A. Nyachieo, A. R. Juma, I. I. Mutai, P. G. Mwetheza, E. O. Mecha, C. O. Omwandho, L. Kassal, M. G'this, C. Mutsvehi and J. A. Obiero	2024	A review: Exposure to bisphenol a analogues in non-human primates as a potential cause of endometriosis	Introduction: Bisphenol A is a synthetic compound widely used in the production of polycarbonate plastics and epoxy resins worldwide. As an environmental toxin, it has been reported to plastic equipment and utensils, leading to widespread human exposure. Consequently, bisphenol A analogues, such as bisphenol S, bisphenol F, and bisphenol AF, have been introduced as substitutes for bisphenol A. However, concerns have emerged regarding the potential toxicity of bisphenol S, bisphenol F, bisphenol AF, and bisphenol B and recommend bisphenol F. Bisphenol A and its analogues can bind to estrogen receptors and trigger multiple cellular responses at the organism level.Methods: A comprehensive literature review was done utilizing electronic databases of PubMed, Google Scholar, Hinari, Connected papers and Science Direct from 1991 onwards. The articles were only included if they reported original relevant research and were limited to articles written in English.Results: Animal models, including non-human primates, have been used to study their effects on the reproductive system. Its endocrine disruption activity is reported to be the most studied effect in reproductive biology indicating that it may potentially cause endometriosis in females. Though non-human primates are closely related to humans, limited data exists on their association between bisphenol A exposure and the pathophysiology of endometriosis.Conclusion: Given the current multifactorial knowledge theory on endometriosis etiology, there is a strong necessity to conduct further bisphenol A research that utilizes non-human primates to study the link between endocrine-disrupting chemicals and its effects on endometriosis.	JOURNAL OF ENDOMETRIOSIS AND PELVIC PAIN DISORDERS Vol.16 Issue 1 Pages 53-60	10.1177/22840265241231323	-	動物	-	不明	不明	不明	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2229	L. An, Y. L. Huang, Y. K. Wang, S. T. Shen, X. X. Luo, X. Y. Liang, L. M. Lu, C. Z. Tang, J. L. Lin, T. Su, M. Q. Zhan, D. Y. Wang, J. Wang, X. Lai and F. Li	2025	Assessment of ovarian dysfunction induced by environmental toxins: a systematic review	Objective: This study systematically assess the potential impact of various environmental pollutants as chemical, silicone, and heavy metal on ovarian function in women, focusing on ovarian reserve such as anti-M & oxidative hormone (AMH) and antral follicle count (AFC), as well as hormone levels like follicle-stimulating hormone (FSH) and estradiol (E2). By reviewing epidemiological evidence, this research aims to elucidate the relationship between these toxins and ovarian health, providing a basis for public health interventions and policy-making.Methods: A systematic review of observational studies published in English was conducted. The search was conducted in PubMed, EMBASE, Cochrane Library, and Web of Science databases to include all relevant studies up to July 28, 2024. The Newcastle-Ottawa Scale (NOS) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach were used to assess study quality.Results: This study ultimately included 20 cohort study reports derived from 20 distinct studies that analyzed the effects of various environmental pollutants on ovarian function in women. The findings indicate that exposure to heavy metals, such as lead (Pb), cadmium (Cd), and mercury (Hg), as well as phthalates, has a significantly negative impact on ovarian function, especially among younger women (<35 years). Long-term exposure to particulate matter (PM2.5 and PM10) is associated with a substantial decrease in ovarian reserve, while heavy metals (e.g., lead and cadmium) also demonstrate reproductive toxicity. However, these conclusions require validation due to both methodological limitations in the original studies (e.g., heterogeneous exposure assessments and residual confounding) and challenges in evidence synthesis (e.g., inconsistent outcome measures across cohorts), highlighting the need for further research to address these constraints.Conclusion: This review underscores that specific pollutants (e.g., PCBs, PFAS, Pb) pose substantial risks to reproductive health in women of childbearing age, particularly in highly polluted environments. The findings, synthesized according to PRISMA guidelines, provide a foundation for stricter regulations and tighter risk-due to occupational or environmental factors. Systematic review registration: PROSPERO CRD42024617181 (accessible at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024617181).	FRONTIERS IN PUBLIC HEALTH Vol.13	10.3389/fpubh.2025.1575418	40809751	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2230	S. Gosnka	2024	Disruption of functions of primary human neonatal melanocytes cultured in the presence of bisphenol A and its analogs bisphenol F and bisphenol S	Bisphenol A (BPA), bisphenol F (BPF), and bisphenol S (BPS) are contaminants of emerging concern (CECs) that humans are exposed to. In silico and zebrafish studies have linked BPA, BPF, and BPS exposure to pigmentation abnormalities, but no studies have examined their impact on primary human melanocytes. Herein, we examined the effects of BPA, BPF, and BPS exposure using human epidermal neonatal melanocytes. BPA reduced the presence cytotoxicity, followed by BPS, whereas BPF did not affect viability. BPA did not affect cellular tyrosinase activity, whereas BPF and BPS diminished it at 100 nM. BPF altered melanin levels, as did BPA although BPF was a potent suppressor of dendricity than BPA. BPA inhibited tyrosinase activity, followed by BPF, while BPS weakly suppressed tyrosinase activity. The tyrosinase activity was mostly recovered after the removal of the chemicals from the culture medium. BPA, BPF, and BPS exposure altered the expression of genes involved in melanogenesis, including those encoding MITF, TYR, and DCT. Additionally, BPA and BPF exposure increased the expression of IL-6 relative secretion to melanocytic cultures treated with bisphenol analogs, but BPF distinct, suggesting that they exacerbate melanocyte inflammation. Collectively, these findings indicate that BPA, BPF, and BPS may impair melanocyte function and pose health hazards, warranting more study.	JOURNAL OF HAZARDOUS MATERIALS LETTERS Vol.5(1):100110	10.1016/j.hazl.2024.100110	-	in vitro	-	-	-	-	-	1	0	0.1, 1, 10, 50, 100, and 200 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2231	P. Sharma and M. B. Mandal	2019	Chronic Ingestion of Bisphenol A and Bisphenol S Attenuated Contractile Activity of Rat Stomach and Small Intestine In-vitro	Introduction: Bisphenol A (BPA) is a chemical used in synthesis of plastic. BPA seeps into food from the plastic containers used to store food items. Exposure to BPA is implicated as a causative factor for detrimental effects on fetal development and various body systems like endocrine, reproductive and immune. Few studies report that BPA ingestion impair overall intestinal contractility in vitro. Government organizations of many countries have posted into the matter and imposed regulations on marketing of BPA. To meet the norms with regulations on BPA, manufacturers are increasingly replacing BPA with Bisphenol S (BPS). BPS has been detected in human urine samples. Objective: The present study was designed to investigate the effects of chronic ingestion of BPA and BPS on contractile activity of rat stomach and small intestine in vitro. Materials and Methods: Healthy male adult albino rats (~250 g) received BPA (50 mg/kg) or BPS (50 mg/kg) or vehicle (Dimethyl sulphoxide) for three months by oral gavage. The animals were partly restrained so that the head is immobilized by retaining the animal in an upright position. Gavage needle was passed along the side of the mouth and moved into the esophagus and towards the stomach. After four months, they were sacrificed and in vitro contractions of gut muscle strips were recorded in an organ bath transducer set at 37 ± 0.5 degrees C using force transducer, computerized polygraph and data acquisition unit (ACT) and chart 5 for Windows, ADI, Sydney, Australia. Results: Acetylcholine (ACh) (0.1 -100 nM) evoked gut contractions. In vitro and the basal tone and maximum contractile tension increased in a concentration dependent manner. However, in both the treated groups, the ACh induced contractions were significantly (p<0.05, two way ANOVA) less as compared to control (vehicle) group. But the treated groups were similar to each other. No difference was found to be similar. The spontaneous intestinal contractions were significantly less (p<0.05, two way ANOVA) as compared to control in both the treated groups, whereas no hypotonic tissue was observed in the treatment (with significantly) skirted the spontaneous contractility. Conclusion: Chronic ingestion of both BPA and BPS may impair gut contractility indicating that BPS might not be a harmless substitute to BPA.	JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH Vol.13 Issue 7 Pages CF1-CF5	10.7860/JCDR/2019/41496.12989	-	動物	-	1	1	1	1	0	50 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2232	M. Aman, T. Kok and I. V. Klun	2024	Endocrine disrupting chemicals and obesity prevention: scoping review	Introduction:Exposure to endocrine disrupting chemicals (EDCs) can result in alterations of natural hormones in the body. The aim of this review article is to highlight the knowledge about EDCs and obesity.Methods:A scoping review of the electronic literature was performed using PubMed platform for studies on EDCs, and obesity published between the years 2011-2021. A total of 22 systematic reviews and meta-analysis studies met our inclusion criteria on more prominent EDCs, focusing mainly on bisphenols, including parabens, triclosan, and phthalates, and their association with obesity.Despite finding mixes Results:EDCs, mostly bisphenols and phthalates, are related to health effects, while there is less information on the impact of parabens and triclosan. A variety of negative physiological effects, leading obesogenic, cardiotoxic, carcinogenic, and inflammatory mechanisms as well as epigenetic and microbiota modulations was related to a prolonged EDCs exposure. A more profound research of particular pollutants is required to illuminate the accelerating effects of EDCs on obesity.Conclusion:Considering the ubiquitous presence of EDCs in the environment, and the heterogeneity of studies, it is necessary to design specific studies of effect tracking and, in particular, education about daily preventive exposure to EDCs for the preservation of long-term public health.	JOURNAL OF HEALTH POPULATION AND NUTRITION Vol.43 Issue 1	10.1186/s41043-024-00627-y	39227884	ヒト	-	-	-	-	-	-	-	スコープレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2258	M. H. Jacobson, C. R. Skoin, M. L. Liu, M. G. Ackerman, J. K. Blakemore, S. E. Lung, G. Flora, R. Romay-Tallon, K. Kannan, H. K. Zhu and L. Trasande	2021	Prenatal Exposure to Bisphenols and Phthalates and Postpartum Depression: The Role of Neurosteroid Hormone Disruption	Context. Postpartum depression (PPD) is a serious psychiatric disorder. While causes remain poorly understood, perinatal sex hormone fluctuations are an important factor, and allopregnanolone in particular has emerged as a key determinant. Although synthetic environmental chemicals such as bisphenols and phthalates are known to affect sex hormones, no studies have measured allopregnanolone and the consequences of these hormonal changes on PPD have not been investigated. Objective: To investigate associations of repeated measures of urinary bisphenols and phthalates in early and midpregnancy with serum progesterone, progesterone metabolites, and allopregnanolone and PPD. Design: Participants were enrolled in the Mount Sinai Children's Environmental Health Study (CHES) cohort. Bisphenol and phthalate biomarkers were measured in early and midpregnancy urine samples. Serum sex hormones were measured in midpregnancy. PPD case was ascertained 6 months postpartum using the Edinburgh Postnatal Depression Scale (EPDS). Multiple informant models were fit using generalized estimating equations. Seven levels of allopregnanolone, progesterone, progesterone, and progesterone were examined as log-transformed continuous variables. PPD symptoms were examined as continuous EPDS scores and dichotomously with scores >= 10 defined as PPD. Results: 33 n= valid phthalate (DnDP) and dicarboxyl phthalate (DCHP) metabolites were associated with reduced progesterone concentrations. Log-unit increases in Sigma DnDP and Sigma DEHP predicted 8.1% (95% CI: -16.3%, -0.3%) and 7.7% (95% CI: -13.3%, -1.7%) lower progesterone, respectively. Sigma DnDP was associated with increased odds of PPD (odds ratio 1.88, 95% CI: 1.18, 2.12). Conclusion: Endocrine disrupting chemicals may influence hormonal shifts during pregnancy as well as contribute to PPD.	J Clin Endocrinol Metab. 2021 Jun 16;106(7):1887-1899.	10.1210/clinem/dgab199	33792735	ヒト	神経(産後うつ)	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2259	A. Ishtiaq, M. U. Qar, N. Ehsan, M. Imran, H. Naz, K. Alvi and G. F. Zhu	2022	Therapeutic Effect of Oroxylin A Against Bisphenol A-induced Kidney Damage in Rats: a Histological and Biochemical Study	Bisphenol A (BPA) is a synthetic chemical compound used in plastic products that adversely affects health. BPA exposure is associated with multiple organ toxicity, particularly renal toxicity. Oroxylin A (ORA) is a flavonoid that has potential therapeutical properties. The current study explored the effect of different doses of ORA on BPA-prompted inflammatory responses and oxidative stress in kidneys. The experiment was executed on forty-six rats (196 +/- 20 g) that were apportioned into 8 groups. The treated rats orally received ORA doses (10 mg/kg, 20 mg/kg, and 40 mg/kg) for 4 weeks before the toxic effects caused by 10 mg/kg of BPA. After 56 days of the experiment, rats were euthanized to detect the level of renal function markers (urea and creatinine), oxidative stress markers, inflammatory markers, antioxidant enzyme activity and histological changes in kidneys. The results revealed that BPA significantly increased the level of urea and creatinine, which indicates impairment of renal function. BPA also caused considerable decrease, while increasing the level of the oxidative stress markers (malondialdehyde, reactive oxygen species and hydrogen peroxide). BPA exposure significantly increased the level of pro-inflammatory cytokines, while decreasing creatinine clearance. Moreover, BPA exposure remarkably increased inflammatory responses by augmenting the activity of cyclooxygenase-2 and levels of nuclear factor-kappa B, tumor necrosis factor-alpha, interleukin-1 and interleukin-1 beta. Besides, histopathological damages were also observed in renal tissues followed by BPA exposure. Co-administration of ORA ameliorated the toxic effects of BPA on renal tissue in a dose-dependent manner. Thus, it is deduced that ORA might be used to counter the harmful effects of BPA on renal tissues.	PAKISTAN VETERINARY JOURNAL Vol.42 Issue 4 Pages 511-516	10.29261/pakvetj/2022.072	-	-	動物	-	1	1	1	1	0	10 mg/kg BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2260	J. Huang, D. Mak, P. Cheung, M. Abraham, T. Clemens and S. Turner	2019	A systematic review of associations between maternal exposures during pregnancy other than smoking and antenatal fetal measurements	Background: Reduced birth weight is associated with many maternal environmental exposures during pregnancy, but the gestational age at onset of this association is unknown. We have previously reported associations between maternal smoking and fetal biometry from 11 weeks gestation. Objectives: To systematically review associations between maternal exposures and antenatal fetal measurements. Search strategy: Electronic databases (OVID and EMBASE) and web sites for cohort studies were searched. Studies were eligible if they examined associations between external environmental exposures (including evidence of exposure, diet and alcohol) and antenatal fetal ultrasound measurements. The Navigation Guide was used to assess the strength of evidence. Results: There were 201 abstracts identified and 36 papers were included in the review. Maternal BMI, alcohol, caffeine, diet, and air pollution were associated with fetal biometry. Conclusions: There is evidence that maternal exposures other than smoking are associated with fetal measurements in 3rd trimester, with second trimester measurements and in 48% of comparisons with third trimester measurements. In third trimester associations can be altered, reduced head size was most commonly (50%) associated with current or previous maternal exposure, with reduced weight being least commonly (12%) associated and reduced weight being intermediate (32%). In the 3rd trimester, increased maternal nitrogen dioxide exposure was associated with reduced head size was associated with in all seven studies. Identified and reduced head weight in five out of six studies. Conclusion: There is sufficient evidence of toxicity in the context of maternal exposure to nitrogen dioxide and reduced third trimester fetal head size. There is currently insufficient evidence of toxicity with regard to maternal exposures to dietary factors, alcohol and environmental chemicals and reduced fetal size.	ENVIRONMENTAL RESEARCH Vol.173 Pages 528-538	10.1016/j.envres.2019.04.005	30991176	ヒト	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2261	L. X. Hong, Y. D. Xu, D. D. Wang, Q. Zhang, X. T. Li, C. F. Xia, J. S. Wu, C. Y. Zhang, G. Gao, Y. Ding and S. S. Geng	2024	Sulforaphane Alleviates Bisphenol A-Induced Glucose Intolerance via Improving Inflammation and Oxidative Stress	Background: Bisphenol A (BPA) disrupts glucose homeostasis via inflammatory pathways in liver cells, affecting insulin sensitivity. This study examines sulforaphane (SFN), known for its anti-inflammatory and antioxidative properties, for counteracting BPA's effects. Methods: We evaluated SFN's impact on BPA-exposed C57BL/6 mice and HepG2 cells, focusing on metabolic parameters, insulin signaling, and inflammatory responses. Results: In mice, SFN significantly reduced BPA-induced weight gain, fasting blood glucose, and insulin resistance. It also improved glucose tolerance and decreased inflammatory responses related to glucose metabolism. In HepG2 cells, SFN enhanced insulin-mediated AKT signaling pathways and reduced inflammation and oxidative stress. Results: SFN reduced blood glucose and improved glucose tolerance of BPA-treated mice. In BPA-treated HepG2 cells, SFN significantly boosted glucose consumption in vitro. Moreover, SFN's treatment enhanced the protein expression of phosphorylated insulin receptor and phosphorylated AKT and lowered glycolytic and gluconeogenic gene expression in HepG2 cells and mice liver. SFN also decreased phosphorylation levels of p38 and JNK and reduced inflammation and oxidative stress markers in vivo and in vitro. Conclusion: Our findings underscore SFN's capacity to ameliorate BPA-induced glucose intolerance and insulin resistance by enhancing hepatic insulin signaling and metabolic functions. This action is likely mediated through SFN's inhibitory effects on inflammatory and oxidative pathways. Consequently, SFN holds promise as an intervention for mitigating BPA-related metabolic disorders.	JOURNAL OF FOOD BIOCHEMISTRY Vol.2024	10.1155/2024/5538651	-	-	動物、in vitro	-	1	0	1	1	0	100 μg/kg	-	-	-	0	0	100 nM	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2262	L. A. Hoepner, R. U. Haldar, B. F. G. Pycke, O. Abulafia, O. M. Sheen and L. A. Geer	2020	Prenatal bisphenol A (BPA) exposure in a Brooklyn study of Afro-Caribbean women	Prior studies suggest ubiquitous fetal exposure to the endocrine disrupting chemical bisphenol A (BPA). Insufficient information is available on the effects of BPA in underserved urban populations in the US. We describe prenatal BPA exposure in a predominantly Afro-Caribbean population. Maternal third trimester urine concentrations of total BPA were measured in 181 mothers in Brooklyn, NY from 2007 to 2008. Mothers aged 18-35 y presenting at a prenatal clinic consented to study participation. Spot urine samples were collected once between the sixth and ninth month of pregnancy. The geometric mean concentration of total BPA was 1.1 ng/mL (95% CI: 0.9, 1.3). Detection frequency was 89%. Urinary BPA concentrations were not significantly associated with maternal age, education, or household income. Mothers who were born in the US had 1.6-fold higher BPA concentrations (95% CI: 1.1, 2.3) compared to mothers who were born outside the US, primarily among African American and Afro-Caribbean immigrant women residing in Brooklyn, NY. These results, contradict evidence of elevated exposure in prior studies of urban populations. Further studies should be conducted to determine whether there are associations between recent immigrant status and BPA exposures during pregnancy.	ENVIRONMENTAL RESEARCH COMMUNICATIONS Vol.2 Issue 4	10.1088/2515-7620/ab8272	-	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2263	N. B. Henderson, C. G. Sears, A. Calafat, A. M. Chen, B. Lanphear, M. Romano, K. Yolton and J. M. Braun	2020	Associations of Breast Milk Consumption with Urinary Phthalate and Phenol Exposure Biomarkers in Infants	Phthalates and phenols are readily detected in human breast milk, but the contribution of breast milk feeding to an infant's exposure to these chemicals is unknown. Among 268 mother-infant pairs in the HOME Study, we assessed breast milk consumption via maternal report and quantified concentrations of eight phthalate metabolites and three phenols. Bisphenol A, triclosan, benzophenone-3 in infants' urine at age 12 months. We estimated covariate-adjusted percent differences in phthalate metabolite and phenol concentrations by breast milk consumption. Seventy infants (26%) were fed some breast milk up to age 12 months. Urinary phenol concentrations were similar in infants who were or were not fed breast milk at 12 months. In contrast, urinary concentrations of monoethylphthalate (MEP) and mono-2-ethylhexyl phthalate (MEHP) were 42% (95% CI: 5, 97) and 26% (95% CI: -8, 62) higher among infants fed breast milk at 12 months, respectively. Moreover, MCOP and MEHP concentrations were positively associated with the quantity of breast milk consumed. Our findings suggest that breast milk is a source of phthalate exposure, but suggesting that breast milk consumption may be a source of exposure to some phthalates. Future studies should examine whether infant feeding habits or pumped milk is a potential exposure source among infants.	ENVIRONMENTAL SCIENCE & TECHNOLOGY LETTERS Vol.7 Issue 10 Pages 733-739	10.1021/acs.estlett.0c00450	-	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2264	H. He, W. J. Chen, Y. Wei, T. F. Zhang, W. F. Geng and J. X. Zhai	2022	Effects of perinatal exposure to endocrine-disrupting chemicals on the reproductive system of F3 generation male rodents: a meta-analysis	To explore the relationship between perinatal exposure to endocrine-disrupting chemicals and the male reproductive system of F3 generation, and to evaluate the toxicological effects of endocrine-disrupting chemicals on the reproductive system of F3 generation male rodents. PubMed and Web of Science databases were searched to obtain the studies, cereal rich value (PRA) with 95% confidence intervals (95% CIs) were used to evaluate the relationship between exposure to endocrine-disrupting chemicals and reproductive system damage in F3 generation male rodents. Nine studies were included for analysis. Endocrine-disrupting chemicals significantly associated with the reproductive system of F3 generation male rodents (SMD = -3.13, 95% CI: -3.18, -3.11, p<0.05; OR = 2.26, 95% CI: 1.27, 3.83, p<0.05; RR = 1.56, 95% CI: 1.37, 1.82, p<0.05; RR = 1.58, 95% CI: 1.13, 2.21, p<0.05), but the current analysis does not prove that EDCs are the adverse factors for puberty abnormalities. The results indicated that the overall associations between anoxia (RR = 1.58, 95% CI: 1.13, 2.21, p = 0.021) and hypospadias (RR = 1.56, 95% CI: 1.37, 1.82, p = 0.000) were significant. Cryptorchidism (OR = 2.26, 95% CI: 1.27, 3.83, p = 0.005) and miniscule (RR = 1.58, 95% CI: 1.13, 2.21, p = 0.021

別添-2　統合文献リスト

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該時点評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2271	R. Grosklaus, K. P. Liesenkötter, K. Daubek, H. Völkel and R. Gaertner	2023	Iodine Deficiency, Maternal Hypothyroxinemia and Endocrine Disrupters Affecting Fetal Brain Development: A Scoping Review	This scoping review critically discusses the publications of the last 20 years on the impact of mild to moderate iodine deficiency and the additional impact of endocrine disrupters during pregnancy on embryonal/fetal brain development. Iodine is an essential micronutrient for the synthesis of thyroid hormones, which are indispensable for normal brain development. Although the WHO has repeatedly emphasized the importance of an adequate iodine supply for all women of childbearing age in order to prevent negative mental and social consequences for their children. An additional threat to the thyroid hormone system is the ubiquitous exposure to endocrine disrupters, which might exacerbate the effects of iodine deficiency in pregnant women on the neurocognitive development of their offspring. Ensuring adequate iodine intake is therefore essential not only for healthy fetal and neonatal development in general, but it might also attenuate the effects of endocrine disrupters. Individual iodine supplementation of women of childbearing age living in areas with mild to moderate iodine deficiency is mandatory as long as worldwide universal salt iodization does not guarantee an adequate iodine supply. There is an urgent need for detailed strategies to identify and reduce exposure to endocrine disrupters, according to the "precautionary principle".	NUTRIENTS Vol.15 Issue 10	10.3390/nu15102249	37242131	ヒト	-	-	-	-	-	-	-	スコープレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2272	L. M. Gosden, E. V. S. Wong, J. Alex, L. Moffin, P. Tocheriaei, M. Bourne, T. Salomonis, E. White, O. Chaudhury, B. J. Seneviratne, Y. R. Mukkera, T. Dale, H. J. Newman, A. Naveed, A. B. Lowe, D. Hendrie, C. Symeonides and S. A. Dunlop	2022	A scoping review protocol on in vivo human plastic exposure and health impacts	Background: Global plastic production has increased exponentially since the 1960s, with more than 8300 million metric tons of plastic waste generated to date. Studies have found a range of human health outcomes associated with plastic exposure, including cancer, reproductive, and developmental outcomes. However, the evidence base has not been systematically reviewed. Methods: We will conduct a scoping review to identify what is known about how long-term exposure to plastic impacts human health. Here is an urgent need to map human in vivo research conducted to date, creating a broad net to searching terms for a comprehensive suite of plastic chemical exposures and the violent range of health domains. Methods: This protocol describes a scoping review that will follow the recommended framework outlined in the 2017 Guidance for the Conduct of Joanna Briggs Institute (JBI) Scoping Reviews, to be reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist. A literature search of primary clinical studies in English from 1960 onwards, will be conducted in MEDLINE (Ovid) and EMBASE (Ovid) databases. References eligible for inclusion will be identified through a quality-controlled, multi-level screening process, conducted by two independent reviewers. Data extraction will be performed using a bespoke tool developed by the authors. Results will be presented descriptively and, if comprehensively, map the primary research undertaken to date on plastic exposure and human health. Secondary outputs will include extensive databases on plastic chemicals and human health outcomes/impacts.	SYSTEMATIC REVIEWS Vol.11 Issue 1	10.1186/s13643-022-02010-6	35790998	ヒト	-	-	-	-	-	-	-	スコープレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2273	S. E. Goh, P. J. Kwong, C. L. Ng, W. J. Ng and K. Y. Ee	2022	Antioxidant-rich Clitoria ternatea L. flower and its benefits in improving murine reproductive performance	C. ternatea is often used as a natural food colouring besides improving the aesthetic value of foods. It contains various antioxidants and bioactive compounds, which exert many functions, such as counteracting oxidative stress, anti-proliferative and anti-inflammatory activities. This study evaluated the antioxidant activity of C. ternatea flower extract and its protective effect on bisphenol A (BPA)-induced oxidative injury in female murine reproductive systems (BPA: free radical scavenging activity (EC50 (22 d) = 2.96 mg/mL) and total phenolic content (3.99 ± 0.09 mg GAE/g dE); C. ternatea flower extract were determined. Then, inclusive Cancer Research (CR) dams were administered with BPA and/or C. ternatea extract to examine its reproductive performance. In the C. ternatea study on uterine histopathology, percentage of pregnancy and offspring development. It was found that the uterine corpora lutea height ratio from dam co-administered with BPA and C. ternatea was lower than dam treated with BPA alone, although no histopathological effect was found. However, the percentage of pregnancy and litter size from C. ternatea-fed group were both higher compared to BPA-fed dam. In conclusion, C. ternatea extract showed high antioxidant activity and exert potential protective effects against BPA on the reproductive performance in terms of improving the percentage of pregnancy and litter size.	FOOD SCIENCE AND TECHNOLOGY Vol.42	10.1590/fst.25921	-	動物	1	1	1	ICR	0	5 mg/kg BW	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2274	M. Ghazal, M. Kadawathagedara, R. Delvert, A. Divaret-Chauveau, C. Rahmioui, S. K. Lioret, A. B?dard, A. C?tyat, V. Sirot, M.-A. Charles, K. Adel-Patient and B. de Lauzon-Guillain	2024	Prenatal dietary exposure to mixtures of chemicals is associated with allergy or respiratory diseases in children in the ELFE nationwide cohort	IntroductionPrenatal exposure to environmental chemicals may be associated with allergies later in life. We aimed to examine the association between prenatal dietary exposure to mixtures of chemicals and allergic or respiratory diseases in children.MethodsWe included 1,238 mother-child pairs from the ELFE nationwide cohort. Dietary exposure to 69 chemicals was assessed using food frequency questionnaires. Exposure to mixtures of chemicals was previously assessed. Allergic and respiratory diseases (eczema, food allergy, wheezing, and asthma) were reported by parents between 6?9 and age 5.5 years. Associations were evaluated with adjusted logistic regressions. Results are expressed as odds ratio (OR[95%CI]) for a variation of one SD increase in mixture pattern.ResultsAdditional dietary exposure to a mixture composed mainly of trace elements, furans and polychlorinated biphenyls (furans-PCBs) was significantly associated with the risk of eczema (1.10 [1.00; 1.22]). In contrast, this association was consistent across sensitivity analyses. Exposure to a mixture of pesticides was positively associated with the risk of food allergy (1.20 [1.01; 1.42]), whereas the exposure to another mixture of pesticides was positively but slightly related to the risk of wheezing (1.14 [1.00; 1.30]). The mixture of furans-PCBs was also positively associated with the risk of asthma (1.15 [1.00; 1.32]). Exposure to a mixture of trace elements was positively associated with the risk of asthma (1.15 [1.00; 1.32]). This association was consistent across sensitivity analyses, except the complete-case analysis.ConclusionWhereas few individual chemicals were related to the risk of allergic and respiratory diseases, some consistent associations were found between prenatal dietary exposure to some mixtures of chemicals and the risk of allergic or respiratory diseases. The positive association between trace elements, furans and PBHs and the risk of eczema, and that between pesticides mixtures and food allergy need to be confirmed in other studies. Conversely, the negative association between perfluoroalkyl acids, PBHs and trace elements and the risk of asthma need to be further explored.	Environ Health. 2024 Jan 9;23(1):5.	10.1186/s12940-023-01046-y	38195595	ヒト	免疫	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2275	A. Gaylord, K. Kannan, M. Lakudzewaran, H. K. Zhu, A. Gharaibeh, M. H. Hoobler, S. K. Lee, H. X. Liu, Y. Alterayma, L. G. Kahn, B. Gu, M. L. Liu, G. S. Mahtte-Lee, S. G. Brubaker and L. Trasande	2022	Variability and correlations of synthetic chemicals in urine from a New York City-based cohort of pregnant women	Fetal exposure to environmental chemicals has been associated with adverse health outcomes in children and later into adulthood. While several studies have examined correlations and variability of non-persistent chemical exposures throughout pregnancy, many do not capture more recent exposures, particularly in New York City. Our goal was to characterize exposure to phthalates, bisphenols, polycyclic aromatic hydrocarbons, and organo-phosphate pesticides among pregnant women residing in New York City who enrolled in the New York University Children's Health and Environment Study (NYU CHES) between 2016 and 2018. We measured urinary biomarkers of exposure in 1st trimester (n = 215), 2nd trimester (n = 215), 3rd trimester (n = 215), and postpartum (n = 183) maternal urine samples. Intra-class correlation coefficients (ICC) were calculated to assess variability of concentrations at each time point across the cohort. We compared ICC values to population-level urinary reproducibility data from adult ongoing cohorts (aged between 18 and 65 years) from the National Health and Nutrition Examination Survey (NHANES). ICCs to quantify inter-individual variability of metabolites across pregnancy. Geometric means and ICCs were compared to time-alike pregnancy cohorts that recruited women in 2012 or later as well as nationally representative cross-sectional data from NHANES (2013?2014). Results: Concentrations of phthalates, bisphenols, and organophosphate pesticides (3,5,6-trichloro-2-pyridinol (TCPy), 4-nitrophenol (PNP), and 2-isopropyl-4-methyl-6-hydroxypyrimidine (IMPY)) were detected in >70% of samples. Bisphenol S (BPS) was detected in 50?60% of samples. Di-2-ethylhexyl phthalate (DEHP) metabolites were detected in 30?40% of samples. Di-n-butyl phthalate (DnBP) metabolites were detected in 50?60% of samples. Mono-2-ethylhexyl phthalate (MEHP) metabolites were detected in 20?30% of samples. Mono-n-butyl phthalate (MnBP) metabolites were detected in 40?50% of samples. Mono-benzyl phthalate (MBzP) metabolites were detected in 10?20% of samples. Mono-ethyl phthalate (MEP) metabolites were detected in >90% of samples. Bisphenol A (BPA) was detected in >70% of samples. Bisphenol F (BPF) was detected in 30?40% of samples. Bisphenol S (BPS) was detected in 50?60% of samples. Bisphenol AF (BPAF) was detected in <10% of samples. Di-2-ethylhexyl phosphate (DEHP) was detected in >90% of samples. Diethyl phosphate (DEP) was detected in >70% of samples. Diphenyl phosphate (DPHP) was detected in >80% of samples. Dimethyl phosphate (DMP) was detected in >60% of samples. Dimethyl thiophosphate (DMTP) was detected in 30?40% of samples. Dimethyl dithiophosphate (DMDTP) was detected in 10?20% of samples. Diethyl thiophosphate (DETP) was detected in 10?20% of samples. Diethyl dithiophosphate (DEDTP) was detected in <10% of samples. Geometric means ranged from 0.33 ng/mL (DMDTP) to 2,010 ng/mL (DEP). Intra-class correlation coefficients (ICC) ranged from 0.1 for DMDTP to 0.6 for DEP. Conclusions: Urinary concentrations of most phthalates, bisphenols, and organophosphate pesticides were detected frequently in pregnant women residing in New York City. Concentrations of DEHP metabolites, DnBP metabolites, and DEP were higher than those measured in other pregnancy cohorts. These results provide a general overview of the chemical metabolites measured in NYU CHES in comparison to other contemporary pregnancy cohorts and highlight directions for future studies.	Environ Pollut. 2022 Sep 15:309:119774.	10.1016/j.envpol.2022.119774	35841991	ヒト	一般毒性	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2276	Y. Gálvez-Ontiveros, S. P?rez, C. Montaraz and A. Rivas	2020	Endocrine Disruptors in Food: Impact on Gut Microbiota and Metabolic Diseases	Endocrine disruptors (EDCs) have been associated with the increased incidence of metabolic disorders. In this work, we conducted a systematic review of the literature in order to identify the current knowledge of the interactions between EDCs in food, the gut microbiota, and metabolic disorders in order to shed light on this complex triad. Exposure to EDCs induces a series of changes including microbial dysbiosis and the induction of metabolic pathways and associated genes, enzymes, and metabolites involved in EDC metabolism. The products and by-products released following the microbial metabolism of EDCs can be taken up by the host; therefore, changes in the composition of the microbiota and in the production of microbial metabolites could have a major impact on host metabolism and the development of diseases. The remediation of EDC-induced changes in the gut microbiome might represent an alternative course for the treatment and prevention of metabolic diseases.	NUTRIENTS Vol.12 Issue 4	10.3390/nu12041158	32326280	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2277	Y. P. Fu, W. Y. Chen, L. Q. Guo, Y. Q. Zhu, J. S. Yuan and Y. H. Liu	2022	The association between hearing threshold and urinary personal care and consumer product metabolites in middle-aged and elderly people from the USA	Endocrine disruptors have been reported to be associated with hearing ability. However, the association between personal care and consumer product chemicals, known as commonly detected endocrine disruptors, and age-related hearing loss still remains unclear. This study aimed to examine the association between exposure to 7 personal care and consumer product chemicals and hearing thresholds in middle-aged and elderly people from the National Health and Nutrition Examination Survey (NHANES) 2011?2012. Weighted multivariate linear regression, restricted cubic spline (RCS), and Bayesian kernel machine regression (BKMR) models were used to evaluate single and joint associations between urinary concentrations of 7 chemicals and pure-tone average (PTA). Exposure to these chemicals was negatively associated with PTA. 2,5-Dichlorophenol had the greatest contribution to the mixture effect. The mixture effect was stronger in women, elderly people. Four pooled clusters were identified according to 7 chemicals exposures. Cluster 3 (high TCS exposure) showed a lower APTT (-9.7?-0.0[95%ci]) than cluster 1(the lowest exposure cluster, as a reference). Our study provides evidence that exposure to personal care and consumer product chemicals might be inversely associated with PTA. More studies are needed to fully understand the association of exposure to these chemicals with hearing threshold.	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH Vol.29 Issue 53 Pages 81076-81086	10.1007/s11356-022-21459-5	35731440	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2278	J. F. Fu, Y. Yao, Z. H. Huang, Z. H. Guo, X. X. Tang, X. L. Chen, X. J. Li, Y. M. Ge, B. J. Lu, Y. J. Shu and S. Y. Lu	2024	Gestational Exposure to Endocrine-Disrupting Chemicals of Emerging Concern and the Risk of Developing Gestational Diabetes Mellitus: A Comprehensive Investigation of Sex-Specific and Trimester-Specific Associations	Gestational diabetes mellitus (GDM) is a type of diabetes that arises during pregnancy, leading to long-term adverse consequences for maternal health and fetal development. However, the specific role of endocrine-disrupting chemicals (EDCs) in GDM remains unclear. This study aimed to investigate the associations between exposure to 11 EDCs of emerging concern and GDM risk in a prospective Ma'anshan birth cohort (MABC) in China. Utilizing liquid chromatography-tandem mass spectrometry, urine samples from 1,362 pregnant women in the MABC were analyzed. Weighted quantile sum regression and Bayesian kernel machine regression (BKMR) models were employed to evaluate the combined effects of exposure to 11 chemicals on pre-pregnancy BMI-stratified GDM risk. Generalized additive models (GAMs) and interaction terms were used to evaluate the nonlinear

別添-2　統合文献リスト

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毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成者間評価へ進め、当該時点評価段階で除外した場合、判断理由を記載。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2297	J. Mari-Jourdes, E. Zimmerman, D. J. Watkins, T. Carpenito, C. M. M'Hari-Vega, G. Huerta-Montalvo, Z. Rosario, I. Ayala, C. Vergara, Z. Feric, M. Ordinas, H. H. Suh, A. Z. Gu, P. Brown, J. F. Cordero, J. D. Meeker and A. Alshawabkeh	2020	Cohort profile: Center for Research on Early Childhood Exposure and Development in Puerto Rico	Puerto Rico children experience high rates of asthma and obesity. Further, infants born in Puerto Rico are more at risk for being born prematurely compared with infants on the mainland USA. Environmental exposures from multiple sources during critical periods of child development, potentially modified by psychosocial factors, may contribute to these adverse health outcomes. To date, most studies investigating the health impacts of environmental exposures in Puerto Rico have been cross-sectional. The Center for Research on Early Childhood Exposure and Development (CRECED) Cohort Study, nested in the Contamination Threats (PROTECT) cohort, and infants and children already born to mothers who participated in the PROTECT study. Findings to date Data collected and processing methods ongoing. Demographic data have been collected on 197 mother–child pairs. Birth outcomes are available for 100 infants; neurodevelopmental outcomes have been collected on 53 children. Concentrations of parabens and phenols in maternal spot urine samples collected during pregnancy (n=197) and in children's urine samples collected at 1 year (n=100) are significantly higher among our participants than among participants in NHANES. Inclusion criteria, to date, have been twelve or seven pregnancies compared to the reference values from a similar population drawn from the National Health and Nutrition Examination Survey. Future plans Data will continue to be collected through recruitment of new births with a target of 600 children. Teens scheduled follow-up visits with existing and new participants are planned. Further, we research team continues to work with healthcare providers, paediatricians and early intervention providers to support parent's ability to access early intervention services for participants.	BMJ Open. 2020 Jul 19;10(7):e036389.	10.1136/bmjopen-2019-036389	32690520	ヒト	発達神経	-	-	-	-	-	-	Cohort profile	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2298	M. Manickathan, N. Sivagurunathan, V. S. Anitalin and J. L. Catherathan	2024	In utero and lactational bisphenol A exposure alters testicular function in adult Wistar rats	Objective Bisphenol A (BPA) is widely used as a plasticiser, and its potential toxicity has been a public concern due to its mimicking effects of estrogen. However, in utero and lactational exposure to BPA during the critical stage of development of the male reproductive system and its effect on the adult offspring's testicular functions remain unclear. In the current study, we sought to investigate the impact of in utero and lactational exposure to BPA on the testicular functions of adult rats. Methods Adult female Wistar rats were administered BPA orally at 50 mg/kg body weight daily from gestational day one until delivery. Results In utero and lactational exposure to BPA alters testicular architecture, as evidenced by the disintegration of the basement membrane of the seminiferous tubules and reduced number of spermatogenic cells, increased mortality of the germ cells, and a decrease in the number of Sertoli cells and Leydig cells. Also, BPA exposure significantly reduced the testicular weight, sperm count, motility, and viability and increased the number of sperm with abnormalities. Moreover, BPA exposure significantly reduced the activities of testicular steroidogenic enzymes, 3β-hydroxysteroid dehydrogenase and 17β-hydroxysteroid dehydrogenase, and hormones, such as testosterone, estradiol, and luteinising hormone. Our results also revealed significantly higher urinary concentrations of dichlorophenols, chlorate and perchlorate, and polyfluoroalkyl substances detected significantly. At the same time, oxidative stress markers, such as malondialdehyde, lipid peroxidation, and hydroxyl radicals in the testicle of the BPA group increased significantly, suggesting that BPA exposure during early development is enough to induce oxidative stress in adults. Further, the terminal deoxynucleotidyl transferase-mediated dUTP nick end labelling showed apoptotic cells localised in the seminiferous tubules. The caudal epididymal sperm count, motility, and viability decreased while sperm abnormalities increased in rats exposed to BPA. Conclusion The present study highlights the detrimental effects of BPA on the male reproductive system, underscoring the potential risks associated with BPA exposure during critical stages of development.	TOXICOLOGY AND ENVIRONMENTAL HEALTH SCIENCES Vol.16 Issue 4 Pages 581-593	10.1007/s13530-024-00236-6	-	動物	1	1	1	1	0	50 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2299	L. R. Macheka, P. Palacci, A. Iglesias-Gonz?lez, C. Zeiss, B. M. P. Appenzeller and F. A. Zeman	2024	Exposure to pesticides, persistent and non - persistent pollutants in French 3.5-year-old children: Findings from comprehensive hair analysis in the ELFE national birth cohort	Introduction Exposure to endocrine disruptors during early childhood poses significant health risks. This study examines the exposure levels of French 3.5-year-old children to various persistent and non-persistent pollutants, including pesticides, PCBs, PBDEs, and PFAS, using hair analysis from the ELFE national birth cohort. Methods Hair samples from 1,000 children were collected during the 3.5-year follow-up visit. Exposure biomarkers from 53 chemical families were analysed using LC-MS/MS and GC-MS/MS. LOD/LOQ values were established for each compound. Descriptive statistics and multivariate analyses, including principal component analysis (PCA) and hierarchical clustering, were performed to identify exposure patterns and correlations between chemicals. Results Detection rates varied significantly among the different French regions. Nicotine presented both the highest concentration (30 pg/mg) and highest median concentration (81 pg/mg) measured in the children 's hair. Statistically significant correlations between the levels of biomarkers found in the hair samples of the mothers and their respective children were observed for Spearman 's correlation coefficient > 0.30, p < 0.001, and Lin 's concordance correlation coefficient > 0.30, p < 0.001 and acceptable 3 correlation coefficient > 0.29, p < 0.001. Conclusions The study highlights the elevated exposure levels of young children to various pollutants, highlighting the influence of sex and geography. Hair analysis emerges as a crucial tool for monitoring endocrine disruptors, offering insights into exposure risks and reinforcing the need for protective measures against these harmful substances.	ENVIRONMENT INTERNATIONAL Vol.190	10.1016/j.envint.2024.108881	39002332	ヒト	-	1	1	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2300	Y. Lu, X. Y. Liu and Y. T. Liu	2024	Novel Therapeutic Targets and Biomarkers Associated with Bladder Cancer-Associated Fibroblasts (CAFs) Promoted by Bisphenol A	The escalating incidence of health issues linked to environmental pollutants, specifically endocrine-disrupting chemicals (EDCs), has emerged as a dire consequence of modern industrialization. Bisphenol A (BPA), a widespread EDC, is under scrutiny for its potential role in exacerbating bladder cancer via the modulation of cancer-associated fibroblasts (CAFs). CAFs are integral to the tumor microenvironment, influencing cancer progression through their interactions with immune cells and secretion of various factors and exosomes. By recognizing the critical role of CAFs, this study delves into their utility as therapeutic targets, focusing on the identification of reliable biomarkers within the CAFs for bladder cancer. Through weighted correlation network analysis, genes associated with CAF activity were pinpointed, culminating in the creation of a CAF-based, immune-related gene prognostic model. Central to this model is BMP6, an enzyme whose expression level not only serves as an indicator of T cell infiltration but also implicates a substantial role in the CAF-mediated immune response within bladder cancer. Furthermore, the study explores the impact of BPA on the CAF-mediated immune response, revealing that BPA can amplify the expression of BMP6 and other genes associated with traditional immunotherapies. Furthermore, BMP6 -targeted strategies could lessen the tumor-mediated burden in bladder cancer patients. Empirical evidence from our proliferation and invasion assays indicates that heightened AMPK expression is correlated with diminished patient survival. These insights pave the way for tailored immunotherapeutic approaches in bladder cancer treatment, emphasizing the modulation of CAFs by BPA/BP.	JOURNAL OF CLINICAL PHARMACY AND THERAPEUTICS Vol.2024	10.1155/2024/3134477	-	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2301	X. L. Lu, T. F. Xia, M. van Faassen, I. P. Kema, A. P. van Beek, X. J. Xu, X. Hua, L. C. Study, B. H. R. Wolffenbuttel, J. V. van Vliet-Ostaptchouk, I. M. Nolte and H. Snieder	2024	Effects of endocrine disrupting chemicals and their interactions with genetic risk scores on cardiometabolic traits	Ubiquitous non-persistent endocrine-disrupting chemicals (EDCs) have inconsistent associations with cardiometabolic traits. Additionally, large-scale genome-wide association studies (GWASs) have yielded many genetic risk variants for cardiometabolic traits and diseases. This study aimed to investigate the associations between a wide range of EDC exposure biomarkers, lipidomic and glycomic (and 31 cardiometabolic traits, and whether these are moderated by their respective genetic risk scores (GRSs). Data were from 1035 participants aged 28 years or older of the LifeLines Cohort Study, a large population-based biobank. GRSs for 10 cardiometabolic traits were calculated based on genome-wide significant common variants from recent GWASs. The concentrations of 15 EDCs in 24 -hour urine samples were measured by liquid chromatography-tandem mass spectrometry technology. The main effects of each specific EDCs and each of the EDC exposure, and their interaction effects on the 10 cardiometabolic traits were examined in multiple linear regression models, adjusted for potential confounders and multiple testing corrections. Results: We found that 1 SD higher urinary MEP, MBzP, MiBP, MCPP, MCOP, MCNP, MEHHP, MEOHP, MECPP, and MEHP+MEOHP+MECPP concentrations were associated with 0.07 to 0.19 SD higher various weight -and body fat-related parameter Z-scores (all P for z > 3.29 $\times 10^{-3}$), and 1 SD higher urinary MEP concentration was associated with 0.07 SD higher waist-to-hip ratio Z-score (all P for z > 3.29 $\times 10^{-3}$). Bonferroni-corrected associations were found between MiBP and MEP with WHR and BMI and body mass index (BMI), and showed that xanthene, bisphenol F, and many other phthalate metabolites significantly contributed to the variance of WHR and BMI. High -density lipoprotein (HDL), eGFR, fasting glucose (FG), and diastolic blood pressure (DBP). Only one association between BMI and bisphenol F was nominally significantly moderated by the GRS explaining 0.3% % of the variance. However, it did not survive multiple testing correction. We showed that non -persistent EDC exposures exerted effects on BMI, WHR and BMI, HDL, eGFR, FG, and DBP. However no evidence for a modulating role of GRSs was found.	Sci Total Environ. 2024 Mar 1:914:169972.	10.1016/j.scitotenv.2024.169972	38211872	ヒト	心血管	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2302	X. L. Lu, T. P. van der Meer, C. Z. Kamali, M. van Faassen, I. P. Kema, A. P. van Beek, X. J. Xu, X. Hua, A. An, L. L. Nolte, I. M. Nolte, B. H. R. Wolffenbuttel, J. V. van Vliet-Ostaptchouk and H. Snieder	2024	A genome-wide association study of 24-hour urinary excretion of endocrine disrupting chemicals	Ubiquitous exposure to environmental endocrine-disrupting chemicals (EDCs) instigates a major public health problem, but much remains unknown on the inter -individual differences in metabolism and excretion of EDCs. To examine this, we performed a two -stage genome -wide association study (GWAS) for 24 -hour urinary excretion of five parabens, two bisphenols, and nine phthalate metabolites. Results: Identified five genome -wide significant (p value < 5x10 -8) and multivariant single nucleotide polymorphisms (SNPs) representing four independent signals that associated with excess 12 -ethyl -5 -carboxypentyl phthalate (MECPP) and mono (2 -ethyl -5 -hydroxyhexyl) phthalate (MEHHP) concentrations. Rs2276307 (p = 1.8x10 -10), rs2276308 (p = 1.8x10 -10), rs2276309 (p = 1.8x10 -10), rs2276310 (p = 1.8x10 -10), and rs11065876 (p = 1.8x10 -10) in SLCO1B1 (solute carrier organic anion transporter family member 1B1) were associated with excess urinary MECPP and MEHHP excretion. Rs1260326 in GCKR (glucokinase regulator) was associated with excess urinary MECPP excretion (p = 3.2x10 -8). Rs11191454 in DGKQ (diacylglycerol kinase theta) was associated with excess urinary MEHHP excretion (p = 2.2x10 -8). Rs1481012 in CELSR1 (cadherin EGF LAG seven -pass G -type receptor 1) was associated with excess urinary MEHHP excretion (p = 4.1x10 -8). Rs1260326 in GCKR was associated with excess urinary MECPP excretion (p = 3.2x10 -8). Rs11191454 in DGKQ was associated with excess urinary MEHHP excretion (p = 2.2x10 -8). Rs1481012 in CELSR1 was associated with excess urinary MEHHP excretion (p = 4.1

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内分泌攪乱性（動物）1：該当、0：該当しない　内分泌攪乱性（疫学）1：該当、0：該当しない　内分泌攪乱性（in vitro）1：該当、0：該当しない　内分泌攪乱性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに内分泌攪乱性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で排除に基づき排除。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2347	A. Punt, J. Louisse, K. Beekmann, N. Pinckaers, E. Fabian, B. van Ravenzwaay, P. L. Carmichael, I. Sorrell and T. E. Moxon	2022	Predictive Performance of Next Generation Human Physiologically Based Kinetic (PBK) Models Based on In Vitro and In Silico Input Data	The goal of the present study was to assess the predictive performance of a generic human physiologically based kinetic (PBK) model based on in vitro and in silico input data and the effect of using different input approaches for chemical parameterization on those predictions. For this purpose, a dataset was created of 38 (72 C-free predictions for 53 compounds by applying different combinations of in vitro and in silico input data for chemical parameterization. Predictions were evaluated by comparing the area under the plasma concentration–time curve (AUC) and maximum plasma concentration (Cmax) based on in vitro–in vivo extrapolation (IVIVE) with those measured in plasma. Linear mixed models were applied to evaluate the effects of species, age, body weight, dose, and selected in vitro and in silico input data. Next, and selected in vitro and in silico input data. Next, and selected in vitro and in silico input data. Next

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2373	R. Q. Yang, J. Y. Sun, S. Y. Zhu, Z. Q. Wang and Y. Liu	2024	Exposure to bisphenol compounds accelerates the conjugative transfer of antibiotic resistance plasmid	Antimicrobial resistance poses the most formidable challenge to public health, with plasmid-mediated horizontal gene transfer playing a pivotal role in its global spread. Bisphenol compounds (BPs), a group of endocrine-disrupting chemicals (EDCs) widely present in the environment, have been reported to promote the conjugative transfer of antibiotic resistance genes (ARGs) that can put bare microbiota at risk. To alternatively assess the BPs-mediated promotion conjugative transfer frequency of RP4-7 and clinically multidrug-resistant plasmids. Furthermore, the promoting effect of BPs on the plasmid transfer was also confirmed in a murine model. Microbial diversity analysis of transconjugants indicated an increase in alpha diversity in the BPAF-treated group, along with the bacterial richness of some beneficial bacteria and checked richness of Faecalibaculum rodentium, which might serve as an intermediate repository for resistance plasmids. The underlying mechanisms along the network conjugative transfer were BPAF treatment-induced exacerbated oxidative stress, disrupted membrane homeostasis, augmented energy metabolism, and the increased expression of conjugation-related genes. Collectively, our findings highlight the potential risk associated with the exacerbated dissemination of ARB both in vitro and in vivo caused by BPs exposure.	Environ Res. 2024 Dec 15;263(Pt 1):120002.	10.1016/j.envres.2024.120002	39278585	in vitro	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2374	L. Y. Xu, Y. Hu, Q. Q. Zh-, C. L. Gu.bin and G. B. Jiang	2022	Several typical endocrine-disrupting chemicals in human urine from general population in China: Regional and demographic-related differences in exposure risk	Endocrine-disrupting chemicals (EDCs) are ubiquitous in the environment, and human exposure to these pollutants has caused great public concern. Five groups of EDCs, including parabens, antimicrobials (triclosan (TCS) and triclocarban (TCC)), bisphenols (BPs), ultraviolet absorbents and its alternatives (UVAs/UVAAs), and benzophenone-type UV filters (BPs), in 24 h urine samples collected from 1,000 participants with different economic levels in China were determined simultaneously to evaluate the exposure levels of such chemicals. The total concentration of target compounds was approximately two times higher in the urines from Chengdu (a first-tier city geometric mean (GM): 4.08 ng/mL) than those from Yangquan (a third-tier city GM: 2.01 ng/mL). Parabens and BPA were the two predominant groups of EDCs in the urine samples. Multivariate models combined with gender, age, body mass index (BMI), education level, occupation, and diet. The estimated daily intakes of target chemicals ranged from 0.002 ng/kg bw/day (triclosan) to 212 ng/kg bw/day (parabens). The exposure estimates showed that females were more vulnerable to exposure to these EDCs. This study profiles the regional and demographic-related differences in the concentrations and exposure risks of several typical EDCs in urines from general populations in three cities with different economic levels in China.	JOURNAL OF HAZARDOUS MATERIALS Vol.424	10.1016/j.jhazmat.2021.127489	34689090	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2375	N. N. Wu, X. N. Li, F. Y. Xu, C. Tian, S. Q. Hu, Y. Wang, L. Li, Q. Q. Kong, B. B. Zhang, G. Eskelan and C. J. Ying	2020	Effects of exposure to a "safe" dose of bisphenol A on male reproductive function and the paternal contribution to the hypothalamic transcriptome profile	The hypothalamus plays key roles in regulating reproduction and energy balance. We determined the transcriptional profile of the hypothalamus (F1) and F2 to identify its relationship with the reproductive function and metabolic phenotypes in male mice after BPA exposure and the paternal contribution. Male mice received 0 (ctrl), 5 μg/kg/day (low BPA), 5 mg/kg/day (high BPA), 5 mg/kg/day bisphenol S (BPS) or vehicle via diet. A PND1 (1 h) intraoral behavior of male F0 rats was assessed before mating. The metabolic and reproductive phenotypes, and the transcriptional profiles of the testis (F0) and hypothalamus were tested in F0 and F1 rats. Male rats exposed to BPA showed a significant increase in the number of pups born alive per litter in the first litter (F1) and a decrease in the number of pups born alive per litter in the second litter (F2). Differentially expressed genes (DEGs) in the F1 testis were identified in the BPA group. Paternal BPA and BPS exposure increased the body weight and food intake of male rats offspring, and 50 and 5,000 DEGs were identified in the hypothalamus of BPA- and BPS-treated rats (F1, male), respectively. The highest-ranked function impaired by BPA and BPS in the F1 hypothalamus was immune function. BPA and BPS exposure induced alterations in the metabolic phenotypes of F1 generation males, and this effect may be related to the altered inflammatory-related signaling pathways in the hypothalamus, but neither treatment affected the F2 hypothalamus. Hundreds of genes in the F1 hypothalamus showed changes upon BPA and BPS treatment. Concern regarding paternal environmental endocrine disruptor exposure should be raised. (C) 2020 Elsevier Ltd. All rights reserved.	CHEMOSPHERE Vol.259	10.1016/j.chemosphere.2020.127447	-	動物	-	1	不明	1	不明	0	35 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2376	A. H. Wu, A. A. Franke and L. R. Wilkens	2021	Risk of breast cancer and prediagnostic urinary excretion of bisphenol A, triclosan and parabens: The Multiethnic Cohort Study (vol 149, pg 1426, 2021)	Exposure to bisphenol A (BPA), triclosan and parabens is widespread but their impact on breast cancer risk remains unclear. This nested case-control study investigated endocrine-disrupting chemicals (EDCs) and breast cancer risk within the Multiethnic Cohort (MEC). We measured pre-diagnostic urinary BPA, triclosan, and parabens in 1,203 newly postmenopausal women with breast cancer (618 African American, 77 Latino, 260 Native Hawaiian, 108 Japanese American, and 270 White) and 1,200 individually matched controls, using a conditional and validated liquid chromatography-mass spectrometry assay. Conditional logistic regression was used to examine risk in three EDCs, with adjustment for creatinine and potential confounders. In all women, breast cancer risk was not associated with BPA (Pmodel = 0.22) but was associated with triclosan (OR = 1.15, 95% CI 0.98-1.35; Pmodel = 0.083) and total parabens (OR = 1.17, 95% CI 0.97-1.41; Pmodel = 0.11). With risk of hormone receptor (HR+) cancer (n = 1,203) lower among women in the upper two tertiles of BPA (OR = 0.81, 95% CI 0.66-1.00; Pmodel = 0.049), risk of HR+ cancer was higher among women in the upper two tertiles of triclosan (OR = 1.23, 95% CI 1.01-1.50; Pmodel = 0.036). An inverse association with triclosan was observed mainly among overweight/obese women (OR*2 vs T1 = 0.76, 95% CI 0.58-1.00; Pmodel = 0.053). In summary, breast cancer risk in a multiethnic population was correlated to BPA and was weakly inversely associated with triclosan and paraben exposure. Studies with multiple urine samples collected before breast cancer diagnosis are needed to further investigate these EDCs and breast cancer risk.	Int J Cancer. 2021 Oct 1;149(7):1426-1434.	10.1002/ijc.33692	34013527	ヒト	発がん	-	-	-	-	-	-	nested case-control	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2377	L. M. Wise, D. HenrYobo-Saawedis, S. M. Boas, Y. S. Pan and J. M. Juraska	2019	Perinatal High-Fat Diet and Bisphenol A: Effects on Behavior and Gene Expression in the Medial Prefrontal Cortex	Both high-fat diets (HFD) and bisphenol A (BPA), an environmental endocrine disruptor, are prevalent in industrialized societies. Previous studies have detected separate effects of BPA and HFD; however, none have investigated the potential interaction between these factors. Here, we exposed female rats to BPA (0, 2.5, 25, or 250 μg/kg/day) and HFD (10% or 45% kcal from fat) during the perinatal period. The eyes were individually closed on PD14, which is the latest developmental time point for this study. Behavioral testing was conducted in the novel object recognition task and a cross-platform maze on PD30–PD35, but no interactive effects were observed. Neither HFD nor BPA exposure changed performance on a social recognition task, and only BPA had an effect on the elevated plus maze. BPA increased novel contact latency in the medial prefrontal cortex (mPFC) of PD2 males but not females. Expression of several genes related to hormone synthesis and receptors, inflammation, oxidative stress, and apoptosis in the mPFC on PD2 and PD8 were altered due to BPA and/or HFD exposure with sex-interactive effects. BPA resulted in an increase in the gene expression of Esr1 in the mPFC of females on both PD2 and PD8. Epigenetic analysis on PD8 did not show a change in methylation or in the levels of per mRNA or its rec.Mtb. Thus, perinatal BPA and HFD have separate effects but rarely interact.	DEVELOPMENTAL NEUROSCIENCE Vol.41 Pages 1-16	10.1159/000494879	30580332	動物	-	1	1	1	1	0	40, 400 μg BPA/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2378	X. P. Wei, N. Zhang, Q. Q. Zhu, Y. Hu, X. Wang, X. Y. Wang, C. Y. Liao and G. B. Jiang	2024	Exposure to Multiple Endocrine-Disrupting Chemicals and Associations with Female Infertility: A Case-Control Study	Parabens (PNs) and their metabolites (MBs), triclocarban (TCC), triclosan (TCS), bisphenols (BPs), benzophenones (BePs), and phthalate metabolites (mPMEs) are typical endocrine-disrupting chemicals (EDCs) used in natural and personal care products (NPCPs). Studies have suggested that these EDCs affect the reproductive system and may cause infertility; however, epidemiological evidence of exposure to infertility is still lacking. Hence, a total of 302 serum samples from women of reproductive age were collected, and six categories of typical EDCs were analyzed. The results revealed that EDCs are ubiquitous in female serum. The geometric mean (GM) concentrations of 4-, iso-PPB-, 4-, iso-MBB-, 4-, iso-TCS-, TCC-, 4-, iso-MBP-, 4-, iso-MBPh-, and 4-, iso-MBPh-, and 4-, iso-MBPh- were 3.58, 767, 1.87, 1.39, 0.267, and 1.58 ng/mL, respectively. The serum concentrations of 4-PPB, 4-MBB, 4-MBPh, 4-MBPh, TCC, TCS, and 4-MBPh- from infertile women (GM: 4.06, 787, 4.01, and 7.01 ng/mL, respectively) were higher than those from fertile women (3.45, 745, 3.65, and 2.27, respectively) (p < 0.05). Elevated serum levels of EDCs, including 4-PPB, 4-MBB, 4-MBPh, 4-MBPh, TCC, TCS, and 4-MBPh-, were significantly associated with the increased infertility risk, and a dose-response relationship was observed. Women's mean daily EDMEX per unit increases in the "Triclosan" score (-0.97–10.7 ng/kg bw/day, 1.602. Conversely, "Women" and "Animal product" patterns, and UPF intake were associated with higher TPHA (e.g., "Women" and 2'-Hydroxypropiophenone-2'4'6'-Trimethoxy-4-Methoxybenzophenone (DHB) (N: 5.63, 1.07–52.1, 1.072), pesticides (e.g., "Animal product" and 3-Phenoxybenzoic acid (3-PBA) (N: 1.22, 1.02–1.47), and phthalates metabolites (e.g., UPF- and Nonmethyl phthalate (1-MIU) (N: 1.002). The association remained significant after correcting for multiple testing. Conclusions: Following a plant-based diet may help reduce the exposure to certain phthalates and organophosphate metabolites, whereas higher consumption of foods from animal origin and high-in-fat/sugar/salt may increase exposure to PAHs, pesticides, and phthalates metabolites in pregnancy.	Environ Health (Wash). 2024 Sep 3;2(12):902-911.	10.1021/envhealth.4c00040	39722846	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2379	X. P. Wei, Y. Hu, Q. Q. Zhu, J. Gao, C. Y. Liao and G. B. Jiang	2022	Co-exposure and health risks of several typical endocrine disrupting chemicals in general population in eastern China	Human exposure to endocrine-disrupting chemicals (EDCs) is a health concern due to their wide use and interference with the human endocrine system. Parabens, bisphenols, benzophenones, triclocarb (TCC), triclosan (TCS), and tetrabromobisphenol A (TBBPA) and its derivatives tetrachlorobisphenol A (TCBPA) and tetrabromobisphenol A (TBBPA), are typical EDCs that are frequently detected in environmental and human samples. However, only a few studies have assessed the co-exposure of these chemicals in humans. In this study, urine samples were collected from the general population in the city of Wuxi (n = 123) and a county, Taishan (n = 116), eastern China, and analyzed for these EDCs. Parabens, bisphenols, TCC, and benzophenones were frequently detected in urine, whereas TBBPA and its derivatives were not detected. The geometric mean concentrations of parabens, bisphenols, and benzophenones in urine from the Wuxi population were 25.7, 2.20, and 2.10 ng/mL, respectively, which were substantially higher than those from the Taishan population (6.60, 0.85, and 0.27 ng/mL, respectively). Co-exposure to parabens, bisphenols, and benzophenones in urine EDCs. The mean intake in these EDCs was estimated based on the measured concentrations in urine and creatinine daily intakes. Wuxi's hazard quotient values for EDCs in humans from both locations were generally less than 1, indicating a low exposure risk of EDCs in these regions. Nonetheless, the health risks caused by co-exposure to such EDCs cannot be ignored.	ENVIRONMENTAL RESEARCH Vol.204	10.1016/j.envres.2021.112366	34774506	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2380	S. Markantis, S. MYtrusi, H. Vesyakis, T. B. Knos, M. Gascon, N. GTil-Guinedi, S. Gunz?ez-Palacios, M. D. G. Roig, C. Lestaele, E. Lliuria, M. Rollard, A. K. Sakhi, C. Thomsen, I. Vioque, M. Bustamante, I. Sunyer and M. Vrijheid	2025	Dietary patterns and exposure to non-persistent endocrine-disrupting chemicals during pregnancy	Background: Exposure to non-persistent endocrine-disrupting chemicals (EDCs) is widespread, causing serious adverse health effects, especially during pregnancy. Diet is a major source of EDCs and the identification of dietary patterns that give rise to higher exposure levels is crucial. We aimed to explore the relationship between dietary patterns during pregnancy and exposure to non-persistent EDCs. Methods: We included 610 pregnant women from the Barcelona Life Study Cohort (BiSC), Spain. Using food frequency questionnaires (2nd trimester), we estimated ultraprocessed food (UPF) consumption and Mediterranean diet adherence, and derived dietary patterns. Metabolites of phthalates, 11 of bisphenols (including A and S), 2 of benzophenone-type UV filters (BP3), chlorpyrifos and pyrethroid, and parabens were measured in urine samples. Mixtures (e.g., UPF- and Mediterranean diet-related phthalates), and parent compounds of phenols and parabens were measured in weekly urine pools (3rd trimester). Associations between dietary patterns and EDCs were evaluated through multivariable linear regression models (MLRMs) and weighted quantile sum regression (WQS). Results: Higher UPF consumption was associated with higher urinary concentrations of several phthalate metabolites. For example, a 10% increase in energy intake from UPF was associated with a 4.3% (95% CI: 0.3%, 8.4%) higher concentration of mono-(carboxynonyl) phthalate (MCNP). Greater mean daily EDMED per unit increases in the "Triclosan" score (-0.97–10.7 ng/kg bw/day, 1.602. Conversely, "Women" and "Animal product" patterns, and UPF intake were associated with higher TPHA (e.g., "Women" and 2'-Hydroxypropiophenone-2'4'6'-Trimethoxy-4-Methoxybenzophenone (DHB) (N: 5.63, 1.07–52.1, 1.072), pesticides (e.g., "Animal product" and 3-Phenoxybenzoic acid (3-PBA) (N: 1.22, 1.02–1.47), and phthalates metabolites (e.g., UPF- and Nonmethyl phthalate (1-MIU) (N: 1.002). The association remained significant after correcting for multiple testing. Conclusions: Following a plant-based diet may help reduce the exposure to certain phthalates and organophosphate metabolites, whereas higher consumption of foods from animal origin and high-in-fat/sugar/salt may increase exposure to PAHs, pesticides, and phthalates metabolites in pregnancy.	ENVIRONMENT INTERNATIONAL Vol.202	10.1016/j.envint.2025.109612	40578114	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2381	T. T. Wang, J. L. Chen, G. Chen and Z. Q. Li	2021	LOW-DOSE BPA PROMOTES PROLIFERATION, INVASION, AND MIGRATION ON TC84113 CELLS THROUGH REGULATING RIP1	Objective: This in vitro research aimed to investigate the association between BPA exposure with the progression of oral squamous cell carcinoma (OSCC). Methods: Tca8113 cells were exposed to BPA with various concentrations (10-10, 10-9, 10-8, 10-7, 10-6, and 10-5 mol/L) and/or cell proliferation by CCK-8. Subsequently, cells were treated with 10-10 mol/L BPA for 72 h, and Transwell was used to measure the cell invasion and migration. Then, cells were co-treated with 10 ng M monastrolum-1 (Sino Cl) during 10-10 mol/L BPA exposure for 72 h. CCK8 and Transwell were used to detect cell proliferation, invasion, and migration. Results: Cell proliferation was significantly promoted by BPA exposure at 10-10 mol/L, 10-9 mol/L, and 10-8 mol/L concentrations for 72 h. BPA exposure at 10-10 mol/L significantly enhanced cell invasion and migration ability. Results: 0.100 nM and 1 BPA accelerated cell proliferation, invasion, and migration of Tca8113 cells at the exposure time of 72 h. Compared with the BPA exposure group, the cell proliferation, invasion, migration, and the expression of the RIP1 gene and protein in the BPA plus Nec-1 group were significantly decreased. 3) RIP1 was silenced effectively by siRNA. Cell proliferation, invasion, and migration in the si-RIP1 group reduced substantially as compared with that in the si-NC group. Conclusion: Low-dose BPA can accelerate cell proliferation, invasion, and migration of Tca8113 cells through regulating RIP1.	ACTA MEDICA MEDITERRANEA Vol.37 Issue 4 Pages 2591-2596	10.19193/0393-6384_2021_4_402	-	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2382	M. Y. Wang, K. Wang, K. Huang, B. Han, R. F. Li, Y. Shen, Z. J. Zhuang, Z. Wang, L. L. Wang, Y. K. Zhou and T. Jing	2024	Human Biomonitoring of Environmental Chemicals among the Elderly in Wuhan, China: Prioritizing Risks Using EPA's ToxCast Database	In line with the "healthy aging" principle, our aim to assess the exposure map and health risks of environmental chemicals in the elderly. Blood samples from 918 elderly individuals in Wuhan, China, were analyzed using high-throughput targeted and untargeted combined gas/liquid mass spectrometry technology to detect levels of 138 environmental chemicals. Cluster analysis identified exposure profiles, while risk indexes and bioanalytical equivalence percentages were calculated using ToxCast data. Results revealed that 113 chemicals were detected in over 50% of samples, with 24 exceeding 90% detection rates. Cluster 2 exhibited significantly higher concentrations of pollutants, including higher concentrations. For volatile pollutants, several serious lifestyles. In cluster 2, which was characterized by higher concentrations of fat-soluble substances, the concentrations of chlorines was higher than those of monosubstituted or nondichloro. Pesticides emerged as the most active environmental chemicals in persistence proliferator-activated receptor gamma antagonist, thyroid hormone receptor (TR) antagonist, TR agonist, and androgen receptor (AR) agonist activity assays. Additionally, PAHs and polycyclic aromatic hydrocarbons played significant roles as active contaminants for the corresponding targets of AR antagonists and estrogen receptor alpha. We proposed a list of priority pollutants linked to endocrine-disrupting toxic effects in the elderly, which may provide the groundwork for further research into environmental etiology.	ENVIRONMENTAL SCIENCE & TECHNOLOGY Vol.58 Issue 23 Pages 10001-10014	10.1021/acs.est.4c00362	38788169	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2383	A. K. R. Vollmer, C. R. Weinberg, D. D. Baird, A. J. Wilcox, A. M. Calafat, N. C. Daniel, C. H. Johnson and A. M. Z. Jukic	2023	Urinary phenol concentrations and fecundability and early pregnancy loss	STUDY QUESTION: Are urinary phenol concentrations of methylparaben, propylparaben, butylparaben, triclosan, benzophenone-3, 2,2-dichlorophenol or 2,5-dichlorophenol associated with fecundability and early pregnancy loss? SUMMARY ANSWER: 2,5-dichlorophenol concentrations were associated with an increased odds of early pregnancy loss, and higher concentrations of butylparaben and triclosan were associated with an increase in fecundability, but these associations were not statistically significant. WHAT IS KNOWN ALREADY: Phenols are widely used in consumer products and have been associated with adverse reproductive outcomes. However, few epidemiologic studies examining phenol exposure and reproductive function in non-fertility treatment populations. STUDY DESIGN, SIZE, DURATION: Secondary and data were from the Fourth Cycle of the Early Pregnancy Study prospective cohort of 221 women attempting to conceive naturally from 1982 to 1986. This analysis includes data from 223 participants across 700 menstrual cycles, with 126 live births, 16 clinical miscarriages and 8 early pregnancy losses. PARTICIPANTS/MATERIALS, SETTING, METHODS: Participants collected daily first-morning urine specimens. For each menstrual cycle, aliquots from these daily specimens across the cycle were pooled within individuals and analyzed for phenol concentrations. To assess sample representativity, we calculated intraclass correlation coefficients (ICCs) for each phenol concentration. We used discrete survival models to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs) for associations between phenol concentrations (GCV), and early pregnancy loss using multivariable logistic regression and GCV. MAIN RESULTS: TO AND THE RISK OF CHANGE (CI) for within-person variability across menstrual cycles and pooled phenol concentrations ranged from 0.22 to 0.75. There was an increased odds of early pregnancy loss with 2,5-dichlorophenol concentrations although the CIs were wide (link to 1st quintile odds ratio (OR): 4.79; 95% CI: 1.06, 21.66). There was a suggestive association between triclosan (OR: 0.61; 95% CI: 0.34, 1.08) and butylparaben (OR: 0.61; 95% CI: 0.34, 1.08) and fecundability. Benzophenone-3 was not associated with fecundability or early pregnancy loss. Associations were observed between these exposures and covariates of older phenols examined. LIMITATIONS, REASONS FOR CAUTION: Limitations include the absence of phenol measurements in male partners, and a limited sample size, especially for the outcome of early pregnancy loss, which reduced our power to detect associations. WIDER IMPLICATIONS OF THE FINDINGS: This study is the first to use repeated pooled measures to summarize phenol exposure and the first to investigate associations with the variability and early pregnancy loss. Within-person phenol concentration variability underscores the importance of collecting repeated samples for future studies. Exposure misclassification could contribute to differences between the findings of this study and those of other studies, all of which used one urine sample to assess phenol exposure. This study also suggests that 2,5-dichlorophenol concentrations may be associated with early pregnancy loss, but more research is needed to confirm this finding. STUDY FUNDING/COMPETING INTEREST(S): This research was supported by the National Institute of Environmental Health Sciences of the National Institutes of Health (National Institutes of Health/NIEHS), the Intramural Research Program of the National Institutes of Health, the National Institute of Environmental Health Sciences (project numbers ES103325 and ES103086) and a doctoral fellowship at the Yale School of Public Health. The authors declare they have no competing interests to disclose.	Hum Reprod. 2023 Jan 5;38(1):139-155.	10.1093/humrep/deac230	36346334	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2384	H. Venkatesan, R. Sauntharajan and H. Sirisewan	2022	Interaction of various types of bisphenols with enzymes involved in melanin synthesis	Objectives:Bisphenol is one of the commercial chemical compounds which finds application in the manufacture of phenol, polyesters, polycarbonates, epoxy resins, etc. Bisphenol A is the most commonly found bisphenol in the environment and is considered to be toxic to humans. Hence, in the present study, the effect of BPA, BPS, BPF, BPC, BPZ, and BPAF on tyrosinase activity was studied.Methods:Bisphenols are commonly found in food packaging and beverage containers and can be easily absorbed by the body. They can enter into the body systems either by direct means like skin contact or by indirect means through food that is stored in a bisphenol-coated containers. Exposure of the human system to this compound may bring about mild to adverse ailments ranging from skin irritations to infertility. Pigmentation disorder is one such health condition that is caused due to the malfunctioning of melanin synthesis. Tyrosinase is the rate-limiting enzyme in the melanin synthesis pathway and is responsible for the pigmentation of skin, hair, and normal eye function. Methods: In vitro analysis has been done to predict the interaction and also description binding parameters when the bisphenol derivatives BPA, BPB, BPC, BPZ, and BPAF have been docked with some of the essential proteins for melanin synthesis such as tyrosinase, tyrosinase related protein-1(TRP-1), dopachrome tautomerase/tyrosinase related protein-2(TRP-2). Results: The interaction has been quantified with the binding energies, and the interacting amino acid residues have also been identified. The results showed strong interactions for both the proteins. TRP-1 and TRP-2 with BPB, BPC, BPZ, BPF, and BPAF. Conclusions: The risk and threats caused by the commercial products made of bisphenol are at higher levels, and thereby, the need for a safe and desirable alternative has been looked.	TOXICOLOGY AND ENVIRONMENTAL HEALTH SCIENCES Vol.14 Issue 1 Pages 19-24	10.1007/s13530-021-00111-8	-	in silico	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2385	C. van Zwol-Janssens, L. Trieraride, A. G. Avrimakopoulos, M. P. Martino-Mirek, K. Kanrar, E. M. Phillips, F. Rivadeneira, V. W. V. Jaddoe and S. Santos	2020	Fetal exposure to bisphenols and phthalates and childhood bone mass: a population-based prospective cohort study	Background: Exposure to bisphenols and phthalates might influence bone health. We hypothesized that exposure to bisphenols and phthalates during fetal life has persistent effects on bone development. Objectives: To analyze the associations of fetal exposure to bisphenols and phthalates with bone health in school-aged children. Methods: Among 1,382 mother–child pairs participating in a population-based cohort study, we measured maternal urinary concentrations of bisphenols and phthalates at first, second and third trimester with high-performance liquid chromatography–electrospray ionization–tandem mass spectrometry. Total body bone mineral content (TBBMC), total body bone mineral density (TBBMD), and cortical thickness (CTh) were measured by dual-energy X-ray absorptiometry at the age of 6 years. We used linear regression models to examine associations of urinary concentrations of bisphenols (BPA, BPS, BPF) and phthalates (sum of di-(2-ethylhexyl) phthalate metabolites (ΣDEHP), mono-n-butyl phthalate (MnBP), mono-benzyl phthalate (MBzP)) with TBBMC, TBBMD, and CTh. Results: Maternal bisphenol concentrations were not associated with childhood bone measures at 6 years. After adjustment for covariates and multiple testing correction, an interquartile range increase in maternal first-trimester bisphenol S (BPS) concentrations was associated with lower BMD and BMC at 6 years (−0.08 SDS; confidence interval (CI): −0.15 to −0.01 and −0.12 SDS; CI: −0.20 to −0.03). Maternal third-trimester low molecular weight (LMW) phthalate concentrations were associated with higher BMC at 6 years whereas, maternal third-trimester di-n-octylphthalate (DNOP) concentrations were associated with lower eBMC at 10 years. However, these associations did not remain statistically significant after multiple testing correction. Discussion: Maternal first-trimester BPS concentrations are associated with lower BMD and eBMC in school-aged children. These findings should be considered as hypothesis generating and need further replication and exploration of potential underlying mechanisms.	Environ Res. 2020 Jul:186:109602.	10.1016/j.envres.2020.109602	32668547	ヒト	骨	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2386	T. F. van der Meer, C. H. L. Thijs, M. van Faassen, A. P. van Beek, H. Snieder, F. N. R. van Berkum, I. P. Kema, K. C. Makris, B. H. R. Wolffenbuttel and J. V. van Vliet-Ostaptchouk	2021	Endocrine disrupting chemicals during diet-induced weight loss - A post-hoc analysis of the LOWER study	The link between exposure to endocrine-disrupting chemicals (EDCs) and the rapid increase in prevalence of obesity has recently been suggested. However, the magnitude and health impact of EDC exposure in at-risk populations remain largely unclear. In this study, we investigated the effects of a dietary intervention-driven reduction in adipose tissue on the magnitude of urinary EDC exposure and mobilization, and whether higher EDC exposure leads to impaired weight loss in obese individuals. In this post hoc analysis of the Lifestyle, Overweight, Energy Restriction (LOWER) study from the Netherlands, 218 subjects were included. For predictors, urinary concentrations of 11 phthalate metabolites, 5 bisphenols, and 7 parabens were measured at baseline and after 4 months of dietary intervention. Associations between adiposity-related traits and EDCs were tested using multivariable linear regression and linear mixed-effects models. A multiple testing correction based on the false discovery rate (FDR) was applied. After the 4-month intervention, urinary parabens and bisphenol excretions remained similar. Excretions of many butyl phthalates and most high-molecular-weight phthalates decreased, whereas mono-ethyl phthalate increased (all FDR < 0.05). Reductions in body weight, waist circumference, and fat mass were associated with decreased excretion of mono-butyl phthalate (MBP), mono-benzyl phthalate (MBzP), and mono-(2-ethylhexyl) phthalate (MEHP). Reductions in waist circumference (in quadratic terms), mono-n-hexyl phthalate, mono-benzyl phthalate, and mono-(2-ethylhexyl) phthalate (MEHP). Associations between parabens and body mass index, and mono-benzyl phthalate and waist circumference and body fat percentage remained after multiple testing correction (all FDR<0.05). In a study of obese participants, we observed a reduction in most phthalates after a weight reduction intervention. A reduction in adipose tissue may not lead to mobilization and successively to higher urinary EDC excretions. Higher baseline paraben and phthalate exposures were associated with reduced weight loss, suggesting obesogenic properties.	ENVIRONMENTAL RESEARCH Vol.192	10.1016/j.envres.2020.110262	33045228	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2387	M. A. van den Dries, A. P. Keil, H. Tiemeier, A. Pronk, S. Spaan, S. Santos, A. G. Asimakopoulos, K. Kannan, R. Gaillard, M. Guxens, L. Trasande, V. W. V. Jaddoe and K. K. Ferguson	2021	Prenatal Exposure to Nonpersistent Chemical Mixtures and Fetal Growth: A Population-Based Study	BACKGROUND: Prenatal exposure to mixtures of nonpersistent chemicals is universal. Most studies examining these chemicals in association with fetal growth have been restricted to single-exposure models, ignoring potential cumulative effects. OBJECTIVES: We aimed to examine associations between prenatal exposure to nonpersistent chemical mixtures and fetal growth. METHODS: Within the Generation R Study, a population-based cohort in Rotterdam, n = 778, urinary concentrations of 11 phthalate metabolites, 5 bisphenols, and 7 alkylphenolic (AP) metabolites were measured at 18, 19.5, and 25 weeks of gestation and averaged. Ultrasound measures of head circumference, femur length, and estimated fetal weight (EFW) were taken at 18 (n = 1,148), 25 (n = 1,148), 30 (n = 1,148), and 33 (n = 1,148) weeks of gestation, and measurements of head circumference, length, and weight were performed at delivery. We examined the difference in each fetal measurement per quartile increase in all exposures within the mixture with quantile g-computation. RESULTS: The average EFW at 18 (95% CI: 0.0, 0.0) and 33 (95% CI: 0.0, 0.0) weeks of gestation was associated with a 0.0 (95% CI: 0.0, 0.0) and 0.0 (95% CI: 0.0, 0.0) g increase in EFW per quartile increase in the mixture, respectively. At 18 (95% CI: 0.0, 0.0), 25 (95% CI: 0.0, 0.0), 30 (95% CI: 0.0, 0.0), and 33 (95% CI: 0.0, 0.0) weeks of gestation, a 0.0 (95% CI: 0.0, 0.0) mm increase in femur length was observed corresponding to a 0.0- (95% CI: 0.0, 0.0) mm difference in femur length per quartile increase in the mixture, respectively. At birth, we observed no differences in weight between Q1–Q2 and Q3–Q4. However, fetuses in Q3–Q4 had 0.0 g (95% CI: 0.0, 0.0) lower birth weight in comparison with those in Q1–Q2. Results observed at 18, 25, and 33 weeks of gestation were similar for femur length; however, no differences were observed at birth. No associations were observed for head circumference. DISCUSSION: Higher exposure to a mixture of phthalates, bisphenols, and OP pesticides was associated with lower EFW in the midgestational period. In late pregnancy, these differences were similar but less pronounced. At birth, the only associations observed between exposure to the mixture and fetal growth were for femur length and weight. This finding suggests that exposure levels of important mixtures may be sufficient to influence growth in early pregnancy, whereas higher levels, representative of those in the general population, affect birth weight, later exposure to nonpersistent chemicals may adversely impact fetal growth, and because these exposures are ubiquitous, this impact could be substantial. https://doi.org/10.1289/EHP9178	Environ Health Perspect. 2021 Nov;129(11):117008.	10.1289/EHP9178	34817287	ヒト	生殖発生	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2388	M. A. van den Dries, K. K. Ferguson, A. P. Keil, A. Pronk, S. Spaan, A. Ghassabian, S. Santos, V. W. V. Jaddoe, L. Trasande, H. Tiemeier and M. Guxens	2021	Prenatal Exposure to Nonpersistent Chemical Mixtures and Offspring IQ and Emotional and Behavioral Problems	Prenatal exposure to nonpersistent chemicals such as phthalates, bisphenols, and organophosphate (OP) pesticides is ubiquitous and occurs in mixtures. So far, epidemiological studies investigating neurodevelopmental consequences of these exposures have mostly been restricted to single pollutant models. Thus, our studied the association between prenatal exposure to nonpersistent chemical mixtures and child IQ and emotional and behavioral problems at age 6 y. We measured 11 phthalate metabolites, 5 bisphenols, and 7 OP pesticide metabolites in urine samples collected from 1,232 pregnant women participating in the Generation R Study. We assessed child IQ at age 6 y using the Wechsler Intelligence Scale for Children-III. Parents reported on their child's emotional and behavioral problems using the Child Behavior Checklist. We used quantile g-computation to estimate the change in each outcome per quartile increase in all chemicals within the mixture. Higher exposure to the mixture was associated with lower nonverbal IQ: 0.0 points (95%CI: −1.5, −0.0), 10.5 years (95%CI: −2.2, −0.9), and −0.5 points (95%CI: −0.8, 0.1) for the second, third, and fourth quartile, respectively, compared to the first quartile. These results were mainly driven by the phthalate mixture. No association was observed with emotional and behavioral problems. Prenatal exposure to nonpersistent chemical mixtures was associated with lower nonverbal IQ in children. Exposure to chemical mixtures during gestation is universal and may impact neurodevelopment.	Environ Sci Technol. 2021 Dec 21;55(24):16502-16514.	10.1021/acs.est.1c04455	34878787	ヒト	発達神経	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2389	C. S. Uldbjerg, T. Koch, Y. H. Lim, L. S. Gregersen, C. S. Olesen, A. M. Andersson, H. Frederiksen, B. A. Coull, R. Hauser, A. Juul and E. Bilsteen	2022	Prenatal and postnatal exposures to endocrine disrupting chemicals and timing of pubertal onset in girls and boys: a systematic review and meta-analysis	BACKGROUND: Globally, the ages at pubertal onset for girls and boys have been decreasing during recent decades, partly attributed to excess body fat accumulation. However, a growing body of literature has recognized that endocrine-disrupting chemicals (EDC) may play an important role in this global trend, but the association has not yet been fully established. OBJECTIVE: AIM NATIONALE EDUCATIVA, a synthesis with normal hormone function and metabolism and play a role in pubertal onset. We aimed to systematically identify and evaluate the current evidence on the timing of pubertal onset in girls and boys following perinatal or postnatal exposures to EDC. METHODS: We searched PubMed, Embase, and Web of Science for epidemiological studies published from 1 January 2000 to 1 March 2021. Eligible studies were those that investigated the association between a combination of early (MUSE and four) two years) terms. Publications were considered if they scored biomarkers of prenatal or postnatal exposures to xenobiotic EDCs (European Commission's list of category 1 EDCs) measured in maternal or child biospecimen and pubertal onset defined by the progression of the following milestones (and assessed in terms of the following measures): menarche (age), characteristic (Tanner staging) and pubarche (Tanner staging). In girls: menarche (age), breast development (Tanner staging), testicular volume (ml) and pubarche (Tanner staging). In boys. OUTCOMES: The literature search identified 1975 references, of which we identified 10 publications fulfilling the eligibility criteria for the qualitative level synthesis and 29 publications for the meta-analysis. The qualitative level synthesis provided data on 101 combinations of associations between exposures to phthalates, bisphenols, parabens, polychlorinated biphenyls, dichlorodiphenyltrichloroethane, and pubertal onset in girls and boys. We found inconsistent associations in the qualitative level synthesis, suggested that postnatal exposure to phthalates may be associated with earlier thelarche and later pubarche. However, our did not find consistent evidence in the meta-analysis for associations between timing of pubertal onset in girls and boys and exposures to any of the studied xenobiotic EDCs. We were not able to identify specific pre- or postnatal windows of exposure to EDC. CONCLUSIONS: Our findings suggest that EDC exposure may affect pubertal onset in girls and boys, but the current literature is inconsistent and the meta-analyses did not support an association. We could not by family confirm EDC exposure as a risk factor for changes in age of pubertal onset in female children. To create a more uniform foundation for future investigations of associations between EDC exposure and pubertal onset, we recommend the use of more standardized approaches in the choice of statistical analyses, with exposure transformations, and in the definitions and assessments of puberty outcomes. The impact of mixtures of EDC exposures on the association also remains unestablished and could be valuable to elucidate for prenatal and postnatal windows of exposure. Future large, longitudinal epidemiological studies are needed to clarify the overall association.	Hum Reprod Update. 2022 Aug 25;28(5):687-716.	10.1093/humupd/dmac013	35466359	ヒト	生殖発生	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2390	Z. N. Zhu, Y. N. Pan, X. Chen, K. Wei, X. Y. Zhou, Z. X. Tang, R. L. Yin, X. Y. Xiao and A. J. Li	2024	Cashiers and bisphenols: Occupational exposure and health implications in south China	Bisphenols are ubiquitous chemicals used in various industries, raising concerns due to their potential to disrupt endocrine systems, particularly among occupational populations. This study concurrently assessed occupational exposure to BPA and its substitutes among cashiers in Guangzhou, China, and explored associations between exposure and health outcomes. Urine samples from 1,000 cashiers were collected in 2019. Analysis revealed 7 bisphenols (BP) and 2 parabens (BP-PC) with detection frequencies ≥ 80 %. BPS exhibited the highest median concentration at 1.26 ng/mL, while bisphenol AF (BPAF) had the highest median concentration of 1.26 ng/mL. Cashiers showed relatively high levels of BPA, BPS and BPC. Highlighting potential occupational exposure implications. Variations in urinary bisphenol concentrations across gender and age groups were explored. Significant correlations were identified between urinary BPS and BPA, as well as BPC and BPAP, indicative of shared exposure sources and pathways. Cashiers had 1.58–2.5 times higher exposure than non-cashiers to these chemicals. The median exposure in the Guangzhou exceeded the established tolerable daily intake for BPA, set at 0.2 ng/kg/day, by 1.5–39 times. This study underscores the urgent need for assessing the potential health implications of bisphenol exposure, especially for those in occupational settings. [Int Hygiene Environ Health 260 (2024) 114395] Graphical abstract.	EMERGING CONTAMINANTS Vol.10 Issue 4	10.1016/j.emcon.2024.100341	-	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2391	Y. X. Zhao, J. Wang, G. S. Liu, Y. Atlasi, C. G. Sonnehag, W. Liu, Q. H. Zhang, J. J. Huang, P. Z. Sun and Y. X. Sun	2024	The CHECH study: A prospective pregnancy cohort study on CHemical exposure and children's health in Tianjin, China	The Chemical Exposure and Children's Health (CHECH) study is an ongoing pregnancy cohort study in Tianjin, China. This paper describes the background, aim and the study design, which can be followed by future researchers to design and conduct similar studies. The abundance and the potential adverse health outcomes of endocrine disrupting chemicals (EDCs) is concerning. Nine weakly developing fetuses and infants are more vulnerable to EDCs exposure. The CHECH study aims to investigate the importance of early life exposure to multiple EDCs (phthalates and their metabolites, bisphenol A and their substitutes, perfluorinated compounds and polycyclic aromatic hydrocarbons) for multiple health outcomes in Chinese children, namely sexual development, neurodevelopment, metabolism and growth, as well as airway and allergy. A total of 2238 pregnant women were recruited in Tianjin from May 2021 to April 2023 with a response rate of 40 %. Among these women, 2196 children were born with available information, including 57 pairs of twins. 4 low samples were excluded from the current analysis. Detailed information on the living environment, dietary habits, socioeconomic status, lifestyle, medical history, and psychological status was collected by questionnaires. Physical examinations and questionnaires. The CHECH study, which collected exposure information and health outcomes at multiple time points, will contribute to the understanding of prenatal exposure to EDCs and their impact on children's health, thereby facilitating the development of risk assessments aimed at reducing exposure and associated health risks.	Hygiene and Environmental Health Advances, Volume 9, March 2024, 100084	10.1016/j.heha.2023.100084	-	ヒト	一般毒性	-	-	-	-	-	-	Cohort profile	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2392	J. Zhao, P. Hirtze, J. Y. Chen and J. Jiang	2020	Causal inference for the effect of environmental chemicals on chronic kidney disease	The impacts of environmental chemicals on the decline of kidney function have been suggested by a limited number of statistical and animal studies. Thus, these exposures may be modifiable risk factors for chronic kidney disease. Some of the chemicals, such as Perfluorooctyl acid (PFOA), are pervasive throughout our environment, determining their health effects is an important public health concern. In this study, we examined cross-sectional data from the 2009-2016 cycle of the National Health and Nutrition Examination Survey (N=9971) using a statistical causal inference method and conventional statistical methods to determine the links between concentrations of several major environmental chemicals and kidney function measured by the estimated glomerular filtration rate (eGFR). Various generalized propensity score estimation methods including the Super Learner algorithm were implemented to estimate the causal effect of environmental chemicals on eGFR. Our results showed that PFOA is a modifiable risk factor for chronic kidney disease and the statistical causal method produces credible results in estimating the effect of environmental exposures on a continuous measure of kidney functions with an observational dataset. © 2020 The Authors. Published by Elsevier B.V. on behalf of Research Network of Computational and Structural Biotechnology.	COMPUTATIONAL AND STRUCTURAL BIOTECHNOLOGY JOURNAL Vol.18 Pages 93-99	10.1016/j.csbj.2019.12.001	31934310	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2393	H. D. Zhao, M. Liu, J. J. Yang, Y. Y. Chen and M. L. Fang	2023	Time-dependent metabolomics uncover dynamic metabolic adaptions in MCF-7 cells exposed to bisphenol A	The biochemical consequences induced by xenobiotic stress are fastened in dose-response and time-related landscapes. Understanding the dynamic process of cellular adaptations is crucial in conducting the risk assessment for chemical exposure. As one of the most phenotype-related omics, metabolomic in response to environmental stress can vary from seconds to days. Up to now, very few dynamic metabolomics studies had been conducted to provide time-dependent mechanistic interpretations in understanding xenobiotics-induced cellular adaptations. This study aims to explore the time-resolved metabolite dysregulation manner and pathway perturbation in MCF-7 cells exposed to BPA. Cells were collected at 6 time points (0.5, 1, 2, 4, 8, and 12 h) for LC-MS/MS analysis. Results showed that 1 mM BPA induced significant dysregulated metabolites were identified, ranging from amino acids, fatty acids, carbohydrates, and nucleotides/nucleotide phosphate compounds. The metabolites in different groups had similar metabolite dysregulation trends but different changing patterns, within those within the common class or same pathways showed similar and synchronized dysregulation behaviors. The pathway enrichment analysis suggested that porter metabolism, pyrimidine metabolism, and glycolysis/gluconeogenesis were significantly perturbed by BPA exposure. Moreover, the dynamic pathway perturbation revealed that BPA exposure induced time-dependent adaptations from cell proliferation to energy metabolism, which indicated an enhancing cellular requirement for elevated energy homeostasis, oxidative stress response and BPA alpha-metabolized cell growth. We further focused on the time-dependent metabolite dysregulation behavior in purine and pyrimidine metabolism, and identified the impaired glycolysis and oxidative phosphorylation by redox imbalance. Lastly, we established a restricted cubic spline-based model to fit and predict metabolite's full range dysregulation compactly, with metabolites' sensitivity components retrieved and novel biomarkers suggested. Overall, the results indicated that 0.1 nM to BPA exposure loaded to global dynamic metabolome adaptions including amino acid, nucleotide and sugar metabolism disorders, and the dysregulated metabolites with intertwined pathways at different stages and of significant temporal distinctions. (C) Higher Education Press 2023.	FRONTIERS OF ENVIRONMENTAL SCIENCE & ENGINEERING Vol.17 Issue 1	10.1007/s11783-023-1604-5	-	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2394	Z. Q. Zhang, M. Xiang, H. H. Yang, W. T. Guo, T. Bai, R. C. Huang, X. M. Zhang and L. L. Yang	2025	Exposure to phenols mixture, oxidative stress, and fasting blood glucose: Association and potential mediation analyses	Phenols exposure may affect glucose metabolism and increase the risk of type 2 diabetes (T2D). However, the underlying biological mechanisms were poorly understood. In this longitudinal panel study of 1223 Chinese adults with three repeated measurements, we aimed to evaluate the associations of multiple phenols exposure with fasting blood glucose (FBG), odds of impaired fasting glucose (IFG), odds of impaired fasting glucose (IFG) and T2D, and further assess the mediating role of oxidative stress in the above associations. FBG and urinary concentrations of 5 phenols and 3 oxidative stress biomarkers were repeatedly measured for each participant. Linear mixed-effect (LME) models were performed to assess the associations of phenols exposure with FBG and oxidative stress biomarkers. Generalized estimating equation (GEE) models were performed to assess the associations of phenols exposure with IFG and T2D. Bayesian kernel machine regression (BKMR) and quantile g-computation (qgcomp) models were implemented to assess the associations of phenols mixture with FBG and IFG/T2D. Mediation analyses were performed to estimate the proportion of the associations of phenols exposure with FBG and IFG/T2D that were mediated by oxidative stress biomarkers. In multiple log-trans exposure-biomarkers-associated with increased FBG and IFG/T2D. Exposure to phenols mixture at log-2 unit or log-3 by two models were marginally linked to increased FBG. No significant relationships of phenols exposure at different log-days with risk of IFG and T2D were observed. In addition, we found that 8-hydroxy-deoxyguanosine (8-OHdG) mediated 36.7 % of the association of urinary phenols mixture at log-1 day with FBG. Our study revealed that phenols exposure, either separately or as a mixture, was related to increased FBG, and oxidative stress is a potential mediating mechanism.	Free Radic Biol Med. 2025 Jul;234:169-177.	10.1016/j.freeradbiomed.2025.04.024	40253013	ヒト	代謝	-	-	-	-	-	-	panel study	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2395	Qingrong Li, Hongmin Zhang, Jun Zou, Xiang Feng, Dan Feng	2019	Bisphenol A induces cholesterol biosynthesis in HepG2 cells via SREBP-2/HMGCR signaling pathway	Bisphenol A (BPA), an environmental chemical to which humans are commonly exposed, has been shown in increase cholesterol level but the molecular mechanism is not clear. Three cholesterol biosynthesis genes as well as SREBP-2 were significantly induced by BPA in HepG2 cells. Moreover, BPA increased the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) and the intracellular cholesterol concentrations. Similar effects were observed when cells were treated with 17β-estradiol (E2). The concentrations of BPA to 20 %, the total cholesterol level and the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) were measured using commercial enzymatic assay kits, and the mRNA and protein expression levels of sterol regulatory element binding protein 2(SREBP-2) and HMGCR were analyzed by qPCR, Western blotting and immunofluorescence, respectively. After treating HepG2 cells with different concentrations (0.1 nM–10 μM) of BPA for 24 h, we found that BPA, at the environmentally relevant concentrations of 1 nM and 10 nM significantly increased the total cholesterol contents, the activity and expression of HMGCR in HepG2 cells, but at 100 nM–1 μM and 10 μM doses, BPA had no stimulatory effect on cholesterol biosynthesis. The whole data response relationship follows non-monotonic dose responses, such as an inverted U-shape. Moreover, BPA induced the translocation of SREBP-2 from the endoplasmic reticulum to the nucleus, which was blocked by the pharmacological inhibitor of SREBP-2 pathway. This study provides important implications for understanding the potential hazards of BPA exposure, and it also indicates that low dose BPA induces hepatic cholesterol biosynthesis through upregulating the SREBP-2/HMGCR signaling pathway. Keywords: 3-Hydroxy-3-methylglutaryl coenzyme A reductase; Bisphenol A; Cholesterol biosynthesis; HepG2 cells; Sterol regulatory element binding protein 2	J Toxicol Sci. 2019;44(7):481-491.	10.2131/jts.44.481	31270304	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	0.1 nM ～10 μM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2396	小林 澄貴, 宮下 ちひろ, 伊藤 佳樹子, 岸 玲子	2023	DOHaD, ライフコースアプローチに よる2040 に及ぶ 前向き出生 コホート研究の成果: 環境と子どもの健康に関する北海道スタディ	「環境と子どもの健康に関する北海道スタディ」(通称、北海道スタディ) は、フクシマからの手紙、環境中毒、強迫神経、女の人生の中で私たちの遺伝子は変わる コホート 日本北海道 コホート研究 北海道スタディ 胎児期 小児期 思春期 DOHaD ライフコースアプローチ 内分泌かく乱化学物質 環境ホルモン 化学物質 PFAS 有害化学物質 ダイオキシン 農薬 環境中毒 化学物質過敏症 アレルギー 喘息 アトピー性皮膚炎 免疫 甲状腺 脳 神経 発達障害 ASD ADHD 自閉スペクトラム症 知的障害 学習障害 LD 言語発達遅滞 運動発達遅滞 睡眠 生活リズム 肥満 体格 思春期 早発乳房発育 月経 初経 妊娠 出産 妊娠高血圧症候群 妊娠糖尿病 早産 低出生体重児 胎児発育不全 先天異常 先天性心疾患 口唇口蓋裂 尿道下裂 停留精巣 男性不妊 女性不妊 不妊治療 生殖補助医療 体外受精 顕微授精 精液所見 卵巣予備能 AMH 月経周期 子宮内膜症 子宮筋腫 多嚢胞性卵巣症候群 PCOS 乳がん 子宮がん 卵巣がん 甲状腺がん 前立腺がん 精巣がん 白血病 小児がん 脳腫瘍 神経芽腫 網膜芽細胞腫 肝芽腫 腎芽腫 ユーイング肉腫 骨肉腫 横紋筋肉腫 悪性リンパ腫 ホジキンリンパ腫 非ホジキンリンパ腫 バーキットリンパ腫 濾胞性リンパ腫 びまん性大細胞型B細胞リンパ腫 T細胞リンパ腫 NK細胞リンパ腫 多発性骨髄腫 形成不全貧血 再生不良性貧血 骨髄異形成症候群 MDS 急性骨髄性白血病 AML 急性リンパ性白血病 ALL 慢性骨髄性白血病 CML 慢性リンパ性白血病 CLL 真性多血症 本態性血小板血症 原発性骨髄線維症 PMF 血友病 フォン・ヴィルブランド病 血小板減少性紫斑病 ITP 血栓性血小板減少性紫斑病 TTP 溶血性尿毒症症候群 HUS 播種性血管内凝固症候群 DIC 血栓症 肺塞栓症 深部静脈血栓症 DVT 脳梗塞 脳出血 くも膜下出血 硬膜下血腫 硬膜外血腫 脳動脈瘤 脳動静脈奇形 もやもや病 てんかん 熱性けいれん 片頭痛 緊張型頭痛 群発頭痛 脳腫瘍 髄膜腫 神経膠腫 星細胞腫 乏突起膠腫 上衣腫 髄芽腫 頭蓋咽頭腫 下垂体腺腫 プロラクチノーマ 成長ホルモン産生腫瘍 クッシング病 アジソン病 原発性アルドステロン症 褐色細胞腫 パラガングリオーマ 甲状腺機能亢進症 バセドウ病 甲状腺機能低下症 橋本病 副甲状腺機能亢進症 副甲状腺機能低下症 骨粗鬆症 骨折 大腿骨近位部骨折 脊椎圧迫骨折 橈骨遠位端骨折 関節リウマチ 変形性関節症 変形性膝関節症 変形性股関節症 椎間板ヘルニア 脊柱管狭窄症 腰痛 頸肩腕症候群 線維筋痛症 全身性エリテマトーデス SLE 強皮症 シェーグレン症候群 皮膚筋炎 多発性筋炎 血管炎症候群 結節性多発動脈炎 顕微鏡的多発血管炎 好酸球性多発血管炎性肉芽腫症 ウェゲナー肉芽腫症 高安動脈炎 巨細胞性動脈炎 リウマチ性多発筋痛症 ベーチェット病 サルコイドーシス 炎症性腸疾患 クローン病 潰瘍性大腸炎 セリアック病 グルテン不耐症 乳糖不耐症 過敏性腸症候群 IBS 胃食道逆流症 GERD 胃潰瘍 十二指腸潰瘍 ピロリ菌 ヘリコバクター・ピロリ 肝炎 ウイルス性肝炎 A型肝炎 B型肝炎 C型肝炎 D型肝炎 E型肝炎 自己免疫性肝炎 原発性胆汁性胆管炎 PBC 原発性硬化性胆管炎 PSC 脂肪肝 非アルコール性脂肪性肝疾患 NAFLD 非アルコール性脂肪肝炎 NASH 肝硬変 肝細胞がん 胆管がん 膵炎 急性膵炎 慢性膵炎 膵がん 膵嚢胞 膵管内乳頭粘液性腫瘍 IPMN 膵神経内分泌腫瘍 膵島細胞腫瘍 インスリノーマ グルカゴノーマ ガストリノーマ VIPoma ソマトスタチノーマ 胆石症 胆嚢炎 胆管炎 胆嚢がん 胆管がん 腎不全 急性腎不全 慢性腎不全 腎臓病 糸球体腎炎 IgA腎症 膜性腎症 微小変化型ネフローゼ症候群 巣状分節性糸球体硬化症 FSGS 膜性増殖性糸球体腎炎 MPGN 急速進行性糸球体腎炎 RPGN 腎盂腎炎 膀胱炎 尿路感染症 UTI 腎結石 尿管結石 膀胱結石 尿路結石 腎がん 腎細胞がん 腎盂がん 尿管がん 膀胱がん 尿路上皮がん 前立腺がん 前立腺肥大症 BPH 過活動膀胱 OAB 尿失禁 腹圧性尿失禁 切迫性尿失禁 溢流性尿失禁 機能性尿失禁 尿閉 排尿障害 夜間頻尿 頻尿 尿意切迫感 残尿感 排尿痛 血尿 膿尿 蛋白尿 尿潜血 尿沈渣 尿検査 腎機能検査 eGFR クレアチニン 尿素窒素 BUN 尿酸 電解質異常 高ナトリウム血症 低ナトリウム血症 高カリウム血症 低カリウム血症 高カルシウム血症 低カルシウム血症 高リン血症 低リン血症 酸塩基平衡異常 代謝性アシドーシス 代謝性アルカローシス 呼吸性アシドーシス 呼吸性アルカローシス 脱水 浮腫 体液貯留 肥満 低体重 やせ 体格指数 BMI 体脂肪率 内臓脂肪 皮下脂肪 腹囲 ウエスト周囲径 ヒップ周囲径 ウエスト・ヒップ比 基礎代謝 エネルギー消費量 活動量 歩数 運動習慣 運動不足 座位時間 睡眠時間 睡眠の質 不眠症 入眠困難 中途覚醒 早朝覚醒 過眠症 日中眠気 昼寝 生活リズム 概日リズム 時差ぼけ シフトワーク 夜勤 交代勤務 ストレス 心理的ストレス 精神的ストレス 身体的ストレス 酸化ストレス 炎症 慢性炎症 急性炎症 免疫機能 免疫抑制 免疫賦活 自己抗体 抗核抗体 ANA 抗DNA抗体 抗ENA抗体 抗リン脂質抗体 抗カルジオリピン抗体 ループスアンチコアグラント 補体 補体価 CH50 C3 C4 C1q 免疫グロブリン IgG IgA IgM IgE IgD 血清蛋白 アルブミン 総蛋白 TP グロブリン 分画 α1 α2 β γ M蛋白 ベンスジョーンズ蛋白 クリオグロブリン 寒冷凝集素 温式自己免疫性溶血性貧血 寒冷凝集素症 発作性夜間ヘモグロビン尿症 PNH 溶血 黄疸 ビリルビン 直接ビリルビン 間接ビリルビン 尿ビリルビン 尿ウロビリノーゲン 便ウロビリノーゲン 便色 白色便 黒色便 タール便 下痢 便秘 便潜血 大腸ポリープ 大腸腺腫 家族性大腸腺腫症 FAP リンチ症候群 遺伝性非ポリポーシス大腸がん HNPCC 遺伝子変異 遺伝子多型 ゲノム ゲノム解析 全ゲノム解析 エクソーム解析 遺伝子検査 遺伝カウンセリング 遺伝子診断 出生前診断 新生児スクリーニング 先天代謝異常 フェニルケトン尿症 PKU メープルシロップ尿症 MSUD ホモシスチン尿症 ガラクトース血症 糖原病 ムコ多糖症 ライソゾーム病 ファブリー病 ゴーシェ病 ポンペ病 ニーマンピック病 テイサックス病 クラッベ病 副腎白質ジストロフィー ALD 異染性白質ジストロフィー 筋ジストロフィー デュシェンヌ型 ベッカー型 福山型先天性筋ジストロフィー 脊髄性筋萎縮症 SMA 筋萎縮性側索硬化症 ALS 多発性硬化症 MS 視神経脊髄炎 NMO 重症筋無力症 ランバート・イートン筋無力症候群 ギラン・バレー症候群 慢性炎症性脱髄性多発神経炎 CIDP 末梢神経障害 多発ニューロパチー 単ニューロパチー 手根管症候群 尺骨神経麻痺 橈骨神経麻痺 腓骨神経麻痺 顔面神経麻痺 ベル麻痺 三叉神経痛 舌咽神経痛 帯状疱疹 後遺症 ヘルペス 単純ヘルペス 水痘 風疹 麻疹 おたふくかぜ 伝染性単核球症 EBウイルス サイトメガロウイルス 結核 非結核性抗酸菌症 肺炎 気管支炎 喘息 COPD 肺気腫 慢性気管支炎 間質性肺炎 特発性肺線維症 IPF 肺塞栓症 肺高血圧症 睡眠時無呼吸症候群 SAS 閉塞性睡眠時無呼吸症候群 OSAS 中枢性睡眠時無呼吸症候群 CSAS 睡眠時低換気症候群 肥満低換気症候群 OHS 慢性閉塞性肺疾患 COPD 気管支喘息 アレルギー性鼻炎 花粉症 通年性アレルギー性鼻炎 アレルギー性結膜炎 春季カタル アトピー性皮膚炎 蕁麻疹 じんましん 血管性浮腫 アナフィラキシー 薬物アレルギー 食物アレルギー 金属アレルギー ラテックスアレルギー 接触皮膚炎 かぶれ 乾癬 白癬 カンジダ症 疥癬 毛嚢炎 せつ 蜂窩織炎 丹毒 壊死性筋膜炎 ガス壊疽 敗血症 菌血症 ウイルス血症 真菌症 寄生虫症 マラリア 住血吸虫症 エキノコックス症 トキソプラズマ症 クリプトスポリジウム症 ジアルジア症 赤痢アメーバ症 腸管出血性大腸菌感染症 O157 サルモネラ腸炎 カンピロバクター腸炎 ノロウイルス ロタウイルス アデノウイルス 腸炎ビブリオ 黄色ブドウ球菌 セレウス菌 ボツリヌス症 破傷風 ジフテリア 百日咳 髄膜炎菌感染症 肺炎球菌感染症 インフルエンザ菌感染症 溶連菌感染症 A群溶血性レンサ球菌 B群溶血性レンサ球菌 緑色レンサ球菌 腸球菌感染症 MRSA VRE 多剤耐性菌 院内感染 市中感染 日和見感染 ウイルス感染症 細菌感染症 真菌感染症 寄生虫感染症 プリオン病 クロイツフェルト・ヤコブ病 狂犬病 ボルナ病 ヒトパルボウイルスB19感染症 伝染性紅斑 リンゴ病 突発性発疹 ヒトヘルペスウイルス6型感染症 ヒトヘルペスウイルス7型感染症 カポジ肉腫 ヒトヘルペスウイルス8型感染症 ヒトT細胞白血病ウイルス1型感染症 ATL HTLV-1関連脊髄症 HAM ヒト免疫不全ウイルス感染症 HIV エイズ AIDS 日和見感染症 カリニ肺炎 ニューモシスチス肺炎 トキソプラズマ脳症 カポジ肉腫 悪性リンパ腫 子宮頸がん ヒトパピローマウイルス HPV 尖圭コンジローマ 性感染症 STD 梅毒 淋菌感染症 クラミジア感染症 性器ヘルペス 尖圭コンジローマ 軟性下疳 鼠径リンパ肉芽腫 トリコモナス症 膣カンジダ症 細菌性膣症 バクテリアルバギノーシス 骨盤内炎症性疾患 PID 子宮内膜炎 子宮頸管炎 卵管炎 卵巣炎 骨盤腹膜炎 Fitz-Hugh-Curtis症候群	DOHaD研究2023年 11 巻 2 号 63-95	10.51057/dohad.11.2_63	-	ヒト	一般毒性	-	-	-	-	-	-	総説	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2397	Tetsuya FUJIMOTO, Hiroshi INOUE, Shun-ichiro HIRANO, Seiji GODA	2019	Effect of bisphenol A exposure on spontaneous behavior using the elevated plus maze test	The elevated plus maze (EPM) test is widely used with experimental animals to evaluate anxiety, which is most often indicated by the open - arm staying time. However, little attention has been focused on general behavioral parameters, such as locomotor activity and rearing, in the EPM test. Therefore, we investigated the effects of bisphenol A (BPA) exposure on these behavioral parameters in the EPM test. There is also no evidence revealed if bisphenol A (BPA), which is an endocrine - disrupting chemical, can induced anxiety-like behavior in the mouse EPM test. Therefore, we investigated significant differences in all parameters between the two

通毒性評価（動物）1：該当、0：該当しない　　通毒性評価（疫学）1：該当、0：該当しない　　通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成段階で評価へ進め、当該物質評価段階で原著に基づき精査。

利用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物飼及び水基礎の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2399	Takahiro Sasaki, Hirokatsu Saito, Yusuke Furukawa, Takeshi Tominaga, Satoshi Kitajima, Jun Kanno, Kentaro Takemura	2023	Exposure to bisphenol A or its phenolic analogs during early life induces different types of anxiety-like behaviors after maturity in male mice	Products used in daily life contain multiple chemicals capable of inducing endocrine disruption in animals, including humans. One such typical substance is bisphenol A (BPA). BPA has been widely used in epoxy resins and polycarbonate plastics and can exert several adverse effects. Furthermore, given their structural similarity to BPA, phenolic analogs of BPA, i.e., synthetic phenolic antioxidants (SPAs), are considered to exhibit similar adverse effects to BPA. In this study, we investigated the effects of BPA or the phenolic analogs 2,6-di-tert-butyl-4-methylphenol (BHT) and 2,6-di-tert-butyl-4-ethylphenol (BHT-C) on BPA and two advanced SPAs, 4,4′-butylidenebis (6-tert-butyl-m-cresol) (BBM) and 2,2′-methylenebis (6-tert-butyl-p-cresol) (AM). We exposed mice in two tests of these chemicals through drinking water during prenatal and postnatal periods. Subsequently, we examined the adverse effects of these chemicals on the central nervous system using a mouse behavioral test battery, comprising the open field test, light/dark transition test, elevated plus maze test, conditioned/unconditioned fear conditioning test, and prepulse inhibition test, at 12–15 weeks old. Based on the behavioral analysis, SPAs, like BPA, may cause affective disorders even at low doses, although significant differences were noted in anxiety-related behaviors. In conclusion, our findings could be valuable for clarifying the potential adverse developmental risks of SPA exposure in early life. Keywords: Central nervous system; Developmental neurotoxicity; Endocrine-disrupting chemicals; Neurobehavioral effects	The Journal of Toxicological Sciences2023年 48 巻 4 号 211-219	10.2131/jts.48.211	37005279	動物	-	1	1	1	1	0	500 μg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2400	Haiou Wang, Yan Li, Chuang Liu, Tianxiang Lu, Qian Zhai, Hongna Wang, Jianfang Zhang	2023	Inhibition of VDAC1 prevents oxidative stress and apoptosis induced by bisphenol A in spermatogonia via AMPK/mTOR signaling pathway	Bisphenol A (BPA), one of the main components of industrial products, is clinically associated with the increased male infertility rate. However, the underlying molecular mechanism of the BPA-resulted reproductive toxicity is not fully elucidated. Voltage-dependent anion channel 1 (VDAC1) is a pore protein and located at the outer mitochondrial membrane. As a mitochondrial gatekeeper, VDAC1 controls the release of most the mitochondrial metabolites. Nevertheless, the potential role of VDAC1 in BPA-induced spermatogonia damage remains unclear. In this study, we found that BPA induced oxidative stress and apoptosis in spermatogonia. The results showed that BPA increased spermatogonia cell line GC-1 spg cell apoptosis and intracellular ROS level, and suppressed AMPK/mTOR signaling pathway at a dose of 50 μM for 48 h. Luciferase-mediated short hairpin RNA targeting VDAC1 (i.e.shVDAC1) silenced VDAC1 expression and enhanced BPA-restricted cell viability. Knockdown of VDAC1 inhibited the apoptosis of BPA-treated GC-1 spg cells determined by cell cytometry. Moreover, silenced VDAC1 decreased the BPA-induced intracellular ROS generation and oxidative stress. Meanwhile, silenced VDAC1 also alleviated the BPA-triggered mitochondrial ROS generation and oxidative stress. Moreover, silenced VDAC1 increased AMPK α1 Ser5 phosphorylation and suppressed mTOR phosphorylation under BPA exposure. Concomitantly, an AMPK inhibitor, partially abolished the effects of VDAC1 gene silencing on BPA-stimulated GC-1 spg cells. In conclusion, inhibition of VDAC1 attenuated the BPA-induced oxidative stress and apoptosis and promoted the cell viability in spermatogonia through mediating AMPK/mTOR signaling pathway. Keywords: AMPK/mTOR signaling pathway; Apoptosis; Oxidative stress; Spermatogonia; Voltage-dependent anion channel 1.	The Journal of Toxicological Sciences2023年 48 巻 3 号 109-119	10.2131/jts.48.109	36858637	in vitro	-	-	-	-	-	1	0	20, 40, 80 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2401	Jing Chen, Shiori Mitatte, Arisa Munetomo, Fumie Magata, Marimo Sato, Sho Nakamura, Masumi Hirabayashi, Yasuhiro Ishihara, Takeshi Yamazaki, Yoshihisa Uenoyama, Hiroko Tsukamura, Fuko Matsuda	2022	Kiss1-dependent and independent release of luteinizing hormone and testosterone in perinatal male rats	Prenatal and postnatal biphasic increases in plasma testosterone levels derived from perinatal testes are considered critical for determining masculinizing the brain mechanism that regulates sexual behavior in male rats. Hypothalamic kisspeptin neurons are indispensable for stimulating GnRH and downstream gonadotropin, as well as the consequent testicular testosterone production/release in adult male rats. However, it is unknown whether kisspeptin neurons are involved in the perinatal testicular activity. Here, we found that the kisspeptin system is not necessary for the perinatal testicular activity for subsequent testosterone increase in male rats by comparing the plasma testosterone and LH profiles of wild-type (Kiss1+/+) and Kiss1 knockout (Kiss1−/−) male rats. Perinatal patterns of plasma testosterone levels, with peaks in the prenatal and postnatal periods, was found in both Kiss1+/+ and Kiss1−/− male rats. Postnatal plasma testosterone and LH levels were significantly lower in Kiss1−/− male rats than in Kiss1+/+ male rats, whereas the levels in the prenatal testicular period were comparable between the two genotypes. Kisspeptin/kisspeptin challenge significantly increased plasma testosterone and LH levels and the number of c-Fos immunoreactive GnRH neurons in neonatal Kiss1−/− and Kiss1+/+ male rats. Kiss1 and Gpr54 (kisspeptin receptor gene) were found in the testes of neonatal rats, but kisspeptin treatment failed to stimulate testosterone release in the cultured testes of both genotypes. These findings suggest that perinatal, but not prenatal, testosterone increase in male rats is mainly induced by central kisspeptin-dependent stimulation of GnRH and consequent LH release. Keywords: Hypothalamic-pituitary-gonadal axis; Kisspeptin; Perinatal testosterone surge; Testes.	Endocrine Journal2022年 69 巻 7 号 797-807	10.1507/endocrj.EJ21-0620	35125377	動物	-	1	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2402	Kaori Kiso-Farmi, Takeshi Yagi, Takahiro Fujimoto, Kyoko Ito	2022	Low Doses of Bisphenol A Disrupt Neuronal Differentiation of Human Neuronal Stem/Progenitor Cells	Bisphenol A (BPA) is an endocrine-disrupting chemical. Human epidemiological studies have suggested that adverse neurobehavioral outcomes are induced by fetal exposure to BPA. The remarkable differences in the corticogenesis between human and agonistically mammals are an increase in the intermediate progenitor cells (IPCs) and a thickening increase in the subplate in the cortex. It is unclear whether low doses of BPA (low-BPA) affect human-only corticogenesis-interbasal progenitor cells (IBPs) produce IPCs resulting in amplified neurogenesis. In this study, human-derived neuronal stem/progenitor cells were exposed to low-BPA in the vehicle only, and the mutated cell type-specific molecular changes and morphology were analyzed. We found that low-dose cells immunoreactive for EOMES (IPCs and IBPs), and fewer neurons for DCX. EOMES-positive cells significantly decreased at day in vitro (DIV) 5 and 7, whereas Ki67-positive cells tended to be higher, while DCX-positive cells significantly increased at DIV7 when exposed to 100 nM of BPA compared with the vehicle. These results suggest that low-BPA exposure may affect human neurogenesis. The increase in multipolar cells at DIV7 when exposed to 100 nM of BPA compared with the vehicle. These results provide insights into the in vitro effect of low-BPA on neuronal differentiation in the human fetal cerebral cortex. Keywords: Bisphenol A (BPA); corticogenesis; differentiation; endocrine-disrupting chemicals; neural stem/progenitor cells.	Acta Histochem Cytochem. 2022 Dec 28;55(6):193-202.	10.1267/ahc.22-00090	36688137	in vitro	-	-	-	-	-	1	0	0.1, 1, 10 and 100 nM	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2403	Munekazu Komada, Tetsuji Nagao, Nao Kagawa	2020	Prenatal and postnatal bisphenol A exposure inhibits postnatal neurogenesis in the hippocampal dentate gyrus	Bisphenol A (BPA), an endocrine disruptor with estrogenic effects, is widely used as a raw material for manufacturing polycarbonate plastic and epoxy resins. Prenatal and postnatal exposure to BPA affects brain morphogenesis. However, the effects of prenatal and postnatal BPA exposure on postnatal neurogenesis in mice are poorly understood. In this study, we developed a mouse model of prenatal and postnatal BPA exposure and analyzed its effects on hippocampal neurogenesis. The hippocampal dentate gyrus is one of the regions in which neurogenesis continues in the region even after birth. It is also known that in mice, prenatal and postnatal BPA exposure decreased the number of type 1, 2a, 2b, and 3 neural progenitor cells, as well as in granule cells, in the hippocampal dentate gyrus on postnatal days 14 and 70. The effect of prenatal BPA exposure on the number of granule cells disappeared on postnatal day 70, whereas that of postnatal BPA exposure remained. In addition, prenatal and postnatal BPA exposure affects the expression of drug transporters on postnatal day 70. Our results suggest that neurodevelopmental toxicity due to prenatal and postnatal BPA exposure might affect postnatal neurogenesis and functional development of the hippocampal dentate gyrus. Keywords: Bisphenol A; Dentate gyrus; Granule cells; Neural stem cells; Neurogenesis.	J Toxicol Sci. 2020;45(10):639-650.	10.2131/jts.45.639	33012732	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2404	Yang Ling, Zhang Qiongqiu, Cui Maosheng, Zhang Leying, Ma Yong	2024	Effects of bisphenol A and taurourodeoxycholic acid on maturation of porcine oocytes and parthenogenetic development of embryos	Prolonged exposure of bisphenol A (BPA) has adverse effects on in vitro maturation (IVM) of oocytes, but treatment with tauroursodeoxycholic acid (TUDCA) can improve the IVM and development of embryos. The purpose of this study was to investigate the effects of BPA and both BPA and TUDCA on IVM and parthenogenetic development of embryos. The results showed that BPA treatment exerted adverse effects on the cumulus expansion index, survival rate, polar body rate, mitochondrial distribution of the oocytes after maturation culture, and that it also decreased the cleavage rate and blastocyst rate of embryos after parthenogenetic development. In addition, BPA treatment upregulated expression of genes related to metaphase-to-anaphase transition, cell apoptosis, and decreased the expression of genes related to maintenance of meiotic arrest, cumulus expansion. However, the supplementation of TUDCA relieved these adverse effects of BPA except polar body rate, blastocyst rate, and expression of BCL-2 and PTGS2. In conclusion, the supplementation of TUDCA could alleviate the adverse effects of BPA exposure on the parthenogenetic development of embryos, possibly by modification of the expression of genes related to metaphase-to-anaphase transition, cumulus expansion, and cumulus expansion, intracellular ROS level, and mitochondrial distribution.	Anim Sci J. 2024 Jan-Dec;95(1):e13966.	10.1111/asj.13966	38845341	in vitro	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2405	Dagdeviren Gulcan, Arslan Burak, Kelles Ayse, Celik Duygu Yuecel, Anal Ozoguz, Caglar Ali Turhan	2023	The evaluation of serum bisphenol A in patients with preeclampsia	Aims: High bisphenol A (BPA) concentration may compromise normal placental development. The aim of this study was to determine maternal serum BPA concentrations in pregnant women with complicated preeclampsia (PE) and normal pregnant women, to compare BPA concentrations, and to examine pregnancy outcomes. Methods: This prospective case-control study was conducted between March 2021 and October 2021. Serum BPA levels of preeclamptic pregnancy and normal pregnancy were statistically evaluated. In addition, the PE groups was divided into three subgroups according to the course of pregnancy. Group 1: patients with non-severe PE who delivered at 37 weeks or later, Group 2: patients with severe PE who delivered at less than 34 weeks, Group 3: patients with severe PE who delivered between 34 and 37 weeks. The association between BPA levels and pregnancy outcome was investigated. Results: Forty-six cases in the PE group were compared with 46 cases of normal pregnancies. The median BPA level was 35.86 ng/mL in the PE group and 28.34 ng/mL in the control group. The median BPA levels in the PE group were significantly higher than those in the control group (p = 0.007). Serum BPA levels were significantly lower in women who delivered at 37 weeks or later than in women who delivered at less than 34 weeks due to severe PE (p = 0.001). Conclusion: Our study highlights the association between elevated maternal serum levels of BPA and PE. Moreover, knowledge of BPA levels in women with PE may provide information about the prognosis of pregnancy. Keywords: bisphenol A; non-severe preeclampsia; severe preeclampsia.	J Obstet Gynaecol Res. 2023 May;49(5):1322-1327.	10.1111/jog.15616	36806798	ヒト	生殖発生	-	-	-	-	-	-	症例対照	1	1	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2406	Tosiriuk Naruporn, Sakorn Natee, Jartsiri Chutima, Nasongmoon Wichit, Anonpakornkul Supitsara, Supornsilchai Vichit	2022	Increased bisphenol A levels in Thai children and adolescents with type 1 diabetes mellitus	Background: The incidence of type 1 diabetes mellitus (T1DM) in children and adolescents continues to increase worldwide. The reason for this is unclear. In addition to the role of genetics, Bisphenol A (BPA) has been investigated as a possible causal factor for T1DM. This study aimed to determine the correlation between urinary BPA levels and T1DM in Thai children and adolescents. Methods: A cross-sectional study was conducted in T1DM patients who were followed at the endocrinology clinic at King Chulalongkorn Memorial Hospital from December 2018 to December 2019 and age-matched healthy controls. The urinary BPA concentrations were measured by high-performance liquid chromatography (HPLC) with fluorescence detection. Clinical data were collected from the T1DM patients. All participants completed a questionnaire regarding possible BPA exposure. Multivariate logistic regression analysis was used to examine the adjusted odds ratio for T1DM. Results: Seventy-five T1DM patients and 113 age-matched controls were included in the study. The mean age for T1DM and control groups were 11.8 ± 4.7 and 11.5 ± 4.2 years, respectively. The T1DM group had a significantly higher median (interquartile range) level of adjusted urinary BPA compared to the control (11.82 [7.81, 18.07] vs. 10.2 [6.10, 16.82] μg/g creatinine, P = 0.022). Urinary BPA of 17 μg/g creatinine or more was significantly associated with T1DM, with adjusted odds ratio (95% Confidence interval, CI) of 2.38 (1.21, 4.66), P = 0.006. Conclusions: Higher urinary BPA level is one of the possible risk factors for T1DM. Keywords: bisphenol A (BPA); high-performance liquid chromatography (HPLC); type 1 diabetes mellitus (T1DM).	Source：Pediatrics International(Print)(1328-8067)64巻1号 Page ped.14944	10.1111/ped.14944	34342913	ヒト	-	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2407	Sugiyama Kei-ichi, Kinoshita Mawo, Cruz Pete, Kasamatsu Toshio, Honma Masamitsu	2022	Bisphenol-A reduces DNA methylation after metabolic activation	Bisphenol-A (BPA) is an important environmental contaminant with adverse health effects suspected to be mediated through epigenetic mechanisms. We had reported that the FLCD dependent flocculation of transgenic yeast expressing human DNA methyltransferase (DNMT) and S-a useful tool in toxicological bioassay studies. In this report, we have investigated the effects of BPA in the presence of metabolic activation (S-9 mix) on the transcription level of the FLCD gene in the DNMT yeast. In the presence of metabolic activation, BPA inhibited the intensity of green fluorescence reporter protein (GFP) driven by the FLCD promoter. A metabolite of BPA (1-methyl-2,2-bis(p-hydroxyphenyl)ethene-1-one (MBP)), also exhibited similar inhibitory effect. Furthermore, BPA in the presence of S-9 mix had only a weak anti-MBP factor inhibitory effect on the expression of modified GFP reporter gene under the control of FLCD promoter with reduced CpG motifs. Aforementioned behavior was confirmed by the inhibition of flocculation as well as FLCD gene mRNA expression. In addition, the global DNA methylation level in the former (WT/B) cells was also reduced by MBP. These results indicate that BPA-metabolites have inhibitory effect on DNA methylation. Our approach offers a novel in vitro method for screening for chemicals that can alter the epigenome by a mechanism dependent on their metabolic activation.	Genes and Environment,2022,Vol44 ,Issue1,No.20	10.1186/s41021-022-00249-y	35879744	in vitro	-	-	-	-	-	1	0	2.5～40 μM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2408	Hirao-Suzuki Masayo, Nagase Keita, Suemori Tetsuya, Tsutsumi Kana, Shigemori Epo, Tanaka Michitaka, Takiguchi Masafumi, Sugihara Naruki, Yoshitake Shin'ichi, Takeda Shuko Source：Biological & Pharmaceutical Bulletin(0918-6158)44巻10号 Page1524-1529(2021.10)	2021	4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene(MBP)はエストロゲン受容体βを標的として、Gタンパク質共役型エストロゲン受容体1アゴニストであるG-1に対するヒト乳腺MCF-7細胞の耐性を誘導する	ビスフェノールA(BPA)の活性化型代謝物であるMBPが、ERαを特異的に活性化するヒト乳腺細胞株MCF-7細胞におけるアゴニスト受容体型エストロゲン受容体GPERの活性に及ぼす影響について検討した。最低24時間のMBP曝露で全細胞増殖を誘導することにより、細胞がアロマターゼ・インヒビターとICI182780（ERαを特異的に阻害するアンタゴニスト）のいずれかに対して耐性を獲得することを示唆した。MBP曝露細胞における増殖は、GPER特異的アゴニストであるG-1の場合とは異なり、ICI182780の影響を受けなかった。GPERおよびERαの発現レベルは、MBP曝露細胞とG-1曝露細胞間で大きく異なっていなかった。MBPによるGPER発現増強では細胞増殖が誘導されないことから、MBPによるGPER発現増強は細胞増殖に関与していないと示唆された。	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2409	Khair Jasmine, Kadir Siti Hamimah Binti Shaikh Abdul, Zuki Wan Nor Ezzeh Wan Mohamad, Kamalludin Rusliana, Rasid Zaidhathak, Rahman Amirah Abdul	2021	Effect of Bisphenol-A on the Morphology of Small Intestine in Pregnant Rats	環境内分泌撹乱化学物質ビスフェノールA(以後BPA)は毒性が強く、その分泌は妊娠中の胎仔発育への影響が懸念されている。また、メタボリックシンドロームの一因であるPPARγ（ペルオキシソーム増殖剤活性化受容体ガンマ）の活性化については、BPAがPPARγに結合し活性化するとの報告がある。そこで、妊娠ラットにBPAを投与し、PPARγアゴニストであるピオグリタゾン（PIO）を同時に投与することで、BPAの影響が軽減されるかを検討した。妊娠ラットを4群に分け、BPA（0.5mg/kg/day）、PIO（10mg/kg/day）、BPA+PIO、コントロールとし、妊娠20日目に安楽死させた。小腸を採取し、組織学的に観察した。BPA投与群では、絨毛の萎縮と上皮細胞の変性・壊死が観察された。PIO投与群では、絨毛の萎縮、変性・壊死は観察されなかった。BPA+PIO投与群では、BPA投与群と同様の絨毛の萎縮、変性・壊死が観察された。以上の結果から、BPAは妊娠ラットの小腸絨毛に対して毒性を示すことが明らかとなった。また、PIOはBPAの毒性を軽減することが明らかとなった。PIOはPPARγアゴニストであることから、BPAの毒性にPPARγの活性化が関与していることが示唆された。	International Medical Journal(1341-2051)28巻2号 Page141-144	-	-	-	動物	-	1	1	1	1	0	単純投 (0.2mg/ml/匹/日)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2410	河村 勝之, 川端 仁, 前田 豊信, 堀井 和恵	2021	Bisphenol-AがNIH/3T3細胞に及ぼす影響	出発物質の違いによって、ウレタンプラットゥ変異に関与する様々なプレポリマーとポリオールが合成されるためにさまざまな物性を有するエラストマーが開発されている。スチレン-ブタジエンゴム（SBR）とアクリロニトリル-ブタジエンゴム（NBR）は、ポリマー主鎖にブタジエンを含むエラストマーであり、ポリマー主鎖にブタジエンを含むエラストマーは、ポリマー主鎖にブタジエンを含まないエラストマーに比べて耐候性が劣ることが知られている。SBRやNBRの耐候性を向上させるために、ポリマー主鎖にブタジエンを含まないエラストマーを用いたブレンドが検討されている。しかしながら、ポリマー主鎖にブタジエンを含まないエラストマーを用いたブレンドでは、ポリマー主鎖にブタジエンを含むエラストマーに比べて、耐候性が向上するものの、耐候性が十分ではないという問題があった。そこで、ポリマー主鎖に含まれるブタジエンの量を減らすことで、耐候性が向上するのではないかと考えた。そこで、ポリマー主鎖にブタジエンを含まないエラストマーであるEPDMとSBRやNBRとのブレンドを検討した。その結果、EPDMとSBRやNBRとのブレンドでは、EPDMとNBRとのブレンドに比べて、耐候性が向上することが明らかとなった。	東京大学農学部(0916-2313)48巻1-2号 Page1-13	-	-	-	in vitro	-	-	-	-	-	1	0	1×10⁻⁶M、1×10⁻⁵M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2411	Kobayashi Yukino, Oguro Aimi, Yagi Eiisa, Mitani Akira, Kudoh Suguru N., Imaoka Susumu	2020	Bisphenol A and rotenone induce S-nitrosylation of protein disulfide isomerase (PDI) and inhibit neurite outgrowth of primary cultured cells of the rat hippocampus and PC12 cells	Bisphenol A (BPA) interferes the function and development of the central nervous system (CNS), resulting in behavioral abnormalities and memory loss. S-nitrosylation of protein disulfide isomerase (PDI) is increased in the brains of patients with neurodegenerative diseases and is involved in neurodegeneration through S-nitrosylation of PDI. In this study, we investigated the effects of BPA on S-nitrosylation of PDI and neurite outgrowth in neurodegeneration through S-nitrosylation of PDI. S-nor used as a positive control. First, rats were treated with BPA and rotenone, and S-nitrosylation of PDI was detected in rat brain microsomes. BPA and rotenone decreased Mitotest oxidative activity of PDI concentration-and S-nitrosylation of PDI. Next, to clarify S-nitrosylation of PDI by BPA and rotenone in rat brains, we treated the rat pheochromocytoma cell line PC12 and primary cultured neurons cells from the rat hippocampus with BPA (5 and 10 μM) and rotenone (100 or 200 nM). BPA induced S-nitrosylation of PDI, while NO-mononitrite 1 arginine (L-NMMA), a NOS inhibitor, exerted the opposite effects. Finally, to evaluate the toxicity of BPA in the CNS, we investigated its effects on neurite outgrowth of PC12 and primary cultured neuron cells. BPA inhibited neurite outgrowth of these cells, while L-NMMA and rotenone did not affect neurite outgrowth. Furthermore, BPA-induced inhibition of neurite outgrowth was recovered by L-NMMA and rotenone. The overexpression of PDI is not a statistically inactive PDI mutant, enhanced neurite outgrowth. These results suggested that S-nitrosylation of PDI induced by exposure to NO caused BPA-induced neurotoxicity. Keywords: Bisphenol A; Neurite outgrowth; Protein disulfide isomerase; Rotenone; S-nitrosylation.	The Journal of Toxicological Sciences(0388-1350)45巻10-12号 Page783-794	10.2131/jts.45.783	33268678	動物	-	1	0	1	1	0	100 mg/kg/day	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2412	Kagawa Nao, Nagao Tetsuji	2020	Maternal administration of bisphenol A alters the microglial profile in the neocortex of mouse weanlings	Bisphenol A (BPA) is known to cause abnormal neurogenesis in the developing neocortex. The mechanisms of BPA toxicity concerning neuroinflammatory related endpoints are incompletely characterized. To evaluate the microglial morphology and the gene expression of pro- and anti-inflammatory cytokines in the developing neocortex, ICR mice were exposed to BPA (0.06 μg/kg/d or 60 μg/kg/d) in the drinking water from embryonic day 15 (E15) through lactation period (postnatal day 21 (P21)). Microglia in the developing neocortex were immunostained and the microglial morphology was analyzed by using the Sholl analysis. Quantitative real-time PCR was performed to measure the mRNA levels of pro-inflammatory cytokines (Il1b, Il6, Tnf) and anti-inflammatory cytokines (Il4, Il10, Tgfb1) in the neocortex. BPA exposure significantly increased the number of intersections and the number of primary processes of microglia at P21. These findings suggest that the low-dose BPA exposure during lactation period induces morphological alterations of microglia in the developing neocortex of mouse weanlings. Because microglia play a crucial role in the development of neural circuits, the present results suggest that BPA may be related to an increased risk of neurodevelopmental disorders. Moreover, the present study suggests that the low-dose BPA exposure during lactation period may affect the microglial function in the developing neocortex. These findings suggest

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2424	Jenkins S et al.	2011	Chronic oral exposure to Bisphenol A results in a nonmonotonic dose response in mammary carcinogenesis and metastasis in mmtv-erbb2 mice	BACKGROUND: Bisphenol A (BPA) is a synthetic compound used to produce plastics and epoxy resins. BPA can leach from these products in appreciable amounts, resulting in nearly ubiquitous daily exposure to humans. Whether BPA is harmful to humans, especially when administered orally in concentrations relevant to humans, is a topic of debate. OBJECTIVES: In this study, we investigated the role of chronic oral exposure to BPA in the development and progression of mammary carcinogenesis and metastasis in mmtv-erbb2 mice. METHODS: Female mmtv-erbb2 mice (FVB/N background; n = 10-15/group) and their MMTV-erbB2 mice were exposed to 0, 25, 250, or 2,500 μg BPA/L drinking water from 8 wk until 122 days of age (for mechanisms of action) or 250 days of age (for carcinogenesis). Cellular and molecular mechanisms of BPA action in the mammary gland were investigated via immunohistochemistry and immunoblotting. RESULTS: Only low doses of BPA significantly decreased tumor latency and increased tumor multiplicity. Some (but not all) low-dose BPA responses, including phosphorylation of erbB2, erbB3, insulin-like growth factor 1 receptor, and Akt in the mammary gland, SRC3/NCOA3-1 co, but not Agt, BPA doses significantly accelerated mammary carcinogenesis and metastasis in MMTV-erbB2 mice. The combined ratio of cell proliferation and apoptosis indices and alterations in protein expression best predicted the ability of each dose of BPA to alter	Environ Health Perspect. 2011 Nov;119(11):1604-9.	10.1289/ehp.1103850	21988766	動物	発がん(乳がん)	1	1	1	———————	4用量：1	0.0.5,50,500 μg/kg/体重・1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	●	-	-	-	-	-	-
統合_2425	Jones BA et al.	2011	Pre- and postnatal bisphenol A treatment results in persistent deficits in the sexual behavior of male rats, but not female rats, in adulthood	Perinatal administration of the endocrine disruptor bisphenol A (BPA) reportedly inhibits the sexual behavior of sexually naive adult male rats. In order to evaluate the effects of BPA administration during early development on the subsequent sexual behavior of adult male and female rats, Sprague-Dawley rats were administered BPA (0, 2.4, 24, or 240 mg/kg/day) via their mothers' drinking water throughout pregnancy and lactation. Treatment with BPA resulted in dose-dependent deficits in the sexual behavior of adulthood. Male rats receiving the highest dose (5 mg/kg bw/day), however, were indistinguishable from controls with respect to consummatory sexual behaviors but showed decreased latencies to engage in those behaviors when sexually naive. Only a significant main linear, n.s. inkazoid, dose-response relationships observed on the first and last day of testing. Adult female sexual behavior was not affected by early BPA administration at any dose tested. These results are consistent with previous reports that BPA exerts behavioral effects especially at low doses, and further indicates that BPA can cause lasting impairment of sexual behavior in males, but does not alter the normal sexual behavior or appetitive or consummatory sexual behaviors. To our knowledge, this is the first report indicating that adult sexual performance is impaired in sexually experienced animals following perinatal exposure to bisphenol A.	Horm Behav. 2011 Feb;59(2):246-51.	10.1016/j.yhbeh.2010.12.006	21185296	動物	発達神経毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	1	-	-	●	-	●	-	-	-	-
統合_2426	Jones BA and Watson NV	2012	Perinatal BPA exposure demasculinizes males in measures of affect but has no effect on water maze learning in adulthood	Bisphenol A (BPA) is an endocrine disrupting agent that can alter the normal gonadal steroid-sensitive sexual differentiation of the brain and behavior. While reproductive behavior and physiology are known to be altered by perinatal exposure to this compound, less is known about BPA's effects on sex differences in learning and measures of affect. In order to evaluate the effects of perinatal BPA treatment on learning and affect in adulthood, we exposed rats to one of five doses of BPA through gestation and lactation then examined adult behavior in the Morris Water Maze (MWM), the Elevated Zero Maze (EZM), and the Forced Swim Test (FST). No effect of BPA was observed in the MWM, but on both the EZM and FST, low doses (5 mcg/kg) of BPA eliminated sex differences found between controls. Furthermore, a non-monotonic dose response observed in previous studies was confirmed for these tasks. Overall, our study adds to the growing data suggesting that BPA interferes with the normal development of affective behaviors in a non-linear, dose-dependent manner.	Horm Behav. 2012 Apr;61(4):605-10.	10.1016/j.yhbeh.2012.02.011	22370244	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	1	-	-	●	-	●	-	-	-	-
統合_2427	Kim ME et al.	2011	Exposure to bisphenol A appears to impair hippocampal neurogenesis and spatial learning and memory	Bisphenol A (BPA) is widely used in the manufacture of plastics and epoxy resins, and is known to affect reproductive organ growth and development. However, the effects of BPA on hippocampal neurogenesis are unclear in young adult mice. Therefore, the present study was conducted to examine the effects of BPA on hippocampal neurogenesis and learning as well as memory performance in young adult mice. BPA (0, 5, and 20 mg/kg/day) was administered orally to mice for 3 weeks. It was found that high-dose BPA (20 mg/kg/day) decreased the number of newly generated cells in hippocampus, but low-dose BPA (5 mg/kg) increased the number of newly generated cells in hippocampus of young mice. Furthermore, high-dose BPA (20mg/kg/day) was found to impair learning and memory performance significantly. However, no significant differences were found between the control group and the low-dose BPA (5 mg/kg/day) group. Taken together, these results suggest that exposure to high-dose BPA may cause a decrease in hippocampal neurogenesis, which may result in loss or damage or astrocyte activation. These data suggest that exposure to BPA causes fluctuations in hippocampal neurogenesis in young adult mice that result in spatial learning and memory impairment via a BDNF-independent pathway.	Food Chem Toxicol. 2011 Dec;49(12):3383-9.	10.1016/j.fct.2011.09.017	21959526	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	1	-	-	●	-	-	-	-	●	-
統合_2428	Kobayashi et al.	2010	Dietary exposure to low doses of bisphenol A: effects on reproduction and development in two generations of C57BL/6J mice	The present study was conducted to examine the effects of low-dose exposure to bisphenol A on reproduction and development in two generations of mice. Pregnant female C57BL/6J mice (F0) were fed a diet containing low doses of BPA (0, 0.33, 3.3, or 33 ppm) from gestational day (GD) 0 through weaning (F1). Female F1 mice were fed a diet containing the same concentrations of BPA as their mothers from weaning to 11 weeks of age and then mated with non-exposed male mice. Body and organ weights, food consumption, and the number of live litters were examined every 3 to 4 days in F0 dams between the control group and bisphenol A groups. Sexuality and viability were similar in all F1 pups. No treatment-related changes were observed in body weight, food consumption, developmental parameters, anogenital distance, or weight and size of the organs. Sires, dams, testes, thymus, ovaries, uterus, or cervical (vT1) and CD (F1) adults in either sex. The epididymis weight was slightly higher with 0.33 and 3.3 ppm in F1 males, but this slight increase was neither dose dependent nor were accessory generations. There were no treatment-related effects of bisphenol A on male epididymal sperm count or sperm motility in F1 or F2 males. These findings indicate that dietary exposure to bisphenol A between 0.33 and 33 ppm does not adversely affect reproduction or development as assessed in two generations of mice.	Congenit Anom (Kyoto). 2010 Sep;50(3):159-70.	10.1111/j.1741-4520.2010.00279.x	20507349	動物	生殖発生毒性/精子	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	●	-	-	-	-
統合_2429	Kobayashi K et al.	2012	Lack of effects for dietary exposure of bisphenol A during in utero and lactational periods on reproductive development in rat offspring	The potential for health effects on humans with exposure to bisphenol A (BPA) has raised concerns, and the adverse effects of low-dose exposure to BPA on reproduction have been controversial. The purpose of the present study was to investigate the effects of low-dose exposure to BPA on reproductive development in F1 rat offspring. Pregnant female Sprague-Dawley rats (F0) were fed a diet containing low doses of BPA (0, 0.33, 3.3, or 33 ppm) from gestational day (GD) 0 through postnatal day (PND) 21. The weanlings (F1) from all dose groups were fed a normal diet ad libitum after weaning and then some subjected to necropsy at 5 weeks, or 3 months of age. No BPA-related changes were observed in body weight or weight of any of the major reproductive organs in F1 males and females. Statistically significant, but very slight increases in the anogenital distance (AGD) of F1 males exposed to 33 ppm BPA. Anogenital distance (AGD), the ratio of AGD to the cube root of body weight, and relative ovary weight were significantly lower in 3-month-old F1 females exposed to 33 and 33 ppm BPA. However, these changes were not dose dependent and were not observed in F1 females at 5 weeks of age. Histopathological examinations revealed no BPA-related changes in F1 reproductive tissues. Serum hormone concentrations were not altered among groups. In either sex. These outcomes indicate that low dose exposure to BPA in the diet does not adversely affect reproductive development in F1 rat offspring.	J Toxicol Sci. 2012;37(3):565-73.	10.2131/jts.37.565	22687996	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	-	-	-	-	-
統合_2430	Marmugi A et al.	2012	Low doses of bisphenol A induce gene expression related to lipid synthesis and trigger triglyceride accumulation in adult mouse liver	Changes in lifestyle are suspected to have strongly influenced the current obesity epidemic. Based on recent experimental, clinical, and epidemiological work, it has been proposed that some food contaminants may exert damaging effects on endocrine and metabolic functions, thereby promoting obesity and associated metabolic diseases such as nonalcoholic fatty liver disease (NAFLD). In this work, we investigated the effect of one such food contaminant, bisphenol A (BPA), in vivo. We used a transcriptomic approach to male C57J mice exposed for 10 days to different doses of BPA (0, 5, 50, 500, and 5,000 mg/kg/day) through food administration. Hepatic steatosis was observed in BPA-treated mice, with a significant increase in liver triglyceride content at 500 mg/kg/day. Gene expression profiling of dose-responsive (adjusted p-value < 0.05) and dose-dependent (adjusted p-value < 0.05 and fold change > 1.5 between two consecutive doses) genes revealed a monotonic dose response curve, with the most significant effects at lower doses than at the highest dose. In addition to lipogenic enzymes (e.g., Fasn, Scd1), the expression of transcription factors such as Srebf1 (sterol regulatory element-binding protein 1c), and the carbohydrate-responsive element-binding protein that governs the expression of lipogenic genes also followed a monomodetic dose-response curve in response to BPA. Consistent with an increased fatty acid biosynthesis, determination of fatty acid composition of liver revealed an accumulation of cholesterol esters and of triglycerides. CONCLUSIONS: Our work suggests that exposure to low BPA doses may influence de novo fatty acid synthesis through increased expression of lipogenic genes, thereby contributing to hepatic steatosis. Exposure to such contaminants should be carefully examined in the etiology of metabolic diseases such as NAFLD and nonalcoholic steatohepatitis.	Hepatology. 2012 Feb;55(2):395-407.	10.1002/hep.24685	21932408	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	-	-	-	-	-
統合_2431	Martini M et al.	2010	Effects of perinatal administration of Bisphenol A on the neuronal nitric oxide synthase expressing system in the hypothalamus and limbic system of CD1 mice	Bisphenol A (BPA) is a well known plastic-derived pollutant that can bind to oestrogen receptors and is considered an endocrine-disrupting chemical. Its impact on different behaviours in rodents has been largely investigated, however, only a few data are available on its effects upon neural circuits. In the present study, we investigated the long-term effects of early exposure of mice of both sexes to BPA on the olfactory system, one of the neural systems involved in the control of sexual behaviour and useful for the assessment of gender-related differences. Effects of both doses were evaluated for eight prenatal and eight postnatal days. rtrBPA dose was administered to the mothers. The maternally exposed mice were sacrificed at the age of 2 months and their testes were sectioned and immunohistochemically treated for the detection of neuronal nitric oxide synthase (nNOS)-containing neurons. The number of nNOS-immunoreactive (-ir) cells was evaluated in the olfactory bulb, in the hypothalamic nuclei and in the medial amygdaloid nucleus. BPA induced a dose-dependent sex difference in the number of nNOS-ir cells in the medial amygdaloid nucleus, a limbic system area more dependent on sex. These results indicate that BPA has a powerful effect on specific portions of the nNOS-immunoreactive system belonging to the accessory olfactory system that are particularly important for the control of sexual behaviour. In addition, they confirm that perinatal exposure to endocrine-disrupting chemicals, in particular to BPA, may have a high impact on the organisation of specific neural pathways that can later affect complex behaviours and functions.	J Neuroendocrinol. 2010 Sep;22(9):1004-12.	10.1111/j.1365-2826.2010.02043.x	20561153	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	●	-	●	-	-
統合_2432	Ryan BC et al.	2010	In utero and lactational exposure to bisphenol A, in contrast to ethinyl estradiol, does not alter sexually dimorphic behavior, puberty, fertility, and anatomy of female LE rats	Many chemicals released into the environment display oestrogenic activity including the oral contraceptive ethinyl estradiol (EE2) and the plastic monomer bisphenol A (BPA). EE2 is present in some aquatic systems at concentrations sufficient to alter reproductive function of fishes. Many concerns have been raised about the potential effects of BPA. The National Toxicology Program noted the potential effects of low doses of BPA on behavior and central nervous system (CNS) as an area of "some concern," whereas most effects were rated as of "negligible" or "minimal" concern. However, the number of studies in this area was limited. The current study was designed to determine if maternal exposure to relatively low oral doses of EE2 or BPA in vivo and during lactation would alter the expression of a well-characterized sexually dimorphic behaviors or alter reproductive development and function in female offspring. Long-Evans rats were exposed to 0, 2.5, 25, or 250 μg/kg/day EE2 or 0, 2.4, 24, or 240 mg/kg/day BPA. Effects on play behavior were examined on PND 35, and the female offspring were studied. EE2 (50 microg/kg/day) increased anogenital distance and reduced vaginoplasty length at PND21, accelerated the age at vaginal opening, reduced F1 fertility, and F2 litter sizes, and induced malformations of the external genitalia (5 microg/kg). F1 females exposed to EE2 also displayed a reduced male-like/Low-lordosis preference (5 microg/kg) and absence of lordosis behavior (25 microg/kg). Indications of differentiation of the CNS. BPA had no effect on any of the aforementioned measures. These results demonstrate that developmental exposure to pharmacologically relevant dosages levels of EE2 can permanently disrupt the reproductive morphology and function of the female rat.	Toxicol Sci. 2010 Mar;114(1):133-48.	10.1093/toxsci/kfp266	19864446	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	●	●	●	-	-
統合_2437	Wu JH et al.	2011	Oral exposure to low-dose bisphenol A aggravates testosterone-induced benign hyperplasia prostate in rats	The declining level of androgen during aging, associated with an inclining level of estrogen, has been hypothesized to be important in the development of benign prostatic hyperplasia (BPH). Within physiologic range, increasing estrogen levels can stimulate prostatic to develop and consequently increase prostatic size. As an estrogenic endocrine disruptor, bisphenol A (BPA) might be a modulator to prostatic development. We further hypothesized that low dose BPA could induce hyperplasia prostate to proliferate and aggravate the symptom of BPH in male SD rats. BPA was indicated by testosterone and then treated with BPA (10, 30, or 90 mg/kg, i.p., 3 days/week) for 4 weeks. Prostatic hyperplasia was induced by testosterone propionate (3 mg/kg, s.c., 3 days/week) for 4 weeks. Testosterone-induced BPH rats showed a significantly increased prostatic index (ventral prostate weight/body weight) and the relative weight of prostate (p < 0.05). For prostatic index, BPA (3 mg/kg) significantly increased prostatic weight of ventral prostate (VP), weight and relative weight of dorsal lateral prostate (DLP) (p < 0.05). Anthropathology results showed that height of epithelial cell (HEC) of VP and DLP in BPH group were significantly higher than that of model control (p < 0.05). BPA could also decrease testosterone-level and increase prostate-specific antigen level. E2 treatment also showed an obvious effect on relative weight of VP and DLP, HEC, and hormone levels. We concluded that environment exposure to low dose of BPA may induce prostate to proliferate and aggravate testosterone-induced benign hyperplasia prostate in rats.	Toxicol Ind Health. 2011 Oct;27(9):810-9.	10.1177/0748233711399310	21415097	動物	内分泌/前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	-	-	-	-	-
統合_2438	Xu X et al.	2011	Changed preference for sweet taste in adulthood induced by perinatal exposure to bisphenol A-A probable link to overweight and obesity	BACKGROUND: The preference of obesity has risen dramatically worldwide over the past decades. Some latest reports showed significant increase of obesity in men compared to women. Implication of environmental endocrine disruptors (EEDs) on obesity has been widely studied. Bisphenol A (BPA) is a well-known EED. Perinatal exposure to BPA has been reported to induce obesity. However, BPA-induced change in gender-specific behaviors which result in obesity, well-unknown. OBJECTIVES: To examine whether perinatal exposure to BPA at relative dose to environmental levels can influence sweet preference of male and female rats, and consequently lead to alteration in bodyweight. METHODS: Rats perinatally exposed to BPA at doses of 0.01, 0.1 and 1.0 mg/L were tested sweet preference for 0.25%, 0.5% saccharin and 10% sucrose by two-bottle choice (water vs. saccharin/sucrose). The food intake, body weight and bodyweight gain of each animal were recorded monthly. At the end of the test, the fat coverage and cell size/diameter were measured. RESULTS: Significant sex difference of preference for 0.25% and 0.5% saccharin was shown in control and all BPA-treated groups ($p < 0.05$), females vs. male1, 0.1 and 1.0 mg/L BPA treatment induced the preference for 0.25% and 0.5% saccharin in male offspring ($p < 0.05$), but not in female offspring ($p > 0.05$), male1 vs. male0.1 and 1.0 mg/L ($p < 0.05$). Male offspring exposed to BPA (0.1 and 1.0 mg/L) showed the increased sucrose preference (control male0 vs male0.1 and 1.0, $p < 0.05$), but female offspring exposed to BPA (0.1 and 1.0 mg/L) showed the decreased sucrose preference (female0 vs female0.1 and 1.0, $p < 0.05$), compared to control. The males treated by BPA showed overweight ($p < 0.05$), high fat percentage ($p < 0.05$) and low blood pressure ($p < 0.05$) than control. CONCLUSION: Perinatal exposure to a low dose of BPA could increase sweet preference of male rats. Caloric intake may be augmented during early life, leading to changes of body weight depending on the gender. Although further researches concerning the mechanism are required, the results of the present study are particularly important with regards to the more significant increasing prevalence of obesity in men and the environmental endocrine disruptors.	Neurotoxicol Teratol. 2011 Jul-Aug;33(4):458-63.	10.1016/j.ntt.2011.06.002	21704699	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_2439	Zhang HQ et al.	2012	Fetal exposure to bisphenol A affects the primordial follicle formation by inhibiting the meiotic progression of oocytes	Bisphenol A (BPA) is an estrogenic environmental toxin widely used for the production of plastics. Frequent human exposure to this chemical has been proposed to be a potential public health risk. The objective of this study was to assess the effects of BPA on germ cell cyst breakdown and primordial follicle formation. Pregnant mice were treated with BPA at doses of 0, 0.02, 0.20, 2.00, 20.00, or 50.00 mg/kg body weight/day from 12.5 day post-coitum (dpc) to 18.5 dpc. BPA was declared exert by pregnant female mice. A dose–response relationship was observed with increased BPA exposure level associated with more oocytes in germ cell cyst and less primordial follicle at postnatal day 3 (PND3). Progression to meiosis prophase I of oocytes was delayed in the 0.08 mg/kg/day treated group (PND3). Decreased mRNA expression of specific meiotic genes including Stra8, Dmc1, Rad51 and Scp3 were observed. In conclusion, BPA exposure can affect the formation of primordial follicle by inhibiting meiotic progression of oocytes.	Mol Biol Rep. 2012 May;39(5):5651-7.	10.1007/s11033-011-1372-3	22187349	動物	卵巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	-	-	-	-	-
統合_2440	Zong J et al.	2013	Effect of Bisphenol A on Rat Metabolic Profiling Studied by Using Capillary Electrophoresis Time-of-Flight Mass Spectrometry	Bisphenol A (BPA), a chemical widely used in the manufacture of polycarbonate plastics, has raised considerable concern in recent decades because of its hormone-like properties. Whether BPA exposure is a health risk remains controversial in many countries. A metabolomics study based on capillary electrophoresis time-of-flight mass spectrometry (CE-TOF/MS) was performed to study the urine metabolic profiles of Sprague-Dawley rats fed with four dose levels of BPA (0, 1, 10, and 100 μg/kg body weight/day) for 35 days. Multivariate pattern recognition directly reflected the metabolic perturbations caused by BPA. On the basis of univariate analysis, 19 metabolites, including amino acids, polyamines, nucleosides, organic acids, carbohydrates, proteins, polyphenols, and sugar alcoholates, were found as the most significantly differential metabolites. The marked perturbations were related with valine, leucine and isoleucine biosynthesis, D-glutamine and D-glutamate metabolism, etc. Significant alterations of neurotransmitters, lipidemia, gamma-aminobutyric acid, and oxidative stress were also observed. Our findings indicate that BPA exposure may induce neurotoxicity, lipidemia, and oxidative stress, which may contribute to its interactions with the neuroendocrine system. Our study demonstrated that metabolomics may offer more specific insights into the molecular changes underlying the physiological effects of BPA.	Environ Sci Technol. 2013 Jul 2;47(13):7457-65.	10.1021/es400490f	23746042	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-

別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2441	Dobrzynska MM and Radzikowska J	2013	Genotoxicity and reproductive toxicity of bisphenol A and X-ray/bisphenol A combination in male mice	This study was designed to investigate the effects of 2 weeks of exposure of male mice to bisphenol A (BPA) alone or in combination with X-rays on the sperm count and quality as well as induction of DNA strand breaks and micronuclei in germ cells and bone marrow cells. Male CBA/H mice were exposed to BPA (0.1 and 1.0 mg/kg b.w.) and/or X-rays (0.5 Gy) for 2 weeks. BPA was administered in drinking water and X-rays were applied as a single dose. X-rays induced DNA strand breaks in spleen cells, whereas BPA induced DNA strand breaks in leukocytes and in cells of the spleen, kidneys, and lungs and in germ cells. After combined exposure to both agents, sperm count and quality were similar as after exposure to each agent alone and significantly reduced, compared to control. Levels of DNA damage in somatic and germ cells after combined exposure to toxic as well as lighter doses were significantly reduced, compared to the effects of BPA alone. Results confirmed the mutagenic ability of BPA. Combined exposure to X-rays and BPA leads to the prevention of DNA damage in somatic and germ cells of mice.	Drug Chem Toxicol. 2013 Jan;36(1):19-26.	10.3109/01480545.2011.644561	22263531	動物	精子/雄性生殖器	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	●	●	-	-	-	-	-
統合_2442	Kendziorski JA et al.	2012	Strain specific induction of pyometra and differences in immune responsiveness in mice exposed to 17alpha-ethinyl estradiol or the endocrine disrupting chemical bisphenol A	Pyometra is an inflammatory disease of the uterus that can be caused by chronic exposure to estrogens. It is unknown whether weakly estrogenic endocrine disruptors can cause pyometra. We investigated whether dietary exposures to the estrogenic endocrine disruptor bisphenol A (BPA) induced pyometra. Pyometra did not occur in CD1 mice exposed to different dietary doses of BPA ranging from 0.1 to >5000mg/kg/d or 17alpha-ethinyl estradiol (EE) at 0.1 mg/kg/d. In contrast, 100% of CBA/J mice exposed to 0.1 mg/kg/d EE developed pyometra. At the time of euthanasia, the CBA/J mice exposed to EE had significantly more pathological alterations of uterine morphology (endometrial cell hyperplasia, endometrial cell hyperplasia with atypia, and pyometra) than CD1 mice exposed to EE or CBA/J mice exposed to BPA. These results suggest that BPA enhances immune responsiveness of the uterus and that heightened responsiveness in CD1NL/H females is related to increased susceptibility to pyometra.	Reprod Toxicol. 2012 Aug;34(1):22-30.	10.1016/j.reprotox.2012.03.001	22429997	動物	子宮	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	●	-	-	-	-	-	-
統合_2444	Stump DG et al.	2010	Developmental neurotoxicity study of dietary bisphenol A in Sprague-Dawley rats	This study was conducted to determine the potential of bisphenol A (BPA) to induce functional and/or morphological effects in the nervous system of F1 offspring from dietary exposure during gestation and lactation according to the Organization for Economic Cooperation and Development and U.S. Environmental Protection Agency guidelines for the study of developmental neurotoxicity. BPA was offered to timed-pregnant Sprague-Dawley Crl:CD (SD) rats (25 per dose group) and their litters at dietary concentrations of 0 (control), 0.1, 1.0, 75, 750, and 2500 ppm daily from gestation day 6 through lactation day 21. F1 offspring were evaluated using the functional observational battery, motor activity, auditory startle habituation, learning and memory (Morris water maze), and neuropathology. Maternal toxicity was observed at 2500 ppm BPA (750 mg/kg/day [mg/kg/day] as test and reference solutions, respectively) and consisted of decreased body weight gain, food consumption, and food efficiency. There was no evidence of developmental neurotoxicity or effects on brain morphometry. Based on maternal and offspring body weight reductions, the no-observed-adverse-effect level (NOAEL) for systemic toxicity was 75 ppm (5.06 and 5.61 mg/kg/day during gestation and lactation, respectively), with no treatment-related effects at lower doses. In nonmonotonic dose-responses observed for sex parameters. There was no evidence that BPA is a developmental neurotoxin in rats, and the NOAEL for developmental neurotoxicity was 2500 ppm, the highest dose tested (166 and 153 mg/kg/day during gestation and lactation, respectively).	Toxicol Sci. 2010 May;115(1):167-82.	10.1093/toxsci/kfq025	20164145	動物	発達神経	1（混餌）	1	1	1	1	1	1（0.1ppm～5,000ppmの5水準）	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	●	-	●	●	-	●	-
統合_2445	Tse W et al.	2013	Bisphenol A differentially activates protein kinase C isoforms in murine placental tissue	Bisphenol A is utilized to make polycarbonate plastics and is an environmental pollutant. Recent research has indicated that it is an endocrine disruptor and may interfere with reproductive processes. Our lab has previously shown that bisphenol A could regulate corticotrophin releasing hormone and aromatase in cultured placental cells. In the present study, the effect of bisphenol A on these two genes in the placenta was investigated in vivo. Pregnant CD1 mice were gavaged with bisphenol A at 0, 20 and 200mg/kg body weight from E7.5 to E18 and were sacrificed at E19. Compared to control mice, those treated with bisphenol A had significantly greater corticotrophin releasing hormone gene abundance (visualized in situ and in vitro). Aromatase RNA quantification indicated that placental cortical and cupE9 was reduced in mice treated with bisphenol A. Testing the related signaling pathways revealed that PKC ζ/λ and PKC ε were activated by bisphenol A treatment in the placenta. Activation of PKC ζ/λ and PKC ε by bisphenol A in JEG-3 cells in vitro also strongly suggested that changes in reproductive organ weights in the 20 day old males and females are the signs of maternal toxicity were seen. The decreased E2/T4 ratio in both sexes indicates effects on prenatal sexual development and provides new evidence of low dose adverse effects of BPA in rats in the microgram per kilogram dose range. The NOAEL in this study is clearly below 5 mg/kg for BPA, which is used as the basis for establishment of the current tolerable daily intake (TDI) by EFSA; thus a reconsideration of the current TDI of BPA appears warranted.	Toxicol Appl Pharmacol. 2013 Jun 1;269(2):163-71.	10.1016/j.taap.2013.03.016	23545179	動物	胎盤	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	●	-	-	-	-	-	-
統合_2446	Christiansen S et al.	2014	Low-dose effects of bisphenol A on early sexual development in male and female rats	Bisphenol A (BPA) is widely detected in human urine and blood. BPA has been reported to impact many endpoints, for reproduction and neurological development. however, it is controversial whether BPA has effects in the microgram per kilogram dose range. The aim of the current study was to examine the influence of BPA on early sexual development in male and female rats, at dose levels covering both regulatory no-observed-adverse-effect levels (NOAELs) of 5 and 50 mg/kg bw per day and to assess in the same experiment the influence on BPA on anogenital distance (AGD) and nipple retention in male offspring. Pregnancy and lactation from gestation day 7 to post day 22 with 0, 0.28, 2.8, 5, or 50 mg/kg bw per day. BPA. From 62,190 mg/kg and above, male anogenital distance (AGD) was significantly decreased, whereas decreased female AGD was observed at 50,000 mg/kg bw per day. Nipple retention was significantly increased in male offspring at 62,190 and 50,000 mg/kg bw per day. Female AGD was significantly decreased at 50,000 mg/kg bw per day. Changes in reproductive organ weights in the 20 day old males and females are signs of maternal toxicity were seen. The decreased E2/T4 ratio in both sexes indicates effects on prenatal sexual development and provides new evidence of low dose adverse effects of BPA in rats in the microgram per kilogram dose range. The NOAEL in this study is clearly below 5 mg/kg for BPA, which is used as the basis for establishment of the current tolerable daily intake (TDI) by EFSA; thus a reconsideration of the current TDI of BPA appears warranted.	Reproduction. 2014 Mar 21;147(4):477-87.	10.1530/REP-13-0377	24298045	動物	発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	●	-	-	-	●	-
統合_2449	Faulk C et al.	2016	Detection of differential DNA methylation in repetitive DNA of mice and humans perinatally exposed to bisphenol A	Developmental exposure to bisphenol A (BPA) has been shown to induce changes in DNA methylation in both mouse and human germ regions; however, the response in repetitive elements and transposons has not been explored. Here we present novel methodology to assess genomic DNA enrichment and methylation in repetitive elements on next-generation sequencing data to determine the effect of perinatal BPA exposure on repetitive DNA in the mice, family, subfamily, and individual insertion level in both mouse and human samples. Mice were treated during gestation and lactation to BPA in mice at 0, 50, or 50,000 ug/g/d/g/d levels and total BPA was measured in the maternal circulation at gestational day 18 (GD18). Sperm DNA was isolated from the F1 male offspring at 6 months of age and subjected to methylated DNA immunoprecipitation and sequencing (MeDIP-seq). Data were analyzed using the methylCRF algorithm, with the resulting hypothesis test compared to methylKit and Bioconductor edgeR and limma packages. Mouse repeat classes, families, and subfamilies did not respond to BPA with significantly detectable differential DNA methylation. In human samples, LINE individual transposon loci were detected as differentially methylated by BPA exposure, but only 19 were detected in mice. Of note, this approach recapitulated the discovery of previously known mouse environmentally labile metastable epialleles, Cabp28Rt1. Thus, by querying repetitive DNA in both mouse and humans, we report the first known transposons in humans that respond to perinatal BPA exposure.	Epigenetics.2016;11(7):489-500	10.1080/15592294.2016.1183856	27267941	動物	-	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2450	Veiga-Lopez A et al.	2015	Impact of Gestational Bisphenol A on Oxidative Stress and Free Fatty Acids: Human Association and Interspecies Animal Testing Studies	Bisphenol A (BPA) is a high production volume chemical and an endocrine disruptor. Developmental exposures to BPA have been linked to adult metabolic pathologies, but the pathways through which these disruptions occur remain unknown. This is a comprehensive interspecific association or causal study to evaluate risk caused by perinatal BPA exposure and to facilitate discovery of biomarkers of influence in BPA toxicity. Samples from human pregnancies during the first trimester and at term, as well as fetal and 5-week-old lambs exposed to BPA from gestational day 30 to 5 weeks old, and mice, were collected to assess the impact of BPA on free fatty acid and oxidative stress dynamics. Mothers exposed to higher BPA during early to mid-pregnancy and their newborns were cord samples displayed increased 3-nitrotyrosine (3-NT), a marker of nitrosative stress. Maternal samples had increased palmitic acid, which was positively correlated with 3-NT. Sheep fetuses and adult sheep and rats prenatally exposed to a human-relevant exposure dose of BPA showed increased systemic nitrosative stress, altered fatty acid profiles, and increased 3-NT. Our results suggest that BPA exposure may influence the balance of nitrosative stress and fatty acid metabolism. This is the first multispecies study to address maternal-fetal-newborn exposure and metabolic disruptions caused by BPA. Our findings support the use of prenatal BPA exposure in metabolic health. This study provides evidence of the induction of nitrosative stress by prenatal BPA in both the mother and fetus at time of birth and is thus supportive of the use of maternal NT as a biomarker for offspring health.	Endocrinology. 2015 Mar;156(3):911-22.	25603046	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2451	Arambula SE et al.	2016	Impact of Low Dose Oral Exposure to Bisphenol A (BPA) on the Neonatal Rat Hypothalamic and Hippocampal Transcriptome: A CLARITY-BPA Consortium Study	Bisphenol A (BPA) is an endocrine disrupting, high volume production chemical found in a variety of products. Evidence of prenatal exposure has raised concerns that developmental BPA may disrupt sex-specific brain organization and, consequently, induce lasting changes on neurophysiology and behavior. We and others have shown that exposure to BPA at doses below the no-observed-adverse-effect level can disrupt the sex-specific pattern of synaptic connectivity in the hypothalamic anteroventral periventricular nucleus (AVPV) and the principal nucleus of the bed nucleus of the stria terminalis (BNSTp). As a part of the CLARITY-BPA program, we extend this work by examining the hippocampal and hypothalamic transcriptome in a population of CD-1 mice exposed to BPA from gestation day 6 through postnatal day 20. Litters were cross-fostered at birth to create 4 groups (10 litters/group): BPA-control (con), or BPA-low dose (2, 20, or 200 mg/kg body weight [bw]/d). Offspring were euthanized on postnatal day 1, hearts were microdissected and gene expression was examined with RNA sequencing (N = 2/3 – and RNA-seq by Ion PI™ proton only) and/or quantitative real time PCR (all remaining groups). BPA-related transcriptional changes were mostly restricted to the hypothalamus. Consistent with our observations, BPA induced sex-specific effects on hypothalamic Dhdh and Dhdh2 (Dia1 and Dia2) expression and hippocampal and hypothalamic cytosine (Cm) expression. These data demonstrate perinatal BPA exposure, even at doses below the current no-observed-adverse-effect level, can alter gene expression in the developing brain.	Endocrinology. 2016 Oct;157(10):3856-3872.	10.1210/en.2016-1339	27571134	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	●
統合_2452	Arambula SE et al.	2017	Effects of perinatal bisphenol A exposure on the volume of sexually-dimorphic nuclei of juvenile rats: A CLARITY-BPA consortium study	Bisphenol A (BPA) is a high volume endocrine disrupting chemical found in a wide variety of products including plastics and epoxy resins. Human exposure is nearly ubiquitous, and higher in children than adults. Because BPA is rapidly metabolized and excreted, exposure is overwhelmingly to the unconjugated (free) BPA. Developmental exposure to BPA has been shown to alter brain and behavior in rodents, at doses below the EPA NOAEL (i.e. 50 mg/kg body weight [bw]/day), and disrupt brain sexual differentiation. The current studies were conducted as part of the CLARITY-BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity) program and examined the full oral gavage (corn) system on perinatal day (PND) 1, with 10 litters/group. Pregnant Sprague-Dawley rats were gavaged from gestational day 6 until postnatal day 20 with BPA (0-, 2.5-, 25-, 250-, 2500-, or 25 000- mg/kg body weight [bw]/d). Ethinyl estradiol was used as a positive control (EE; 0.1 mg/kg/day [bw]/d). Offspring were euthanized on PND1, and brains were microdissected and gene expression was examined with RNA sequencing (N = 2/3 – and RNA-seq by Ion PI™ proton only) and/or quantitative real time PCR (all remaining groups). BPA-related transcriptional changes were mostly restricted to the hypothalamus. Consistent with our observations, BPA induced sex-specific effects on hypothalamic Dhdh and Dhdh2 (Dia1 and Dia2) expression and hippocampal and hypothalamic cytosine (Cm) expression. These data demonstrate perinatal BPA exposure, even at doses below the current no-observed-adverse-effect level, can alter gene expression in the developing brain.	Neurotoxicology. 2017 Dec;63:33-42.	10.1016/j.neuro.2017.09.002	28890130	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	●	-	-	-	-	●
統合_2453	Arambula SE et al.	2018	Prenatal bisphenol A (BPA) exposure alters the transcriptome of the neonate rat amygdala in a sex-specific manner: a CLARITY-BPA consortium study	Bisphenol A (BPA) is a widely recognized endocrine disruptor prevalent in many household items. Because experimental and epidemiological data suggest links between prenatal BPA exposure and altered affective behaviors in children, even at levels below the current US FDA No-Observed-Adverse-Effect-Level (NOAEL) of 5mg/kg body weight (bw)/day, there is concern that early life exposure may alter neurodevelopment. The current study was conducted as part of the CLARITY-BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity) program and examined the full oral gavage (corn) system on perinatal day (PND) 1, with 10 litters/group. Pregnant Sprague-Dawley rats were gavaged from gestational day 6 until postnatal day 20 with BPA (0-, 2.5-, 25-, 250-, 2500-, or 25 000- mg/kg body weight [bw]/d). Ethinyl estradiol was used as a positive control (EE; 0.1 mg/kg/day [bw]/d). Offspring were euthanized on PND1, and brains were microdissected and gene expression was examined with RNA sequencing (N = 2/3 – and RNA-seq by Ion PI™ proton only) and/or quantitative real time PCR (all remaining groups). BPA-related transcriptional changes were mostly restricted to the hypothalamus. Consistent with our observations, BPA induced sex-specific effects on hypothalamic Dhdh and Dhdh2 (Dia1 and Dia2) expression and hippocampal and hypothalamic cytosine (Cm) expression. These data demonstrate perinatal BPA exposure, even at doses below the current no-observed-adverse-effect level, can alter gene expression in the developing brain.	Neurotoxicology. 2018 Mar;65:207-220.	10.1016/j.neuro.2017.10.005	29097150	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	●
統合_2454	Belcher SM et al.	2015	Bisphenol A Alters Autonomic Tone and Extracellular Matrix Structure and Induces Sex-Specific Effects on Cardiovascular Function in Male and Female CD-1 Mice	The aim of this study was to determine whether bisphenol A (BPA) has adverse effects on cardiovascular functions in CD-1 mice and define sex-specific modes of BPA action in the heart. Dams and analyzed progeny were exposed to environmentally relevant doses of BPA (0.5, 5, 50, 500, and 5000 μg/kg/d) or 17β-estradiol (E2; 0.1 μg/kg/d) in drinking water. Cardiac function was assessed in adult male and female mice at 4 and 8 months of age (0.5, 5, 50, 500, and 5000 μg/kg/d) or as an oral bioavailable estrogen control. Assessment of electrocardiogram parameters using noninvasive methods found that ventricular function is altered in both male and female mice exposed to BPA or E2. However, exposure-related changes in the rates of ventricular contraction, suggestive of a shift in sympathovagal balance of heart rate control toward increased parasympathetic activity, was detected in males. Decreased systolic blood pressure was observed in males exposed to BPA (≥ 5 μg/kg/d) or E2 (0.1 μg/kg/d). In females, BPA exposure (≥ 5 μg/kg/d) or E2 (0.1 μg/kg/d) increased systolic blood pressure. Histological measures revealed sexually dimorphic changes in the composition of the cardiac collagen extracellular matrix, increases in fibrosis, and evidence of modest exposure-related remodeling. Experiments using the alpha-adrenergic agonist phenylephrine revealed that BPA exposure augmented the pressor response in males, but not females. Collectively, these data indicate that BPA exposure is associated with changes in the cardiovascular system that are sex specific and dependent on the dose and duration of exposure. Males are more sensitive to the cardiotoxic effects of the toxic elements, while females are more sensitive to the adverse effects of BPA. Sex-specific changes in gene expression in response to BPA that were consistent with the observed supplement-induced ischemic damage and hypertrophy. The results of RNA sequence analysis identified significant sex-specific changes in gene expression in response to BPA that were consistent with the observed exposure-related phenotypic changes in the collagenous and noncollagenous extracellular matrix, cardiac remodeling, altered autonomic responses, changes in ion channel and transporter functions, and altered glycolysis and lipid metabolism.	Endocrinology. 2015 Mar;156(3):882-95.	10.1210/en.2014-1847	25594700	動物	心血管	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2455	Berger A et al.	2016	The effects of in utero bisphenol A exposure on the ovaries in multiple generations of mice	Bisphenol A is used in polycarbonate plastics and epoxy resins. Previous studies show that in utero BPA exposure inhibits germ cell nest breakdown in the F1 generation of mice, but its effects on germ cell nest breakdown and on the ovary in the F1 generation were unknown. Thus, we tested the hypothesis that BPA has transgenerational effects on the ovary. We in utero exposed mice to BPA (0, 25, 50, or 50mg/kg/day), and ovaries were collected at postnatal days (PND) 0 and 21 from the F1-F3 generations and subjected to histological evaluations and gene expression analyses. In utero BPA exposure did not have transgenerational effects on germ cell nest breakdown and gene expression on PND 0, but it caused transgenerational changes in expression in multiple genes on PND 21. Collectively, these data indicate that in utero BPA exposure has some transgenerational effects in mice.	Reprod Toxicol. 2016 Apr;60:39-52.	10.1016/j.reprotox.2015.12.004	26746108	動物	卵巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	●	-	-	-	-	-
統合_2456	Bertram HF et al.	2018	Decreased macrophage phagocytic function due to xenobiotic exposures in vitro, difference in sensitivity between various macrophage models	Rich autoimmune disease prevalence and exposure to immunotoxic chemicals have increased the last decades. As a first screening of immunotoxic chemicals possibly affecting development of autoimmunity through attenuated macrophage function, we demonstrate a promising model measuring macrophage function in isolated peritoneal macrophages (PCM) from Wistar rats and C57BL/6 mice. Immunotoxic effects of bisphenol A (BPA) and a selection of perfluoralkyl acids (PFAA) were analysed in vitro assessing phagocytic function of macrophages, from different species. Phagocytosis was reduced in PCM of C57BL/6 mice and Wistar rats after BPA and perfluorooctanoic acid (PFOA)(0) exposure, but not in macrophages derived from human and rat monocyte derived macrophages (MDM). On the other hand, in vitro exposure to mixtures of persistent organic pollutants (POPs) showed similar reductions in rat PCM and rat and human MDM phagocytosis. Reduced phagocytosis was partly due to cytotoxicity. PCM isolated from non-obese diabetic (NOD) mice, a model for type 1 diabetes, showed a similar reduction in phagocytosis after in vitro exposure to BPA and PFOA(0). Isolated PCM from NOD mice and Wistar/NSP exposure also decreased the number of pancreatic macrophages in pancreatic islets, reflecting early signs of autoimmunity development, similarly as previously described for BPA.	Food Chem Toxicol.2018;112:86-96	10.1016/j.fct.2017.12.024	29258957	動物	-	1	1	1	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階で除外。当該性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2457	Biasiotto G et al.	2016	Municipal wastewater affects adipose deposition in male mice and increases 3T3-L1 cell differentiation	Toxic concentration of EDs (endocrine disrupting compounds) in water bodies caused by wastewater treatment plant effluents is a recognized problem for the health of aquatic organisms and their potential to affect human health. In this paper we show that continuous exposure of male mice from early development to the adult life (120 days) to unprocessed drinking of wastewater collected from a municipal sewage treatment plant, is associated with an increased adipose deposition and weight gain during adulthood because of altered body homeostasis. In parallel, bisphenol A (BPA) at the administration dose of 5 mg/kg/body weight, shows an obesogenic effect similar to that of wastewater. Pre-adipocytes 3T3-L1 cell line was used to investigate the effects of BPA and wastewater on cell differentiation. The wastewater at a medium-term cytotoxic concentration of BPA at 0.40 and 0.60 nM and 50 nM respectively

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2473	Huang CY et al.	2018	Oral exposure of low-dose bisphenol A promotes proliferation of dorsolateral prostate and induces epithelial-mesenchymal transition in aged rats	Bisphenol A (BPA) is a well-known endocrine-disruptor compound reported to have prostate toxicity. This study aimed to assess the effect of BPA on the proliferation of dorsolateral prostate (DLP) and the expression of epithelial-mesenchymal transition (EMT) markers in aged rats. Thirty-six 18-month-old male Wistar rats were randomly divided into 3 groups (n = 12/group) and orally administered 0 (control), 0.5, or 50 μg/kg bw/day BPA for 90 days. Increased the relative weights of PCNA, DLP, Ki-67-and Ezh2-stained cells and Ki-67-stained cell counts were found in the 50 μg/kg BPA group compared with the control group (P < 0.05). Moreover, the 50 μg/kg BPA group significantly increased the serum estrogen to androgen ratio (P < 0.05). The EMT-like changes in the DLP, including a significant upregulation of vimentin, Snail, Twist1, and transforming growth factor beta 1, as well as the downregulation of E-cadherin in the DLP, were also found in the 50 μg/kg BPA group. Immunohistochemical data revealed that the expression of vimentin, estrogen receptor α, and androgen receptor increased and the expression of E-cadherin decreased in the 50 and 50 μg/kg BPA groups. It was concluded that environmental exposure to low doses of BPA might promote the proliferation of DLP in aged rats by increasing the estrogen to androgen ratio and inducing EMT.	Sci Rep. 2018 Jan 11;8(1):490.	10.1038/s41598-017-18869-8	29323181	動物	前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	●	-	-	-	-	-	-
統合_2474	Jeong JS et al.	2017	Low-Dose Bisphenol A Increases Bile Duct Proliferation in Juvenile Rats: A Possible Evidence for Risk of Liver Cancer in the Exposed Population?	Increasing concern is being given to the association between risk of cancer and exposure to low dose bisphenol A (BPA), especially in young aged population. In this study, we investigated the effects of repeated oral treatment of low to high dose BPA in juvenile Sprague-Dawley rats. Exposing juvenile rats to BPA (0.5, 5, 50, and 250 mg/kg/day) for one week (early stage) or four weeks (late stage) did not affect body weights. In biliary ductal effect relatively. Male mammary glands were unaffected at high dose, which coincided with unusual pre-maturation of females. Notably, proliferative changes with abnormal cell foci and foci of cellular alteration were observed in the liver of male rats exposed to 250 mg/kg BPA for 4 weeks. Hepatocellular hypertrophy was also observed in the 250 mg/kg BPA group. Consistent exposure to BPA has greater effects on body weight gain, and the liver is the most susceptible organ to BPA exposure in juvenile rats. Considering consistent exposure to BPA has greater at early age (e.g., 250 fold to Dose, and 26 fold in SLC at 50 mg/kg to make no day 1, which might have stemmed from either age- or gender-dependent differences in metabolic capacity. These results may serve as evidence for the association between risk of cancer and exposure to low-dose BPA, especially in young children, as well as for varying toxicity of xenobiotics in different age and gender groups.	Biomol Ther (Seoul). 2017 Sep 1;25(5):545-552.	10.4062/biomolther.2017.148	28822992	動物	一般毒性(主に肝臓)	1	1	1	SD rat:1	4用量：1	0.5,5,50,250 mg/kg:1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	-
統合_2475	Jiang X et al.	2018	Bisphenol A induced male germ cell apoptosis via IFN beta-XAF1-XIAP pathway in adult mice	Bisphenol A (BPA) impairs male fertility by acting as an endocrine disruptor. However, the mechanisms by which BPA causes reproductive toxicity are not fully elucidated. Here, we explored the role of XAF1, a novel pro-apoptotic molecule, in BPA-induced abnormal spermatogenesis and the hypothalamic-pituitary-testicular mechanism of BPA-induced XAF1. BPA exposure detrimentally impacted spermatogenesis by inducing excessive germ cell apoptosis in the testes of adult mice. Moreover, BPA exposure significantly increased the expression of XAF1 and its upstream regulator IFN beta in the testes of adult mice. Knockdown of XAF1 expression significantly inhibited the apoptosis in GC-2 cells, suggesting that the activation and accumulation of endogenous XAF1 induced by BPA exposure to the testes. BPA exposure also significantly suppressed the expression of XIAP, a natural inhibitor of XAF1, in the testes of adult mice and in GC-2 cells. Furthermore, IFN beta knockdown reduced the expression of XAF1 and increased the expression of XIAP in BPA-treated GC-2 cells. Together, these data indicated that BPA triggers male germ cell apoptosis in vitro via the IFN beta -XAF1-XIAP pathway, which may contribute to BPA-induced testis toxicity.	Toxicol Appl Pharmacol. 2018 Sep 15;355:247-256.	10.1016/j.taap.2018.07.009	30017639	動物	精子	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	●	-	-	-	-	-	-
統合_2477	Jones BA et al.	2016	The Effects of Bisphenol A Exposure at Different Developmental Time Points in an Androgen-Sensitive Neuromuscular System in Male Rats	The industrial plasticizer bisphenol A (BPA) is a ubiquitous endocrine disruptor to which the general human population is routinely exposed. Although BPA is well known as an estrogenic mimic, there have been some suggestions that this compound may also alter activity at the androgen receptor. To determine whether BPA does have antiandrogenic properties, we evaluated BPA effects in the spinal nucleus of the bulbocavernosus, an androgen-sensitive nucleus, sexually dimorphic groups of motor neurons in the lumbar spinal cord that are critically dependent on androgens for survival and maintenance as well as the dendritic arborization of their cell membranes. In experiment 1, we administered varying concentrations of BPA to juvenile rats per- and postnatally and examined both the number and size of motor neurons in adulthood. In experiment 2, different doses of BPA were given to adult male rats for 28 days, and we examined androgen receptor (AR) immunoreactivity in the nucleus of the bulbocavernosus. In experiment 3, we examined the effects of BPA on androgen-induced growth in the levator ani muscle. Developmental exposure to BPA at 0.2 mg/kg/day, a dose within the range of typical human exposure, resulted in a decrease in some—but not all—motor neurons and, after chronic exposure in adulthood. These findings are discussed with regard to putative antiandrogenic effects of BPA, we argue that BPA is not antiandrogenic but is acting through nonandrogen receptor–dependent mechanisms.	Endocrinology. 2016 Aug;157(8):2972-7.	10.1210/en.2015-1574	27022676	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	1	-	-	-	-	-	-	-	-	-
統合_2478	Kalb AC et al.	2016	Maternal Transfer of Bisphenol A During Nursing Causes Sperm Impairment in Male Offspring	The health effects of environmental chemicals on animals and humans are of growing concern. Human epidemiological and animal study data indicate that reproductive disorders and diseases beginning early during prenatal and postnatal development. An increase of human male reproductive disorders in the past several decades was associated to chemicals called endocrine disruptors (ED). Bisphenol A (BPA) is a ubiquitous organic environmental contaminant with ED activity. This study quantified the effect of BPA exposure on breast milk during the lactation period, and examined the effects on male offspring. Female rats were administered three doses of BPA and BPF (0, 25, and 125 mg/kg/d by gavage for 35 consecutive days in 2014-2015, and a 2-ml blood sample was taken from each treated rat. Concentrations of BPA and NP in the blood were determined using the HPLC-fluorescence detection method. The male offspring were examined for their sperm quality, testicular histology, and fertility. The results showed that BPA and NP were detectable in the breast milk of the treated rats. Exposure to BPA and NP caused histological damage and morphology of the sperm (WHO, 21). The weight of the testes and prostate in the rats receiving BPA and NP treatment showed significant decreases compared to the control group. Similarly, NP-treated higher concentration than BPA in the serum (e.g., 6.48 +/- 0.46 vs. 1.36 +/- 0.24, at 125 mg/kg). Compared to the control group, dose-dependent significant decreases in count and motility in the sperm were observed following the administration of BPA (25 and 125 mg/kg) and NP (all three doses). Morphology exams of the rats' sperm were changed in various doses of BPA and NP. CONCLUSIONS: According to our findings, BPA and NP induced dose-dependent toxic effects on various parameters, i.e., sperm toxicity, weight of the testes, and weight of the prostate gland.	Electron Physician. 2016 Aug 25;8(8):2772-2780.	10.19082/2772	27757188	動物	精子	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	●	-	-	-	-	-	-
統合_2480	Kazemi S et al.	2016	Histopathology and histomorphometric investigation of bisphenol a and nonylphenol on the male rat reproductive system	BACKGROUND: Bisphenol A (BPA) and nonylphenol (NP) have harmful effects on the endocrine system of humans and animals. AIM: We sought to investigate the effect of three doses of BPA and NP on the reproductive parameters of rats. MATERIALS AND METHODS: Adult Wistar rats was outgoing 180-200g were used for a consecutive 70 day study. BPA and NP were given by gavage in three doses (5, 25, and 125 μg/kg). At the end of the study, the rats were anesthetized and 2 ml blood sample was obtained from the auxiliary venous plexus for the assessment of sex hormone levels. The testes were removed and kept in 10% formalin for the histomorphometric and histopathologic analyses. RESULTS: BPA and NP significantly decreased the body weight of the animals compared to the controls (P < 0.05). The seminiferous tubule diameter and thickness of the seminiferous epithelium were significantly decreased in the groups receiving BPA and NP compared to the control (P < 0.05). The number of seminiferous tubules in every experimental group increased, except for the BPA and NP (125 μg/kg) groups, which significantly decreased compared to the control (P < 0.05). The number of Leydig cells in the BPA and NP (125 μg/kg) groups (especially) in the group receiving NP (125 μg/kg) was significantly decreased compared to the other groups. Serum levels of luteinizing hormone, FSH, testosterone, and estradiol did not show any significant changes compared to the controls. CONCLUSION: Based on the results, all three doses of BPA and NP significantly produced weight loss, as well as destruction of the testis tissue and impairment of the spermatogenesis.	N Am J Med Sci. 2016 May;8(5):215-21.	10.4103/1947-2714.183012	27298816	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	●	-	-	-	-	-	-
統合_2481	Kazemi S et al.	2017	Low dose administration of Bisphenol A induces liver toxicity in adult rats	BACKGROUND: Bisphenol A (BPA) is one of the most widely used chemicals, often used in epoxy resins, health products and colors. This study aims to investigate the effect of various doses of BPA on hepatotoxicity in rats. METHOD: This experimental study was conducted using 20 male adult Wistar rats older than 2 months weighing 150-200g. 15, 75 and 125 μg/kg BPA was administered by gavage for 35 consecutive days. The animals were weighed at the beginning and the end of the experiment. The livers were removed, and the histological changes, alanine aminotransferase and aspartate aminotransferase were determined using colorimetric method. The liver tissue was kept in the freezer at -80° C for histological studies. FINDINGS: The body weight of rats receiving BPA decreased significantly compared to control group and this weight loss was more evident at doses of 75 and 125 μg/kg BPA. Administration of BPA significantly increased the liver weight in the treated groups ($P < 0.05$). CONCLUSION: Results of this study demonstrated that BPA could significantly increase Mean Corpuscular Hemoglobin (MCH) in the group receiving BPA (125 μg/kg) was significantly decreased compared to the other groups. Serum levels of luteinizing hormone, FSH, testosterone and estradiol did not show any significant changes compared to the controls. CONCLUSION: Based on the results, all three doses of BPA and NP significantly produced weight loss, as well as destruction of the testis tissue and impairment of the spermatogenesis.	Biochem Biophys Res Commun. 2017 Dec 9;494(1-2):107-112.	10.1016/j.bbrc.2017.10.074	29050942	動物	肝臓	1	1	1	Wistar rat:1	3用量：1	5,25,125 μg/kg:1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	-
統合_2482	Kazemi S et al.	2016	Induction Effect of Bisphenol A on Gene Expression Involving Hepatic Oxidative Stress in Rat	Background and Objective. Bisphenol A (BPA) is an abundantly used xenoestrogenic chemical which may cause various disorders in body. In the present study, we sought to investigate the effects of various doses of BPA on hepatic oxidative stress- related gene expression in rats. Methods. Male Wistar rats weighing 150-200 g were used in this study. Three doses of the BPA (5, 25, and 125 mg/kg/day) or corn oil were administered as gavage during 35 consecutive days. After the experiment, the rats were injured and the livers were removed and stored at -80 degrees C freezer for RNA extraction. Findings. The Real Time PCR showed increased expression of Nrf2 gene in the treated groups ($P < 0.05$). Administration of BPA significantly increased the liver weight in the treated groups ($P < 0.05$). The Catalase (CAT) gene expression was significantly increased in various doses BPA was increase (CAT) gene expression compared to control group. That expression was significantly increased in the lowest dose (5 mg/kg) of the BPA ($p < 0.05$). The final body weights (168.2 +/- 10.6 g) in the treatment group (BPA (125 mg/kg)) showed a significant decrease compared to control group (191.60 +/- 4.56 g). Conclusion. These findings demonstrate that BPA generated ROS and increased the antioxidant gene expression that causes hepatotoxicity.	Oxid Med Cell Longev. 2016:2016:6298515.	10.1155/2016/6298515	27143994	動物	肝臓	1	1	1	Wistar rat:1	3用量：1	5,25,125 μg/kg:1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	-
統合_2483	Kendziorski JA et al.	2015	Strain-specific induction of endometrial periglandular fibrosis in mice exposed during adulthood to the endocrine disrupting chemical bisphenol A	The aim of this study was to compare effects of bisphenol A (BPA) on collagen accumulation in uteri of two mouse strains. Adult C57BL/6N and CD-1 mice were exposed to dietary BPA (0.004-40mg/kg/day) or 17alpha-ethinyl estradiol (0.00002-0.02mg/kg/day) as effect control. An equine endometrosis-like phenotype with increased gland nesting and periglandular collagen accumulation was characteristic of unexposed C57BL/6N, but not CD-1, mice. Periglandular collagen was more commonly, increased gland area density and periglandular collagen accumulation in both strains, increased collagen I and fibronectin, decreased matrix metalloproteinase-2 (MMP2), and MMP13 expression, and impaired uterine memory response were associated with the endometrosis phenotype in the C57BL/6N mouse uterine. Bisphenol A (BPA) (10 μg/kg/day) exposure between the pre-collagen with increased collagen expression and decreased MMP2 expression and activity implies that strain differences and BPA exposure alter regulation of endometrial remodeling and contribute to increased fibrosis, a component of several human uterine diseases.	Reprod Toxicol. 2015 Dec;58:119-30.	10.1016/j.reprotox.2015.08.001	26307436	動物	子宮	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	●	-	-	-	-	-	-
統合_2484	Kendziorski JA et al.	2015	Effects of whole life exposure to Bisphenol A or 17 α -ethinyl estradiol in uterus of nulligravida CD1 mice	Bisphenol A (BPA) is an endocrine disrupting chemical (EDC) with known estrogenic activity. Exposure to BPA in adult mice was shown previously to increase uterine pathology with associated alterations in the immune response and fibrosis. Reported here are uterine fibroblast findings from CD1 mice exposed to BPA or 17alpha-ethinyl estradiol at multiple doses from conception through parturition. By 40 days, with uterine pathology, impacts of exposure on collagen accumulation and TLR9 positive macrophage numbers, as an indicator of immune response in the endometrium and myometrium, are presented. These comparisons are from offspring (F1) of females dosed for chronic exposure (gestation and lactation) published in the Reproductive Toxicology manuscript titled "Exposure to Mixtures of Endocrine Disruptors Induces Uterine Responses and Pathology in a Mouse Model of Uterine Fibroids and Endometriosis, and Is Associated with Changes in Fibroid Estrogen Receptor Expression" (Kendziorski et al. 2014). Additional findings from this study are described in the Endocrine Disrupting Chemical Bisphenol A" (doi: 10.1016/j.reprotox.2015.08.001).	Data Brief. 2015 Nov 3;5:948-53.	10.1016/j.dib.2015.10.034	26702426	動物	子宮	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	●	-	-	-	-	-	-
統合_2486	Klint H et al.	2017	Low-dose exposure to bisphenol A in combination with fructose increases expression of genes regulating angiogenesis and vascular tone in juvenile Fischer 344 rat cardiac tissue	OBJECTIVES: Epidemiological studies report associations between exposure to the high-volume chemical and endocrine disruptor bisphenol A (BPA) and cardiovascular disorders, but there is a lack of experimental evidence. Fructose is also suggested to be a risk factor for cardiovascular disease. We investigated the effects of BPA and fructose, alone and in combination, on the cardiovascular system. METHODS: Juvenile female rats were exposed to BPA in a human exposure range (0.5 μg/kg bw/day) and/or fructose (10% in drinking water) from 5 to 15 weeks of age, in combination with 5% fructose. Further, cultured human cardiomyocytes were exposed to 12 nM BPA (= 3 × 10(3) nM BPA in 1 × 10(3) nM BPA) for 24 hours. Expression of markers for cardiovascular function and BPA target receptors was analyzed by microarray and RT-qPCR. RESULTS: Fructose-induced hypertension was not affected by BPA co-exposure. Cardiac microarray revealed that BPA + fructose co-exposure altered the expression of 1,010 mRNA in comparison with BPA or fructose and 0.5, as well as 5. Bisphosphonates known to regulate inflammatory response, CCRL2, and CXCR4. Low-dose exposure of juvenile rats to BPA and fructose induced up-regulation of expression of genes controlling angiogenesis and vascular tone in cardiac tissues. The observed effects of BPA in rat heart were in line with our present and previous studies of BPA in human endothelial cells and cardiomyocytes. These findings may aid in understanding the mechanisms of the association between BPA exposure and cardiovascular disorders reported in epidemiological studies.	Ups J Med Sci. 2017 Mar;122(1):20-27.	10.1080/03009734.2016.1225870	27622962	動物	心血管	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2487	Kuwahara R et al.	2014	Bisphenol A Does Not Affect Memory Performance in Adult Male Rats	Bisphenol A (BPA) is an estrogenic endocrine disruptor used for producing polycarbonate plastics and epoxy resins. This study investigated the effects of oral BPA administration on memory performance, general activity, and emotionality in adult male Sprague-Dawley rats using a battery of behavioral tests, including an appetite-motivated two-way SMOR task used to assess spatial memory performance. In addition, in order to confirm the effects of BPA on spatial memory performance, we examined whether intrahippocampal injection of BPA affects spatial memory consolidation. In the SMOR test, although oral BPA administration at 10 mg/kg significantly altered the number of entries into the incorrect area compared to those of vehicle-treated rats, male rats given BPA through either oral administration or intrahippocampal injection failed to show significant differences in latencies to reach the reward. Also, oral BPA administration did not affect their motivated memory performance in the one-trial passive avoidance test. Oral BPA administration at 0.05 mg/kg, the lowest dose used in this study, did not affect the performance of the SMOR task. Furthermore, oral BPA administration at 10 mg/kg, a dose used in this study, was correlated with a light anxiolytic effect in the elevated plus maze test. The present study suggests that BPA is adulthood has little effect on spatial memory performance in male rats.	Cell Mol Neurobiol. 2014 Apr;34(3):333-42.	10.1007/s10571-013-0017-6	24326521	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該物評価段階で除害に基づき除害。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2488	Lee HS et al.	2018	Proteomic Biomarkers for Bisphenol A-Early Exposure and Women's Thyroid Cancer	PURPOSE: For the target treatment and prevention of women's increased thyroid cancer, we focused on risks of environmental exposure to endocrine disrupting chemicals, particularly bisphenol A (BPA), and its high exposure population. We identified BPA-responsive proteins in vitro and in vivo and verified their clinical significance in thyroid cancer tissues. METHODS: We treated BPA-responsive proteins in vitro-favorite liver-derived liver cholangiocarcinoma cell line and performed a large analysis, and the microscopic behavior was observed. We further analyzed expression of the BPA-responsive proteins in women thyroid cancer patients (n=28). RESULTS: We found the altered 17 proteins, in BPA dose-dependent manner among the thyroid tissues of all young mice and identified nine proteins of them, including Vimentin, Rab5a, Thioredoxin, and Cyp, etc. In addition, we observed the positive association between these BPA levels and mRNA expression of the VIM, RAB and CYP not in normal but thyroid cancer tissues. CONCLUSION: Our study provides VIMENA and HCP as proteomic biomarkers for BPA to verify the exposure and their potential for women's thyroid cancer.	Cancer Res Treat. 2018 Jan;50(1):111-117.	10.4143/crt.2017.001	28279065	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_2489	Lejzerkiss MH et al.	2016	Low-dose developmental exposure to bisphenol A alters the femoral bone geometry in wistar rats	BACKGROUND: Bisphenol A (BPA) is a chemical produced in large volumes for use in manufacturing of consumer products and industrial applications, and an endocrine disruptor known to affect several hormonal systems. Developmental exposure to BPA is associated with adverse effects on bone development and growth. METHODS: Pregnant Wistar rats were gavaged with 0.5 ml/kg/day of 0.1% carboxymethylcellulose (CMC) or 2.5 μg BPA/kg bw/day (0.0025 mg BPA/kg bw/day) from gestational day 7 until weaning at postnatal day 21. The male offspring were sacrificed at postnatal day 90 and right femurs collected for length measurements, geometrical measurements by peripheral quantitative computed tomography (pQCT), as well as for analysis of biomechanical properties using the three-point bending method. RESULTS: The femur was elongated in female offspring of dams exposed to 2% or 500% μg BPA/kg bw/day (5.0% and 1.1%, respectively), and increased cortical thickness (6.7% and 4.7%, respectively), and increased cortical thickness (6.7%) was observed in male offspring of dams exposed to 2% μg BPA/kg bw/day, compared to controls (p < 0.005). The biomechanical properties of the bone were not significantly altered. CONCLUSIONS: In vivo and translational exposure to the normal BPA tolerable daily intake (TDI) established by the European Food Safety Authority (EFSA) (0.05 mg BPA/kg bw/day) and the temporary TDI (0.5 mg BPA/kg bw/day) established by the European Food Safety Authority (EFSA) (0.05 mg BPA/kg bw/day) established by the European Food Safety Authority (EFSA) applied by EFSA to set a temporary TDI (500 μg BPA/kg bw/day), and far lower than the No Observed Adverse Effect Level (NOAEL) (5000 μg BPA/kg bw/day) on which the US FDA TDI is based.	Chemosphere. 2016 Dec;164:339-346.	10.1016/j.chemosphere.2016.08.114	27592323	動物	骨	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-
統合_2490	Leung YK et al.	2017	Gestational high-fat diet and bisphenol A exposure heightens mammary cancer risk	In utero exposure to bisphenol A (BPA) increases mammary cancer susceptibility in offspring. High-fat diet is widely believed to be a risk factor of breast cancer. The objective of this study was to determine whether maternal exposure to BPA in addition to high-butterfat (HBT) intake during pregnancy further influences carcinogen-induced mammary cancer risk in offspring, and to dose-response curve. In this study, we found that gestational HBT intake in addition to a low dose BPA (25 microg Bw/day) exposure increased mammary tumor incidence in a 50-day rat age-chemical carcinogen administration model and altered mammary gland morphology. Gene expression profiling revealed that maternal exposure to BPA and HBT altered the expression of genes involved in cell cycle, DNA damage response, and mammary gland development through DNA methylation, compared with HBT alone in the absence of BPA. Two HBT + BPA-upregulated genes (SLC9A3R1, SATB1, CAV1, CAV2, ILF3/NF90) are associated with poorer overall survival in The Cancer Genomic Atlas (TCGA) human breast cancer cohort (n = 1,068). Furthermore, the prognostic power of the identified genes was further enhanced in the survival analysis of Caucasian patients with estrogen receptor-positive tumors. In conclusion, concurrent HBT dietary and a low dose BPA exposure during pregnancy increases mammary tumor incidence in offspring, accompanied by alterations in mammary gland development and gene expression, and possibly through epigenetic reprogramming.	Endocr Relat Cancer. 2017 Jul;24(7):365-378.	10.1530/ERC-17-0006	28487351	動物	発がん(乳がん)	1	1	1	SD rat：1	4用量：1	[illegible]	-	-	-	-	-	-	-	1	1	-	-	●	-	-	-	-	●	-	-	●	-	-	●	-
統合_2491	Li J et al.	2018	CLARITY-BPA: Effects of chronic Bisphenol A exposure on the immune system: Part 1 - Quantification of the relative number and proportion of leukocyte populations in the spleen and thymus	Bisphenol A (BPA) is extensively used in manufacturing of a broad range of consumer products worldwide. Due to its widespread use, human exposure to BPA is virtually ubiquitous. Broad human exposure coupled with a large scientific literature describing emergent activities of BPA in animals has raised public health concerns. To comprehensively evaluate the health effects of BPA exposure, a chronic toxicity study using a wide range of BPA doses (2.5-25000mcg/kg/day) was conducted jointly by the FDA (Women-NIEHS-supported grantees, and the FDA, which is called the Consortium Linking Academic and Regulatory Insights on Toxicity of BPA (CLARITY-BPA). As a participant in the CLARITY-BPA project, the objective of the current study was to evaluate the effects of chronic BPA exposure in Sprague-Dawley rats on the relative numbers and proportions of defined leukocyte populations in the spleen and the thymus. Toward this end, lymphoid tissues from a total of 402 rats were assayed after being continuously dosed with BPA or controls for up to one year. To comprehensively characterize the immunophenotypes of leukocytes in the spleen and thymus, multiparameter flow cytometry was used to identify T cells, NK cells, monocytes, granulocytes, macrophages and dendritic cells. Overall, 420 different measurements in BPA-treated rats were performed which 56 measurements were statistically different from vehicle controls. The most substantive alteration associated with BPA treatment was the augmentation of lymphocytes in response to adrenal cell-type stimulation. In Spear cell male rats, which was also observed in the reference estrogen ethinyl estradiol treated group. With the exception of the aforementioned, the statistically significant changes induced by BPA treatment were mostly bounded and those dependent on BPA dose and the duration of the BPA dosing were relatively limited. In addition, the observed BPA associated alterations were mostly moderate in magnitude and relevant to persistent deviation the one-year time period. Based on these findings, we conclude that the observed BPA-mediated changes observed in this study are unlikely to alter immune competence in adult rats.	Toxicology. 2018 Mar 1:396-397:46-53.	10.1016/j.tox.2018.01.004	29428349	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	●	-	-	●	-	-	●	●
統合_2492	Li J et al.	2018	CLARITY-BPA: Effects of chronic bisphenol A exposure on the immune system: Part 2 - Characterization of lymphoproliferative and immune effector responses by splenic leukocytes	Bisphenol A (BPA) is commonly used in the manufacturing of a wide range of consumer products, including polycarbonate plastics, epoxy resin that lines beverage and food cans, and some dental sealants. Consumption of food and beverages containing BPA represents the primary route of human BPA exposure, which is virtually ubiquitous. An increasing number of studies have evaluated potential effects of BPA on immune response, in laboratory animals, that have reported a variety of effects some of which have been contradictory. To address the divergent findings surrounding BPA exposure, a comprehensive chronic treatment study of BPA was conducted jointly by the FDA (Women-NIEHS-supported grantees, and the FDA, which is called the Consortium Linking Academic and Regulatory Insights on Toxicity of BPA (CLARITY-BPA). As a participant in the CLARITY-BPA project, the objective of the current study was to evaluate the effects of chronic BPA exposure in Sprague-Dawley rats on the relative numbers and proportions of defined leukocyte populations in the spleen and the thymus. Toward this end, lymphoid tissues from a total of 402 rats were assayed after being continuously dosed with BPA or controls for up to one year. To comprehensively characterize the immunophenotypes of leukocytes in the spleen and thymus, multiparameter flow cytometry was used to identify T cells, NK cells, monocytes, granulocytes, macrophages and dendritic cells. Overall, 420 different measurements in BPA-treated rats were performed which 56 measurements were statistically different from vehicle controls. The most substantive alteration associated with BPA treatment was the augmentation of lymphocytes in response to adrenal cell-type stimulation. In Spear cell male rats, which was also observed in the reference estrogen ethinyl estradiol treated group. With the exception of the aforementioned, the statistically significant changes induced by BPA treatment were mostly bounded and those dependent on BPA dose and the duration of the BPA dosing were relatively limited. In addition, the observed BPA associated alterations were mostly moderate in magnitude and relevant to persistent deviation the one-year time period. Based on these findings, we conclude that the observed BPA-mediated changes observed in this study are unlikely to alter immune competence in adult rats.	Toxicology. 2018 Mar 1:396-397:54-67.	10.1016/j.tox.2018.02.004	29427786	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	●	-	-	●	-	-	●	●
統合_2493	Li Q et al.	2018	Bisphenol A and phthalates modulate peritoneal macrophage function in female mice involving SYMD2-H3K36 dimethylation	Ample evidence suggests that environmental and occupational exposure to bisphenol A (BPA) and phthalate, two chemicals widely used in the plastics industry, disrupts homeostasis of innate immunity and causes immunotoxicity. However, the underlying epigenetic mechanisms remain poorly understood. Here, we investigated the effects of BPA and phthalates on peritoneal macrophages in vivo and in vitro. Chronic exposure to BPA or phthalates at levels relevant to human exposure, either in vivo or in vitro, on the inflammatory reprogramming of peritoneal macrophages. Our studies revealed that BPA and phthalates adversely affected expression levels of the proinflammatory cytokines and mediators in response to lipopolysaccharide stimulation. Exposure to these toxicants also affected gene expression of scavenger receptors and phagocytic capacity of peritoneal macrophages. Our studies revealed that the epigenetic inhibitors differentially modulated target gene expression in these cells. Further analysis revealed that certain histone modification enzymes were aberrantly expressed in response to BPA or phthalate exposure, leading to alterations in the levels of H3K36 acetylation and dimethylation, two chromatin modifications that are critical for transcriptional efficiency and fidelity. Specifically, we found that SYMD2, a histone methyltransferase that catalyzes H3K36 dimethylation, was significantly upregulated in peritoneal macrophages from BPA- or phthalate-exposed mice. Moreover, the same enzyme-faster alpha expression level decreased the phagocytic capacity of peritoneal macrophages. In summary, our results indicate that peritoneal macrophages are vulnerable to BPA or phthalate at levels relevant to human exposure. These environmental toxicants affect phenotypic programming of macrophages via epigenetic mechanisms involving SSMD2-mediated H3K36 modification.	Endocrinology. 2018 May 1;159(5):2216-2228.	10.1210/en.2017-03000	29718165	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	●	-	-	-	-	-	-	-
統合_2494	Liu XL et al.	2013	Effects of exposure to bisphenol A during pregnancy and lactation on the testicular morphology and caspase-3 protein expression of ICR pups	Bisphenol A (BPA), a xenoestrogen and endocrine-disrupting chemical, is a cause for concern due to its being a potential human carcinogen. The aim of this study was to investigate the effects of continued maternal exposure to BPA on the testicular structures and expression of caspase-3 protein in male ICR offspring during pregnancy and lactation and explore its possible mechanisms. Pregnant ICR mice were divided into two control groups, which were either given a rat grain the solvent dimethyl sulfoxide (DMSO) and three treatment groups, which were gavaged with water-soluble BPA dissolved in DMSO at three different concentrations from gestation day 0 (GD0) to postnatal day 21 (PND21). Testicular histopathology, caspase-3 protein expression, and ultrastructural changes were observed by light microscopy, immunohistochemistry, and transmission electron microscopy, respectively. Moreover, the testicular coefficients were measured and statistically analyzed. Remarkable histopathological changes, such as obvious necrosis in the seminiferous epithelium, were found in the testes of male offspring mice exposed to BPA. Meanwhile, there was no significant difference between offspring of the control group and the treatment group in the testicular coefficient in the latter decreased (P<0.05). Specifically, compared with offspring of the control group, in addition to increased cell apoptosis, those of the treatment groups were found to have changes in mitochondrial and endoplasmic reticulum in their spermatogenic cells. Legally and particularly rapid cells, which were concomitant with an elevated expression of caspase-3 in the cytoplasm (P<0.01). In conclusion, exposure of pregnant mice to BPA during pregnancy and lactation has numerous effects on the testes of male ICR offspring and these may originate from increased apoptosis.	Biomed Rep. 2013 May;1(3):420-424.	10.3892/br.2013.79	24648961	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	●	-	-	-	-	-	-	-
統合_2496	Lv Q et al.	2017	Bisphenol A promotes hepatic lipid deposition involving Kupffer cells M1 polarization in male mice	Bisphenol A (BPA), one of the most common environmental endocrine disruptors, is considered to promote hepatic lipid deposition. However, the mechanisms have not been fully elucidated. The polarization of Kupffer cells (KCs) plays an important role in the maintenance of liver homeostasis and metabolic disorders. This study aimed to investigate the effects of BPA exposure on KC polarization and its role in BPA-induced hepatic lipid deposition in male mice. In this study, we examined hepatic lipid content and quantified M1/M2 in BPA-treated (50) mice, and further evaluated the interactions between KCs and hepatocytes using conditioned HepG2 cell culture. BPA treatment significantly increased hepatic fat contents. In CCl4 mice, accompanied by increased number of pro-inflammatory M1/KCs and enhanced secretion of inflammatory cytokines. Increased lipid contents were also observed in HepG2 cells treated with BPA. Interestingly, higher TG contents were observed in HepG2 cells treated with conditioned media from BPA-treated KCs, compared with those treated with BPA directly. Incubation of KCs with BPA promoted the polarization of KCs to pro-inflammatory M1 dominant subtypes, which was blocked by estrogen antagonists ICI182780. Taken together, our results revealed that M1/KCs polarization, treated in BPA-induced hepatic fat deposition, which is possibly associated with the estrogen receptor-signaling pathway.	J Endocrinol. 2017 Aug;234(2):143-154.	10.1530/JOE-17-0028	28500084	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-	-	-
統合_2497	Mahalingam S et al.	2017	The effects of in utero bisphenol A exposure on ovarian follicle numbers and steroidogenesis in the F1 and F2 generations of mice	Bisphenol A (BPA) is a commonly used plasticizer. Previous studies show that in utero exposure to BPA affects reproductive outcomes in the F1 F1 generations of mice. However, its multigenerational effects on ovarian histology and steroidogenesis are the reproductive lifespan are unknown. Thus, we tested the hypothesis that BPA has multigenerational effects on follicle numbers and steroidogenesis. Mice were exposed in utero to vehicle (0.1% EtOH), BPA (50 μg/kg/day), or ethinyl estradiol (EE2, 0.1 μg/kg/day) from gestation day 9 to birth. Ovaries were collected from F1 and F2 generations at 4 months of age. Follicle numbers, cytochrome P450 aromatase mRNA levels, and estradiol levels in the F1 generation, whereas 3-beta-hydroxysteroid dehydrogenase levels and altered steroidogenic acute regulatory protein, cytochrome P450 cholesterol side-chain cleavage, 3beta-hydroxysteroid dehydrogenase 1, and cytochrome P450 aromatase mRNA levels in the F1 generation. These data suggest that BPA has multigenerational effects on the ovary in mice.	Reprod Toxicol. 2017 Dec;74:150-157.	10.1016/j.reprotox.2017.09.013	28970132	動物	卵巣	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	●	-	-	-	-	-	-	-
統合_2499	Mamuqi A et al.	2014	Adverse effects of long-term exposure to bisphenol A during adulthood leading to hypeglycaemia and hypercholesterolemia in mice	Bisphenol A (BPA) is a suspected endocrine disrupter highly prevalent in our environment since it is used as monomer of polycarbonate plastics and epoxy resins. Recent epidemiological and animal studies have suggested that BPA exposure may influence the development of obesity and related pathologies such as type 2 diabetes, and cardiovascular diseases. However, experimental studies have often focused on short-term exposures. In this study, we investigated the effect of several months of BPA exposure on hepatic and plasma metabolic markers in adult mice. Male CD1 mice were exposed during 6 months to five different BPA doses below or above the tolerable daily intake (TDI) established by the European Food Safety Authority (EFSA) (0.05 mg BPA/kg bw/day) and the temporary TDI (0.5 mg BPA/kg bw/day) established by the European Food Safety Authority (EFSA) applied by EFSA to set a temporary TDI (500 μg BPA/kg bw/day), and far lower than the No Observed Adverse Effect Level (NOAEL) (5000 μg BPA/kg bw/day) on which the US FDA TDI is based. Results: BPA exposure induced a dose-dependent increase in body weight gain, fasting glycaemia and cholesterolemia. Correlations with the hypercholesterolemia in BPA-treated animals, HFD and SD performed on hepatic mRNA transcriptomic demonstrated an overexpression of key genes involved in cholesterol biosynthesis, namely Sfrp4, Lss, Fdps, and Sqle. BPA also induced the expression of the sterol regulatory element binding proteins, 2, a master regulator of hepatic cholesterol biosynthesis. As shown by the plasma lathosterol to cholesterol ratio, a surrogate marker for cholesterol biosynthesis, whole-body cholesterol de novo synthesis was also increased in BPA-exposed animals. These original results are consistent with many epidemiological studies reporting on a link between BPA exposure and the onset of cardiovascular diseases.	J Toxicology. 2014 Nov 5:325:133-43.	10.1016/j.tox.2014.08.006	25168180	動物	代謝	1	1	1	1	1	BPA/kg bw/day	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-	-	-
統合_2500	Mathisen GH et al.	2013	Prenatal exposure to bisphenol A interferes with the development of cerebellar granule neurons in mice and chicken	In mice, prenatal exposure to low doses of bisphenol A has been shown to affect neurogenesis and neuronal migration in cortex, resulting in disturbance of both neuronal packaging and the network formation between thalamus and cortex in the offspring brain. In the present study we investigated whether prenatal exposure to bisphenol A disturbs the neurodevelopment of the cerebellum. Two different model systems were used, offspring from two strains of mice from northern Norway exposed to the bisphenol A via the drinking water during pregnancy and lactation, and chicken embryos exposed to bisphenol A in the egg; an embryonic day 18 to 20in before preparation of cerebellar granule cell cultures. In the cerebellum, light regulation of the level of transcription factor Pax6 is critical for correct development of granule neurons. During the development, the Pax6 positive granule cells migrate from the external granular layer to the internal granular layer. Our results show that prenatal exposure to BPA at human relevant doses affects granule cell migration, resulting in increased thickness of the external granule layer and also an increase in the total cerebellar Pax6 level in 11 day old mice offspring. In cultured chicken cerebellar granule neurons from bisphenol A exposed eggs the Pax6 level was increased day 6 in vitro. Together, these findings indicate that bisphenol A may affect the granule neurons in the developing cerebellum and thereby may disturb the correct development of the cerebellum.	Int J Dev Neurosci. 2013 Dec;31(8):762-9.	10.1016/j.ijdevneu.2013.09.009	24091367	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2501	Menard S et al.	2014	Food intolerance at adulthood after perinatal exposure to the endocrine disruptor bisphenol A	The food contaminant bisphenol A (BPA) is pointed out as a risk factor in development of food allergy and food intolerance, two adverse food reactions increasing worldwide. We evaluated the consequences of perinatal exposure to BPA on the development of food intolerance in adulthood. Pregnant mice were exposed to BPA (0.5 mg/kg/day) from gestation day 0 to weaning. Adult offspring were challenged by oral increase of anti-OVA IgG1/IgG2a titers, at all BPA dosages (1–50%) reached one, and of mg/kg/day 0.5–50% increased mast compromise control cells mast cells effects. In BPA-treated animals, the development OVA-IgE titers were associated with higher IFNgamma secretion by the spleen. This result is in accordance with the increase of activated CD3(+)CD69(high)CD62L(low) T lymphocytes observed in spleen of BPA-exposed mice compared to controls. Finally, when BPA-treated OVA-tolerized rats were orally challenged with OVA, colonic inflammation occurred, with increased mMCP-1 infiltration, increased IFNgamma, and decreased TGFbeta. We show that perinatal exposure to BPA altered oral tolerance and immunization to dietary antigens (OVA). In summary, the naive immune system of neonate is vulnerable to low doses of BPA that trigger food intolerance later in life.	FASEB J. 2014 Nov;28(11):4893-900.	10.1096/fj.14-255380	25085925	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	●	-	-	-	-	-	-	-	-
統合_2503	Nowicki BA et al.	2016	Adverse effects of bisphenol A (BPA) on the dopamine system in two distinct cell models and corpus striatum of the Sprague-Dawley rat	The aim of this study was to examine the effects of bisphenol A (BPA) on the brain dopamine (DA) system utilizing both in vitro models (SH5-cells, a rat pituitary cell line, and SH-SY5Y cells, a human neuroblastoma cell line) and an animal model such as Sprague-Dawley (SD) rats. First, cellular DA uptake was measured 1 or 6 h following BPA exposure (0.2 NM) in SH-SY5Y cells, where a significant increase in DA uptake was noted. BPA exerted no marked effect on dopamine active transporter levels in SH5-cells exposed for 6 or 24 h. However, SH-SY5Y cells displayed an increase in dopamine transporter (DAT) levels following 24 h of exposure to BPA in contrast to DAT levels. BPA exposure produced no marked effect on D2 DA receptor levels in SH-SY5Y cells, yet a significant decrease in SH5-cells following both 6- and 24-h exposure periods was noted, suggesting that BPA exerts differential effects dependent upon cell type. BPA produced no significant effects on prolactin levels at 2 h, but a marked fall occurred at 24 h of exposure in SH-cells. Finally, to examine the effects of BPA on striatal DA release, striatal slices were exposed to BPA (0.2 NM) and DA release was measured. BPA significantly increased DA release, and DA levels were measured in perchloric acid (PCA)-DA using high-performance liquid chromatography (HPLC). Data demonstrated that chronic exposure to BPA did not significantly alter striatal DA levels in the SD rat.	J Toxicol Environ Health A. 2016;79(20):912-24.	10.1080/15287394.2016.1204577	27494678	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-

通毒性評価（動物）1：該当、0：該当しない　通毒性評価（疫学）1：該当、0：該当しない　通毒性評価（in vitro）1：該当、0：該当しない　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2505	O'Brien E et al.	2014	Perinatal bisphenol A exposure beginning before gestation enhances allergen sensitization, but not pulmonary inflammation, in adult mice	Bisphenol A (BPA), a monomer of polycarbonate plastics and epoxide resin, is a high production volume chemical implicated in asthma pathogenesis; when exposure occurs in the developing fetus. However, few studies have directly examined the effect of in utero and early life BPA exposure on the pathogenesis of asthma in adulthood. This study examines the influence of perinatal BPA exposure through maternal diet on allergen sensitization and pulmonary inflammation in adult offspring. Female C57BL/6 mice were fed a diet containing 0 (control), 10, 100, or 1000 μg BPA/kg body weight/day (BW/day) for 2 weeks prior to mating and throughout gestation and lactation until postnatal day (PND) 21 when offspring were weaned onto the control diet. Twelve week old offspring were sensitized to ovalbumin (OVA) and subsequently challenged with aerosolized OVA. Sera, splenocytes, bronchoalveolar lavage fluid and whole lungs were harvested to assess allergen sensitization and pulmonary inflammation after OVA challenge. Serum OVA-specific IgE was significantly increased in offspring exposed to 10 μg BPA/kg BW/day during gestation and lactation, relative to control. However, BPA exposure did not affect proliferation, production of interleukin-13 and interferon-gamma were increased in OVA-stimulated splenocytes recovered from BPA-exposed mice. Pulmonary inflammation, as indicated by total and differential leukocyte counts in bronchoalveolar lavage fluid, cytokines, chemokines, and pulmonary histopathology inflammatory scores, however, was either not different or was reduced in offspring exposed to BPA. Although these data suggest that perinatal BPA exposure beginning before gestation enhances allergen sensitization by increasing serum IgE and splenocyte cytokine production, a substantial impact of BPA on OVA-induced pulmonary inflammation in adulthood was not observed.	J Dev Orig Health Dis. 2014 Apr;5(2):121-31.	10.1017/S204017441400004X	24847698	動物	免疫	1	1	0	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	●	-	-	-	-	-
統合_2506	O'Brien E et al.	2014	Perinatal bisphenol A exposures increase production of pro-inflammatory mediators in bone marrow-derived mast cells of adult mice	Bisphenol A (BPA) is a widely used monomer of polycarbonate plastics and epoxide resin that has been implicated in asthma pathogenesis; when exposure occurs in the developing fetus. However, few studies have examined the relationship between perinatal BPA exposure and asthma pathogenesis in adulthood. This study used an isogenic mouse model to examine the influence of perinatal BPA exposure via maternal diet on inflammatory mediators associated with asthma in 6-month-old adult offspring by measuring bone marrow-derived mast cell (BMMC) production of pro-inflammatory cytokines and prostaglandin (PG) synthesis. Interleukin (IL)-1, -5, -6, -9, -13, and tumor necrosis factor (TNF)-alpha, and leukotriene (LT)B4 and PGD2 were measured in BMMC supernatants. Female C57BL/6 mice were fed a diet containing 0 (control), 10, 100, or 1000 μg BPA/kg body weight/day (BW/day) for 2 weeks prior to mating and throughout gestation and lactation until postnatal day (PND) 21 when offspring were weaned onto the control diet. Following BMMC activation, increases in cytokine production by 1.5-10.5 and TNFalpha by ~2.500, and production of LTB4 and PGD2 by ~1.500 and 6-13.5-fold, respectively, were observed in the high exposure group. Additionally, BMMCs from adult mice in all exposure groups displayed a decrease in global DNA methylation compared to control animals. Thus, perinatal BPA exposure displayed a long-term influence on mast cell-mediated production of pro-inflammatory mediators associated with asthma and global DNA methylation levels, suggesting a potential for mast cell dysregulation, which could affect pulmonary inflammation associated with allergic airway disease into adulthood.	J Immunotoxicol. 2014 Jul-Sep;11(3):205-12.	10.3109/1547691X.2013.822036	23914806	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	●	-	-	-	-
統合_2507	Özaydın T, Özmurlu V, Su E, Çelik İ, Uluışık D.	2018	The effects of bisphenol A on some plasma cytokine levels and distribution of CD8(+) and CD4(+) T lymphocytes in spleen, ileal Peyer's patch and bronchus associated lymphoid tissue in rats	The effects of bisphenol A on the some plasma cytokine levels and distribution of CD8(+) and CD4(+) T lymphocytes in spleen, ileal Peyer's patch and bronchus- associated lymphoid tissue in rats were investigated. A total of twenty-eight female Wistar albino rats were divided into four groups including 8 rats in each one: control, vehicle, BPA 5, BPA 50 and BPA 500 groups. Doses of 5, 50 and 500 mg/kg BPA were dissolved in ethanol, then mixed with corn oil. The control group received no treatment. The vehicle group was given the ethanol- corn oil mixture. BPA 5, BPA 50 and BPA 500 groups were given, respectively, 5, 50, and 500 mg/kg/day orally. In blood samples, IL-1, IL-6, IL-10, and TNF- alpha plasma levels were determined with ELISA. Tissue samples taken from spleen, ileal Peyer's patches and bronchus were processed by means of routine histological techniques. CD8 and CD4 were stained immunohistochemically. Data obtained from this study showed that, BPA causes the alteration on immune parameters including cytokine profile, distribution of CD8(+) and CD4(+) T lymphocytes in spleen and ileal Peyer's patches. Present study indicated that BPA may affect immune systems even at lower doses.Disruption of immune system cells and cytokine levels can result in harmful outcomes triggering autoimmune diseases and immunodeficiencies.	Acta Histochem. 2018 Nov;120(8):728-733.	10.1016/j.acthis.2018.08.002	30107890	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	-
統合_2508	Özaydın T et al.	2018	Effects of bisphenol A on antioxidant system and lipid profile in rats	We investigated the effects of bisphenol A (BPA) on antioxidant system enzymes, blood lipid profile and histologic structure of liver and pancreas in rats. We used 32 8-week- old male Wistar albino rats. The animals were divided into four groups of eight: control, vehicle, BPA 5, BPA 50 and BPA 500. BPA was dissolved in ethanol, then mixed with corn oil. The control group was untreated. The vehicle group was given the ethanol- corn oil mixture. The BPA 5, BPA 50 and BPA 500 groups were given 5, 50, and 500 mg/kg body weight/day, respectively. After 8 weeks, blood and tissue samples were obtained from the animals under ether anesthesia. TBARS, SOD, GPx, CAT, NO, total cholesterol, triglyceride, HDL, LDL, insulin and glucose were measured. The cavities were stained using Hale-Hematoxylin-Eosin-Mallory-Heidenhain trichromic methods. BPA significantly decreased the SOD, GPx, CAT, NO, HDL and insulin levels and increased the TBARS, total cholesterol, triglyceride, LDL and glucose levels in a dose-dependent manner. Histopathologically, BPA caused degeneration in the hepatocytes and immunoreactive cells in islets, increased significantly in the BPA 500 group. The H-score of the BPA 5 and BPA 50 groups decreased significantly compared to controls. We found that BPA caused oxidative stress and disruption of pancreatic beta-cell function. Therefore, BPA is a risk factor for animal and human health.	Biotech Histochem. 2018;93(4):231-238.	10.1080/10520295.2017.1420821	29388445	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	-
統合_2512	Rashid H et al.	2018	Bisphenol A-Induced Endocrine Toxicity and Male Reproductopathy are Mediated by the Dietary Iron Deficiency	INTRODUCTION: Bisphenol A (BPA) is suspected to cause hormonal imbalance in humans. Dietary factors are known to bring changes in hormonal profile. In order to study chemico-biological interactions of iron deficiency on toxicity outcome of BPA exposure, we studied the modulatory effects of iron deficiency on the hormone levels in rats chronically exposed to BPA. METHODS: Weanling rats maintained on normal and iron deficient diet were exposed to low level of BPA at 0, 5, 5 and 10 μg/rat/day for six months through drinking water. The serum levels of thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone, progesterone, estradiol, prolactin and corticosterone were measured in the serum by enzyme linked immunosorbent assay (ELISA). Histopathology was performed to check the pathological changes in gonads. RESULTS: No significant change was observed in TSH, progesterone and estradiol levels at 5 and 10 μg/rat/day BPA exposure in iron deficient rats. However, 5 μg/rat/day BPA exposure in iron deficient rats showed significant increase in LH, FSH, testosterone and prolactin levels. Sham (0 μg/rat/day BPA) and 10 μg/rat/day BPA exposure in iron deficient rats were used as a reference category. Exposure-operated gestation and lactation with dams gavaged from gestational day 5 until birth and then the offspring gavaged directly from postnatal day 5 until birth and then the offspring gavaged directly from postnatal day 5 until later began. Offspring were then gavaged directly from the day after birth until the day before scheduled sacrifice on postnatal days 21 or 90. Using in vitro hybridization, one or more BPA doses produced significant increases in the number of cells expressing mRNA for ERα, ERβ, and AR in the anterior pituitary gland, hypothalamus, and testis. Similarly, there was a dose-related increase in the adult female and BPA-and male animals were BPA50, relative to vehicle controls. BPA did not simply reproduce ER effects, indicating that BPA is not acting solely as an estrogen mimic. The possible consequences of long- term changes in hypothalamic ESR expression resulting from subchronic low dose BPA exposure on neuroendocrine effects are discussed and being addressed in ongoing, related work.	Endocr Metab Immune Disord Drug Targets. 2018;18(6):626-636.	10.2174/1871530318666180521095443	29779488	動物	ホルモンレベル	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	●	-	-	-	-	-
統合_2513	Rebuli ME et al.	2015	Impact of Low-Dose Oral Exposure to Bisphenol A (BPA) on Juvenile and Adult Rat Exploratory and Anxiety Behavior: A CLARITY-BPA Consortium Study	Bisphenol A (BPA) is a high volume production chemical and has been identified as an endocrine disruptor, prompting concern that developmental exposure could impact brain development and behavior. Rodent and human studies of BPA effects on ER-dependent behaviors have yielded inconsistent findings, and the CLARITY-BPA program was designed to address potential sources of variability in the literature. To address this, the present studies were conducted as part of the CLARITY- BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity) program. The impact of perinatal BPA exposure (2.5, 25, or 2500 microg/kg body weight (bw)/day) on behaviors related to anxiety and exploratory activity was assessed in juvenile (prepubertal) and adult (NCTR Sprague-Dawley) rats of both sexes. Oil/ethinyl estradiol (EE) microg/kg bw/day) was used as a reference category. Exposure spanned gestation and lactation with dams gavaged from gestational day 6 until birth and then the offspring gavaged directly from postnatal day 1 until later. Offspring were then gavaged directly from the day after birth until the day before scheduled sacrifice on postnatal days 21 or 90. Using in vitro hybridization, one or more BPA doses produced significant increases in the number of cells expressing mRNA for ERα, ERβ, and AR in the anterior pituitary gland, hypothalamus, and testis. Similarly, there was a dose-related increase in the adult female and BPA-and male animals were BPA50, relative to vehicle controls. BPA did not simply reproduce ER effects, indicating that BPA is not acting solely as an estrogen mimic. The possible consequences of long- term changes in hypothalamic ESR expression resulting from subchronic low dose BPA exposure on neuroendocrine effects are discussed and being addressed in ongoing, related work.	Toxicol Sci. 2015 Dec;148(2):341-54.	10.1093/toxsci/kfv163	26209558	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-	●
統合_2514	Rebuli ME et al.	2014	Investigation of the Effects of Subchronic Low Dose Oral Exposure to Bisphenol A (BPA) and Ethinyl Estradiol (EE) on Estrogen Receptor Expression in the Juvenile and Adult Female Rat Hypothalamus	Concerns have been raised regarding the long-term impacts of early life exposure to the ubiquitous environmental contaminant bisphenol A (BPA) on brain organization. Because BPA has been reported to affect estrogen signaling, and steroid hormones play a critical role in brain sexual differentiation, there is also concern that BPA exposure could alter neural sex differences. Here, we examine the impact of subchronic exposure from gestation to adulthood to oral doses of BPA below the current no-observed-adverse-effect level (NOAEL) of 5 mg/kg body weight (bw)/day on estrogen receptor (ESR) expression in sexually dimorphic brain regions of prepubertal and adult female rats. The dams were gavaged daily with vehicle (0.3% carboxymethylcellulose), 2.5, 25, 250, or 2500 mg BPA/kg bw/day, or 0.1 or 1.0 mg ethinyl estradiol (EE)/kg bw/day from gestational day 6 until later began. Offspring were then gavaged directly from the day after birth until the day before scheduled sacrifice on postnatal days 21 or 90. Using in situ hybridization, one or more BPA doses produced significant increases in the number of cells expressing mRNA for ERα, ERβ, and androgen receptor (AR) in the anterior pituitary gland, hypothalamus, and testis. Similarly, there was a dose-related increase in the adult female and BPA-and male animals were BPA50, relative to vehicle controls. BPA did not simply reproduce EE effects, indicating that BPA is not acting solely as an estrogen mimic. The possible consequences of long- term changes in hypothalamic ESR expression resulting from subchronic low dose BPA exposure on neuroendocrine effects are discussed and being addressed in ongoing, related work.	Toxicol Sci. 2014 Jul;140(1):190-203.	10.1093/toxsci/kfu074	24752507	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_2515	Rebuli ME et al.	2016	Sex differences in microglial colonization and vulnerabilities to endocrine disruption in the social brain	During development, microglia, the resident immune cells of the brain, play an important role in synaptic organization. Microglial colonization of the developing brain is sexually dimorphic in some regions, including nuclei critical for the coordination of social behavior, suggesting steroid hormones have an influence on microglia cells and their response to estrogens. By extension, microglial colonization may be a mechanism for endocrine disruption. Concerns have been raised regarding the potential for endocrine disrupting compounds (EDCs) to alter brain development and behavior. Developmental exposure to Bisphenol A (BPA), a ubiquitous EDC, has been associated with altered sociosexual and rough-and-tumble behaviors in various animal models and children. Through a comparison of the parent-to-sexual Wistar rat (Rattus norvegicus) and the socially monogamous prairie vole (Microtus ochrogaster), we are the first to observe that developmental exposure to the synthetic estrogen ethinyl estradiol (EE) or BPA alters the sex-specific colonization of the hippocampus and amygdala by microglia.	Gen Comp Endocrinol. 2016 Nov 1;238:39-46.	10.1016/j.ygcen.2016.04.018	27102938	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_2516	Sadowski RN et al.	2014	Effects of perinatal bisphenol A exposure during early development on radial arm maze behavior in adult male and female rats	Previous work has shown that exposure to bisphenol A (BPA) can affect anxiety behavior. However, no studies have examined whether administration of this endocrine disruptor during the perinatal period has the potential to induce alterations in cognitive behavior in both adult males and females, as assessed in an appetitive spatial learning task. The goal of the current study was to determine whether exposure to different doses of BPA during early development alters performance on the 17-arm radial maze in adulthood in Long-Evans rats. Oral administration of corn oil (vehicle), 0 mg/kg, 50 mg/kg, or 500 mg/kg BPA to the dams occurred daily throughout gestation and lactation. Subjects were tested on the 17-arm radial maze beginning on postnatal day (PND) 90. Rats were trained to locate food rewards at the ends of 8 arms during 15 daily sessions. Various indices of learning and memory, including working memory errors, reference memory errors, and latency to locate food, were evaluated. Results indicated that after exposure to BPA at both 0 and 500 mg/kg/day, rats of both sexes had decreased levels of HVA at weaning. There were no significant effects of BPA on performance on the radial arm maze in males or females. In conclusion, exposure to BPA during early development had modest effects on circulating hormones but did not affect performance on a spatial learning and memory task.	Neurotoxicol Teratol. 2014 Mar-Apr;42:17-24.	10.1016/j.ntt.2014.01.002	24440629	動物	内分泌、発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_2517	Sadowski RN et al.	2014	Early exposure to bisphenol A alters neuron and glia number in the rat prefrontal cortex of adult males, but not females	Previous work has shown that exposure to bisphenol A (BPA) during early development can alter sexual differentiation of the brain in rodents, although few studies have examined effects on areas of the brain associated with cognition. The current study examined if developmental BPA exposure alters the total number of neurons and glia in the medial prefrontal cortex (mPFC) in adulthood. Pregnant Long-Evans rats were orally exposed to 0 mg/kg, 50 mg/kg, or 500 mg/kg BPA to the dams throughout gestation and lactation. Offspring were euthanized on PND 90 and the mPFC was dissected. The density of neurons and glia in three layers was quantified stereologically with the optical fractionator, and brain region volume was estimated by volume Cavalieri. Males exposed to 500 mg/kg BPA were found to have increased numbers of neurons and glia in layers 5/6. Although there were no significant effects of BPA in layers 1/2, the pattern of increased neuron number in males exposed to 500 mg/kg BPA was similar to that seen in layers 5/6. No effects of BPA were seen in females, or in males exposed to the other doses of BPA. This study indicates that males are more susceptible to the long-lasting effects of BPA on anatomy of the mPFC, an area implicated in neurological disorders.	Neuroscience. 2014 Oct 24:279:122-31.	10.1016/j.neuroscience.2014.08.038	25193849	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_2518	Saura M et al.	2014	Oral administration of bisphenol A induces high blood pressure through angiotensin II/CaMKII-dependent uncoupling of eNOS	Bisphenol A (BPA) is found in human urine and fat tissue. Higher urinary BPA concentrations are associated with arterial hypertension. To shed light on the underlying mechanism, we orally administered BPA (5 still to 350 mg/kg/d) in drinking water to 8- to- and 250- mice over 30 d. Mice developed dosage- dependent high blood pressure (systolic 138 +/- 7 (2 vs. 170 +/- 12 mmHg (C57BL/6 male)). Impairment of endothelium (Ach- induced carotid relaxation (0.66 +/- 0.06 vs. 0.41 +/- 0.1 rad; n.5-7 fold increase in animal angiotensin II (AngII; an 87-fold increase in eNOS mRNA and protein, and significant eNOS-dependent superoxide and peroxynitrite accumulation. AngII inhibition (olmesartan) or BPA withdrawal reduced oxidative stress and normalized blood pressure and endothelium dysfunction. BPA exposure in human endothelial cells (HUVEC) induced eNOS uncoupling and peroxynitrite formation, which suggests that BPA- induced endothelial dysfunction by promoting oxidative and nitrosative stress. Microarray analysis of mouse aortic endothelial cells revealed a 2.5-fold increase in expression of calcium/calmodulin-dependent protein kinase II (CaMKII) gene (Camk2d) by BPA. Western blot analysis confirmed CaMKII activation (phosphorylation) by BPA. Pharmacological inhibition of CaMKII (KN-93) or its selective inhibitor (AIP) reduced BPA-mediated increase of superoxide. Administration of CaMKII alpha inhibitor tat-CN-21 reduced BPA-induced blood pressure and endothelial dysfunction in mice, and restored BPA-mediated carotid constriction in response to treatment with AngII. Given that CaMKII alpha inhibition prevents BPA-mediated high blood pressure, our data suggest that BPA regulates blood pressure by inducing AngII/CaMKII alpha-uncoupling of eNOS.	FASEB J. 2014 Nov;28(11):4719-28.	10.1096/fj.14-252460	25103225	動物	心血管	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-	-
統合_2519	Shi M et al.	2018	Prenatal exposure to bisphenol A analogues on male reproductive functions in mice	This study was performed to examine whether prenatal exposure to bisphenol (BP) A analogues, BPS and BPF, negatively impacts male reproductive functions and toxic development using mice as a model. CD-1 mice were orally administered with vehicle (0.5% carboxymethylcellulose), BPA, BPS or BPF at 0.2 mg/kg/day from gestation day 0 to postnatal day 21. Male offspring were sacrificed at 8 weeks of age. Compared to BPA, BPS or BPF at environmental dose (EPA 50 μg/kg/day) or BPA exposure at human dose (5 mg/kg/day), exposure to BPS, BPF and BPA altered the expression of genes and proteins involved in steroidogenesis, reduced testosterone synthesis, and exhibited an abnormal distribution of the stages of spermatogenesis. Furthermore, BPS with a dose of 50 mg/kg/day increased a level of serum estradiol (Tukey's post-hoc, 2H-PAGO). BPS and BPF significantly increased TUNEL-positive cells in neonatal testis, following disruption of the expression of apoptosis, autophagy, and oxidative stress-related factors. In addition, the expression of methyltransferases for DNA methylation and histone modification was also affected by prenatal exposure to BPA, BPS, or BPF in neonatal testis. These results suggest that prenatal exposure to BPS and BPF still physiologically relevant doses affects male reproductive functions probably due to spermatogenic defect in the developing testis.	Toxicol Sci. 2018 Jun 1;163(2):620-631.	10.1093/toxsci/kfy061	29741722	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	●	-	-	-	-	-
統合_2520	Srivastava S and Gupta P	2016	Genotoxic and infertility effects of bisphenol a on wistar albino rats	The plastic monomer and plastic lure bisphenol A (BPA) is one of the highest volume chemicals produced worldwide. It is used in the production of polycarbonate plastics and epoxy resins used in many consumer products. The study was designed to determine genotoxic and infertility effect of BPA. Adult male wistar albino rats were orally administered with various doses of BPA (5 mg, 50 μg and 100 μg/100g bw) and mated. 5 mg/100g bw) once a day for 90 days. Decline in testicular protein and DNA level and increases in the frequency of micronucleus in polychromatic erythrocytes and nonchromatic erythrocytes were observed at various dose levels as compared to control and vitamin E intervention groups. Study concludes that, BPA exposure partly inhibit the reproductive function in male rat and cause genotoxicity whereas, supplementation of vitamin E during BPA exposure have certain protective effect on reproductive inhibition caused by BPA exposure.	International Journal of Pharmaceutical Sciences Review and Research.2016;41(1):126-131	-	-	動物	遺伝毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	●	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2522	Sullivan AW et al.	2014	A Novel Model for Neuroendocrine Toxicology: Neurobehavioral Effects of BPA Exposure in a Prosocial Species, the Prairie Vole (Microtus ochrogaster)	Impacts on brain and behavior have been reported in laboratory rodents after developmental exposure to bisphenol A (BPA), raising concerns about possible human effects. Epidemiological data suggest links between prenatal BPA exposure and altered affective behaviors in children, but potential mechanisms are unclear. Disruption of neurotrophic oxytocin (OT)/vasopressin (AVP) pathways have been proposed, but supporting evidence is limited. We used a novel animal model, the prairie vole (Microtus ochrogaster), to investigate the effects of BPA exposure on OT and AVP systems in socially relevant brain regions. Voles were orally exposed to 0 mg/kg body weight/day (bw/d), 50 mg/kg bw/d, or 50 mg/kg bw/d BPA in addition to potential dose (5, 0.5, 5 pbw) to corn kernel and sweet cereal mash and fed to parties preference as adults. Brains were then collected and assessed for immunoreactive OT/oxytocin hydroxylase (TH) to dopamine-marked neurons in the principal bed nucleus of the stria terminalis (pBNST) and TH-ir neurons in the ventral tegmental area (VTA). Results: Adult female voles exposed to 50 mg/kg bw/d BPA showed a significant increase in OT-ir neurons in the pBNST, but not in the VTA. Exposure to 50 mg/kg bw/d BPA was associated with a significant increase in OT-ir neurons in the posterior PVN and fewer OT-ir neurons in the posterior PVN. At the 5 lowest doses, BPA administered sex differences in PVN TH-ir neuron numbers and reversed this sex difference at the highest dose. Minimal behavioral effects were observed in BPA-exposed males. These data support the hypothesis that BPA alters affective behaviors, potentially via disruption of OT/AVP pathways.	Endocrinology. 2014 Oct;155(10):3867-81.	10.1210/en.2014-1379	25051448	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2523	Tarapore P et al.	2016	Data on spermatogenesis in rat males gestationally exposed to bisphenol A and high fat diets	This data article contains supporting information regarding the research article entitled "High butter fat diet and bisphenol A additively impair male rat spermatogenesis" (P. Tarapore, M. Hennessy, D. Song, J. Ying, B. Ouyang, Y. Govindarajah, et al.,). Sprague-Dawley females were fed 60% high fat butter, 2 (butter only) or ad libitum, or high fat butter plus four bisphenol A doses (2500 micrograms/liter or 250 micrograms/liter in 0.25% micrograms/liter in 0.25% micrograms/liter in 0.25%

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2537	Weinhaus C et al.	2015	Stat3 is a candidate epigenetic biomarker of perinatal Bisphenol A exposure associated with murine hepatic tumors with implications for human health	Bisphenol A (BPA) is an endocrine disrupting chemical (EDC) that has been implicated as a potential carcinogen and epigenotoxicant. We have previously reported dose-dependent incidence of hepatic tumors in 10-month-old isogenic mice perinatally exposed to BPA. Here, we evaluated DNA methylation at 3 candidate genes (Esr1, Stat3, and Stat5) in liver tissue of BPA-exposed mice collected at 2 time points: post-natal day 21 (PND21) and 10 months (10M). Bisulfite sequencing revealed that Stat3 was significantly hypermethylated in 10M tumors relative to 10M normal tissue (p = 0.0001) and PND21 normal tissue (p = 0.0001). 10M tumors from mice BPA-treats. Candidate genes were chosen based on dose-dependent changes in gene expression observed in both rodent and human hepatocellular carcinoma (HCC). Regions for bisulfite sequencing were chosen by mining whole genome next generation sequencing methylation datasets of both mice and human liver samples with known perinatal BPA exposures. One of 3 candidate genes, Stat3, displayed dose-dependent DNA methylation changes in both 10-month mice with liver tumors as compared to those without liver tumors and in and in utero mice from the same exposure study, implicating Stat3 as a potential epigenetic biomarker of both early life BPA exposure and adult disease in mice. DNA methylation profiles within STAT3 varied with liver tissue (BPA liver) in human total liver samples as well, suggesting STAT3 may be a translationally relevant candidate biomarker. These data indicate Stat3 as a potential early life biomarker of adult murine liver tumor risk following early BPA exposure with early evidence of relevance to human health.	Epigenetics. 2015;10(12):1099-110.	10.1080/15592294.2015.1107694	26542749	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-
統合_2538	Weinhaus C et al.	2016	Epigenome-wide DNA methylation analysis implicates neuronal and inflammatory signaling pathways in adult murine hepatic tumorigenesis following perinatal exposure to bisphenol A	Developmental exposure to the endocrine active compound bisphenol A (BPA) has been linked to epigenomics and potential carcinogenic effects in rodent liver, prostate, and mammary glands. A dose-dependent increase in hepatic tumors in 10-month-old mice perinatally exposed to one of three doses of BPA (50 ng, 50 microg, or 50 mg BPA/kg chow) was previously reported. These tumors represent early-onset disease and lack classical sexual dimorphism in its incidence. Here, adult epigenome-wide DNA methylation profiles in BPA-induced liver tumors were investigated. Mice with hepatic tumors showed 12,802 (1.8%) probes with differential methylation as compared with non-tumor controls, of which 8,496 (67.6%) were hypermethylated. A significant enrichment of hypermethylated CpG probes in CpG islands located within the promoter regions of genes was observed in tumors. Pathway analysis revealed that genes associated with hypermethylated tumor-specific probes were involved in neuronal signaling pathways linked to energy regulation and metabolic function, supporting metabolic consequences in the liver as BPA-induced disruption of neuronal signaling pathways. Hypothesis-driven pathway analysis revealed mouse and human genes linked to BPA exposure related to intracellular Ca(2)(+) and MAPK signaling pathways. Taken together, these findings are indicative of the relevance of the hepatic tumor phenotype seen in BPA-exposed mice to human health. This work demonstrated that epigenome-wide discovery experiments in animal models were effective tools for identification and understanding of xenobiotic mechanisms salient to human disease. Environ. Mol. Mutagen. 57:439–456, 2016. (c) 2016 Wiley Periodicals, Inc.	Environ Mol Mutagen. 2016 Jul;57(6):435-46.	10.1002/em.22024	27334623	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-
統合_2539	Wise LM et al.	2016	Long-term effects of adolescent exposure to bisphenol A on neuron and glia number in the rat prefrontal cortex: Differences between the sexes and cell type	Bisphenol A (BPA), an endocrine disruptor used in a variety of consumer products, has been found to alter the number of neurons in multiple brain areas in rats following exposure to perinatal development. Both the number of neurons and glia in the prefrontal cortex (PFC) undergo significant changes during adolescence, and are susceptible to disruption by gonadal hormones. The present study examined Long-Evans male and female rats that were administered BPA (0, 0.40, or 400mg/kg/day) during adolescent development (postnatal days 27-58). In adulthood (postnatal day 150), the number of neurons and glia in the mPFC were stereologically assessed in methylene blue/azure II stained sections. There were no changes in the number of neurons, but there was a significant dose by sex interaction in number of glia in the mPFC. Pairwise comparisons between controls and each dose revealed a significant increase in the number of glia between 0 and 40mg/kg/day in females, and a significant decrease in the number of glia between 0 and 400mg/kg/day in males. In order to determine the type of glial cells that were changing in these groups, in response to adolescent BPA administration, adjacent sections were labelled with S100beta (astrocytes) and IBA1 (microglia) in the mPFC of the groups that differed. The number of microglia was significantly higher in females exposed to 40mg/kg/day than controls and more in males exposed to 0mg/kg/day than controls. There were no significant effects of adolescent exposure to BPA on the number of astrocytes in male or females. Thus, adolescent exposure to BPA produced long-term alterations in the number of microglia in the mPFC of rats, the functional implications of which need to be explored.	Neurotoxicology. 2016 Mar;53:186-192.	10.1016/j.neuro.2016.01.011	26828634	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2540	Wong RLY et al.	2019	Identification of Secretaglobin Scgb2a1 as a target for developmental reprogramming by BPA in the rat prostate	Secretaglobins are a superfamily of secreted proteins thought to participate in inflammation, tissue repair, and tumorigenesis. Secretaglobin family 2A member 1 (Scgb2a1) is a component of prostatein, a major androgen-regulated protein secreted by the rat ventral prostate (VP). Scgb2a1 is also expressed in the human prostate. We have shown that perinatal exposure to bisphenol A (BPA) results in the increased of adult rat's terminally exposed to bisphenol A (BPA), with increased gene expression confirmed by quantitative RT-PCR and immunohistochemistry/western blot in the VP of acinar/ductal epithelium. Bisulfite analysis of both CpG islands located within 10 kb of the Scgb2a1 promoter identified significant hypomethylation of the CpG island upstream of the transcription start site of this gene in the reprogrammed prostate. These data suggest that expression of Scgb2a1 in the adult prostate could be epigenetically reprogrammed by BPA exposure during prostate development, with potential implications for cancer risk and exposure to chemotherapeutics associated with prostatein binding.	Epigenetics. 2015;10(2):127-34.	10.1080/15592294.2015.1009768	25612011	動物	メカニズム	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	●	-	-	-	-
統合_2541	Wu JH et al.	2016	Oral administration of low-dose bisphenol A promotes proliferation of ventral prostate and upregulates prostaglandin D-2 synthase expression in adult rats	This study aims to assess the effect of low oral dose of bisphenol A (BPA) on proliferation of ventral prostate (VP) and expression of related genes in adult rats. Three-month-old male Sprague-Dawley rats were treated with BPA (0, 0.5, 5, 50, and 500 mg/kg/day) for 28 days. Histological examination revealed that BPA induced hyperplasia of the VP epithelium. Immunohistochemical staining showed that BPA increased the height of epithelial cells in the VP. Treatment with BPA increased serum testosterone levels and VP weight. Interestingly, BPA increased serum E2 and induced testosterone levels and significantly increased the estrogen to androgen ratio (p < 0.05). In addition, BPA significantly increased dihydrotestosterone (DHT) levels. Immunohistochemistry data showed that BPA significantly upregulated proliferating cell nuclear antigen expression (p < 0.01). Furthermore, microarray and reverse transcription-polymerase chain reaction analysis showed that BPA induced upregulation of prostaglandin-D synthase (Ptgds), Fas, Fasl1, and complement factor B (Cfb)as well as downregulation of Ptgs2 and Fasl1 in the VP. These results indicated that environmental exposure to low doses of BPA may induce proliferation of VP in adult rats by increasing the estrogen to androgen ratio and upregulating expression of Ptgds to promote production of DHT.	Toxicol Ind Health. 2016 Nov;32(11):1848-1858.	10.1177/0748233715590758	26088557	動物	前立腺	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	●	-	-	-	-
統合_2542	Wyatt BS et al.	2016	Sex- and Strain-dependent Effects of Bisphenol A Consumption in Juvenile Mice	Children are directly exposed to bisphenol A (BPA) and other putative environmental obesogens through both diet and household products. The purpose of this study was to investigate sex- and genetic-dependent effects of BPA consumption on traits relevant to obesity and Type 2 diabetes in juveniles, using mice as a models. Two strains of mice (C57BL/6J and DBA/2J) were chosen to represent divine genetic backgrounds that differ in susceptibility to obesity and insulin resistance. Male and female mice of each strain consumed BPA at three doses in drinking water from four to eleven weeks of age. Male but not female mice of each strain consuming BPA were significantly taller than controls. BPA induced correspondingly changes in adipose tissue gene expression and metabolite abundance that indicate effects on adipogenesis and energy utilization. BPA consumption also altered the synthesis of adipokines, circulating factors that modulate insulin sensitivity and atherogenesis, in C57BL/6J but not DBA/2J males. Conversely, effects of BPA on plasma insulin were only observed in DBA/2J males. Thus, BPA consumption has sex-specific effects in the two strains. These results suggest that dietary BPA may exacerbate childhood obesity and its consequences, and that sex and genetic background are important determinants of the physiological impact of BPA.	Journal of Diabetes & Metabolism.2016;7(8):10	10.4172/2155-6156.1000694	-	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2544	Yang ML et al.	2016	Bisphenol A Promotes Adiposity and Inflammation in a Nonmonotonic Dose-response Way in 5-week-old Male and Female C57BL/6J Mice Fed a Low-calorie Diet	A growing body of epidemiological research show that Bisphenol A (BPA) is positively correlated with obesity and metabolic disorders. However, the mechanisms of BPA on adiposity remain largely unknown. In this study, we found that 5-week-old male and female C57BL/6J mice exposed to low dosages of BPA (5, 50, 500, and 5000 mug/kg/d) by oral intake for 28 days showed significantly increased body weight and fat mass in a nonmonotonic dose-dependent manner when fed a chow diet. The effect occurred even at the lowest concentration (5 mug/kg/d), lower than the tolerable daily intake of 50 mug/kg/day for BPA. However, no significant difference in body weight and fat mass was observed in either male or female mice fed a high-fat diet. Our findings suggest that BPA may interact with diet to promote obesity risk. In vivo study revealed that BPA treatment altered the differentiation of white adipocyte progenitors, from the stromal vascular fraction, partially through glucocorticoid receptor. BPA exposure increased circulating inflammatory factors and the local inflammation in white adipose tissue (WAT) of male mice fed a chow diet. Moreover, BPA treatment induced hepatic steatosis and inflammation, which was associated with increased circulating inflammatory factors and elevated TNFalpha in female subjects. Body mass index (~23.0 kg/m(2)) but not in female subjects or in both sexes of overweight/obese subjects; body mass index (~31.0 kg/m(2)). In conclusion, we demonstrated the nonmonotonic dose-effects of BPA on adiposity and chronic inflammation in 5-week-old mice, which is related to caloric uptake.	Endocrinology. 2016 Jun;157(6):2333-45.	10.1210/en.2015-1926	27145005	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2545	Yang SM et al.	2017	Dysregulated Autophagy in Hepatocytes Promotes Bisphenol A-Induced Hepatic Lipid Accumulation in Male Mice	Accumulating evidence suggests that bisphenol A (BPA) exposure is associated with nonalcoholic fatty liver disease. Disruption of autophagy causes lipid accumulation in hepatocytes. Whether and how BPA regulates autophagy remains to be explored. We investigated the effect of BPA on autophagy in hepatocytes and examined the influence of BPA-regulated autophagy on hepatic lipid accumulation. Male CD1 mice were treated with BPA (0, 0.05, 5, or 50 mg/kg/day) by oral gavage for 28 days. BPA exposure induced hepatic lipid accumulation and autophagosome formation. BPA treatment increased the number of autophagosomes in hepatocytes and cells. Lipid content in HepG2 cells and in primary hepatocytes was increased obviously after BPA exposure. In addition, BPA exposure increased accumulation of autophagosomes in HepG2 cells and enhanced colocalization of fluoxy (RS)-583 with microtubule-associated protein light chain 3. These changes were accompanied with increased expression levels of a mammalian target of rapamycin, p-mTOR kinase, p-ULK1 and decreased expression of Beclin 1 and autophagy-related gene 7 (ATG7). Moreover, BPA treatment increased the number of acidic autophagic vesicles in HepG2 cells. The increased autophagic degradation was further evidenced by increased levels of p62 in BPA-treated HepG2 cells. At the whole animal level, BPA treatment induced dysfunction between fusions of mature CD1 mice, which was accompanied with changes in hepatic autophagy-related proteins. Moreover, induction of autophagy by Torin1 protected against BPA-induced lipid accumulation whereas suppression of autophagy by chloroquine exacerbated BPA-induced lipid accumulation in HepG2 cells. BPA dysregulates autophagy in hepatocytes, which is linked to BPA-induced hepatic lipid accumulation.	Endocrinology. 2017 Sep 1;158(9):2799-2812.	10.1210/en.2016-1479	28323964	動物	代謝	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_2546	Ye Y et al.	2019	Bisphenol A exposure alters placentation and causes preeclampsia-like features in pregnant mice involved in reprogramming of DNA methylation of WNT2	Preeclampsia leads to adverse outcomes for pregnant women. Bisphenol A (BPA) is an environmental endocrine disruptor and has been shown to be positively associated with increased risk of preeclampsia in human studies. We investigated whether BPA exposure causes preeclampsia-like features in pregnant mice and the associated underlying mechanisms. Experiments were performed in animal models and cell cultures. In pregnant mice, BPA exposure induced hypertension, proteinuria, and fetal growth restriction, which were accompanied with placental dysfunctions, including impaired placentation, placental oxidative stress, and glomerular atrophy. Urinary proteins was not affected. These preeclampsia-like features correlated with increased retention of smooth muscle cells and reduced vessels area at the junctional zone of the placenta. In addition, there were decreased expression of invasion-related genes including increased tissue inhibitors of metalloproteinases, decreased metalloproteinases, and Ets family member ERF(Ets6 r.)-which correlated with increased DNA methylation in its promoter region and upregulation of DNA methyltransferase (Dnmt3). BPA exposure impeded the interaction between the histone acetyltransferase cell line, HTR-8/SVneo, and endothelium cells. BPA exposure down-regulated WNT2 expression, and stimulated the DNA methylation of WNT2. These results were consistent with in vivo observations. Inhibition of DNMT in HTR-8/SVneo cells by 5-aza-2'-deoxycytidine (5-Aza) reversed the BPA-induced WNT2 down-regulation. Moreover, BPA exposure induced endoplasmic reticulum stress and apoptosis in placental trophoblasts, which may lead to the development of preeclampsia-like features in pregnant mice. Our results suggest that this phenomenon involves the epigenetic reprogramming and down-regulation of WNT2 mediated by DNMT1. Ye, Y., Tang, Y., Xiong, Y., Feng, J., Li, X. Bisphenol A exposure alters placentation and causes preeclampsia-like features in pregnant mice involved in reprogramming of DNA methylation of WNT2.	FASEB J. 2019 Feb;33(2):2732-2742.	10.1096/fj.201800934RRR	30303745	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	●	-	-	-	-
統合_2547	Yin L et al.	2017	The regulation of cellular apoptosis by the ROS-triggered PERK/EIF2 alpha chop pathway plays a vital role in bisphenol A-induced male reproductive toxicity	Bisphenol A (2,2-bis(4-hydroxyphenyl)propane; BPA) is ubiquitous in the environment, wildlife, and humans. Evidence from past studies suggests that BPA is associated with decreased semen quality. However, the molecular basis for the adverse effect of BPA on male reproductive toxicity remains unclear. We evaluated the effect of BPA on mouse spermatocyte GC-2 cells and adult mice, and we explored the potential mechanism underlying the BPA-induced male reproductive toxicity. Our results revealed that BPA induced GC-2 cell apoptosis and decreased sperm quality in adult male mice in a dose-dependent manner. In addition, BPA caused reactive oxygen species (ROS) accumulation. Previous study has verified that reduction-based ROS are the ingredients affecting the BPA-triggered ROS accumulation. We found that BPA induced damage to the endoplasmic reticulum (ER) in addition to mitochondria, and most ER-stress related proteins were activated in cellular and animal models. Knocking down of the PERK/EIF2 alpha pathway, one of the ER-stress pathways, partially recovered the BPA-induced cell apoptosis. In addition, an ROS scavenger attenuated the expression of the PERK/EIF2 alpha pathway related proteins. Taken together, these data suggested that the ROS-regulated PERK/EIF2 alpha pathway played a vital role in BPA-induced male reproductive toxicity.	Toxicol Appl Pharmacol. 2017 Jan 1;314:98-108.	10.1016/j.taap.2016.11.013	27894913	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	●	-	-	-	-
統合_2548	Yuan M et al.	2018	Environmentally relevant levels of bisphenol A affect uterine decidualization and embryo implantation through the estrogen receptor/serum and glucocorticoid-regulated kinase 1/epithelial sodium ion channel alpha-subunit pathway in a mouse model	OBJECTIVE: To investigate whether bisphenol A (BPA) exposure is associated with uterine decidualization and embryo implantation failure in mice. DESIGN: Experimental animal study and in vivo study. SETTING: University-based infertility center. ANIMALS: ICR mice. INTERVENTION(S): Mice treated with different doses of BPA. Isolated cells cultured in medium at different concentrations of BPA. MAIN OUTCOME MEASURE(S): Embryo implantation sites, uterine weight, quantitative real-time reverse transcriptase-polymerase chain reaction, Western blot analysis, hematoxylin and eosin staining, immunohistochemical, cell proliferation, and statistical analysis. RESULT(S): In the experiment of mouse model, administration of 1,000 mg/kg/day of BPA by gavage led to reduction of the number of embryo implantation sites in a dose-dependent manner. The uterine weight of the decidualized uterine horn of the mouse in groups exposed to BPA (100,000 and 1,000,000 mg/kg/day) was significantly lower than that of the control group. Hematoxylin and eosin staining revealed that the total weight of the decidualized uterine horn of the mouse in groups exposed to BPA (100,000 and 1,000,000 mg/kg/day) was significantly lower than that of the control group. Immunohistochemical results demonstrated that administration of 100, 1,000, or 10,000 mg/kg/day of BPA by gavage statistically significantly down-regulated the expression of epithelial Na(+) channel alpha-subunit (ENaCalpha) in the luminal epithelial cells and stromal cells in decidual cells of the rat's reduced decidualization uterine horns. Administration of 100 mg/kg/day BPA in embryo days 0.5-5.5 by gavage statistically significantly decreased the level of uterine serum and glucocorticoid-regulated kinase 1 (SGK1) protein expression on embryo days 5 and 6. After treatment with 100(2), 0.01, 0.1, or 1.0 mg/mL of BPA for 30 hours, the SGK1, ENaCalpha, and phospho-SGK1 (p-SGK1) protein expression in the mouse uterine epithelial cells was significantly down-regulated. CONCLUSION(S): Environmentally relevant levels of BPA (100 mg/kg/day) by gavage can impair embryo implantation in mice and BPA can affect decidualization of the uterus in mouse model. Our results suggest that BPA can down-regulate SGK1 and ENaCalpha protein expression through estrogen receptors in luteinous cells.	Fertil Steril. 2018 Apr;109(4):735-744.e1.	10.1016/j.fertnstert.2017.12.003	29605410	動物	子宮	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	●	-	-	-	-
統合_2549	Zhang Q et al.	2014	Exposure to bisphenol-A affects fear memory and histone acetylation of the hippocampus in adult mice	Bisphenol A (BPA), an environmental endocrine disruptor, has been reported to possess weak estrogenic, and non-estrogenic, and anti-androgen properties. Previous evidence indicates that perinatal exposure to low levels of BPA can affect hippocampal synaptic plasticity and learning and memory in offspring. However, the effects of BPA exposure on hippocampal function in adulthood remain unclear. In the present study, we investigated the effects of BPA in fear conditioning in adult male mice. The results indicated that exposure to BPA increased the freezing time in the fear conditioning training. Further molecular analysis revealed that BPA exposure increased the level of H3K9ac in the hippocampus and the mRNA level of dopamine receptor subunit D4(D4R) receptor subunit D4(D4) and increased the expressions of histone deacetylase 2 (HDAC2) before fear conditioning training in the hippocampus of male mice. One and twenty-four hours after fear conditioning training, BPA enhanced the changes of the expressions of NR2, phosphorylated extracellular-regulated protein kinases (ERK1/2), and histone acetylation induced by fear conditioning in the hippocampus. These results suggest that long-term exposure to BPA enhanced fear memory by the concomitant increased level of H3K9A receptor and/or the enhanced histone acetylation in the hippocampus, which may be associated with activation of ERK1/2 signaling pathway.	Horm Behav. 2014 Feb;65(2):106-13.	10.1016/j.yhbeh.2013.12.004	24333847	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	-	-	-	-	-
統合_2551	Zu-Gai A et al.	2015	The effects of in utero bisphenol A exposure on reproductive capacity in several generations of mice	In utero bisphenol A (BPA) exposure affects reproductive function in the first generation (F1) of mice; however, not many studies have examined the reproductive effects of BPA exposure on subsequent generations. In this study, pregnant mice (F0) were orally dosed with vehicle, BPA (50, 25, and 50 mug/kg/day) or diethylstilbestrol (DES; 0.05 mug/kg/day) daily from gestation day 11 until birth. F1 females were used to generate the F2 generation, and F2 females were used to generate the F3 generation. Breeding studies at the ages of 3, 6, and 9 months were conducted to evaluate reproductive capacity over time. Further, studies were conducted to evaluate the estrous cycle, histology of the ovaries, and serum hormone levels in the F1 generation. Exposure to 50 mug/kg/day BPA or 0.05 mug/kg/day DES significantly delayed the age of first estrus in the F1 generation compared to vehicle control. BPA or DES also delayed the age at vaginal opening in the F1 generation compared to vehicle control. Both DES (0.05 mug/kg/day) and BPA (50 mug/kg/day) significantly delayed the age of first estrus in the F1 generation compared to vehicle control. BPA exposure reduced gestational index in the F1 and F2 generations compared to control. Further, BPA exposure (0.5 mug/kg/day) compromised the fertility index in the F2 generation compared to control. Finally, in utero BPA exposure reduced the ability of female mice to maintain pregnancies as they aged. Collectively, these data suggest that BPA exposure affects reproductive function in female mice and that some effects may be transgenerational in nature.	Toxicol Appl Pharmacol. 2015 May 1;284(3):354-62.	10.1016/j.taap.2015.03.003	25771130	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	●	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2552	Vahdati HF et al.	2017	Protective effect of crocin on BPA-induced liver toxicity in rats through inhibition of oxidative stress and downregulation of MAPK and MAPKAP signaling pathway and miRNA-122 expression	Bisphenol A (BPA) is an artificial environmental endocrine-disrupting chemical and commonly used as a monomer of polycarbonate plastics and epoxy resins. The aim of the present study is to investigate the hepatoprotective effects of crocin, a constituent of saffron, against BPA-induced liver toxicity. We showed that treatment of male Wistar rats with 0.5 mg/kg BPA for 30 days increased the level of 8-isoprostane, malondialdehyde (MDA), and nitrotyrosine, and decreased the activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) in liver tissues. Administration of BPA increased the phosphorylation of c-Jun N-terminal kinase (JNK), extracellular-signal-regulated kinase (ERK) 1/2, and mitogen-activated protein kinase-activated protein kinase 2 (MAPKAPK2), but not p38. BPA also reduced the Akt signaling activation and upregulated microRNA (miR)-122 expression. Moreover, we showed here that crocin (25 mg/kg, administration ameliorated liver damage and improved elevated levels of TG and liver enzymes of BPA-treated rats possibly through antioxidant activity, downregulation of miR-122 transcript level and lowering the phosphorylation of JNK, ERK1/2, and MAPKAPK2 and subsequently liver activities. Overall, our findings suggest that crocin possesses hepatoprotective effects against BPA-induced liver toxicity by enhancing the antioxidative defense system and regulation of important signaling pathway activities and miR-122 expression.	Food Chem Toxicol. 2017 Sep;107(Pt A):395-405.	10.1016/j.fct.2017.07.007	28689058	動物	肝毒性	1	1	単独カラ：1	Wistar rat:1	3用量：1	0.5,5,50 mg/kg：1	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-
統合_2553	Weinhaus C et al.	2014	Dose-Dependent incidence of hepatic tumors in adult mice following perinatal exposure to Bisphenol A	BACKGROUND: Bisphenol A (BPA) is a high production volume chemical with hormone-like properties that has been implicated as a potential carcinogen. Early life exposure has been linked to increased risk for precancerous lesions in mammary and prostate glands and the uterus, but to prior study has shown a significant association between BPA exposure and cancer development. OBJECTIVE: We explored the effects of BPA exposure during gestation and lactation on adult incidence of hepatic tumors in mice. METHODS: Swiss CD-1 mice were given nine perinatal oral exposures to BPA through maternal feeding while undergoing one of four environmentally relevant doses of BPA (0, 10 ug, 10 mg, or 10 mg per kilogram of diet), and we followed approximately one male and one female per litter until they were 20 months of age. Animals were tested for known risk factors for hepatocellular carcinoma (HCC), including sex, litter effects, and body weight. Livers were examined for histopathological changes, and HCC was confirmed by immunohistochemistry. Serum was tested for BPA and liver tumors or preneoplastic lesions. We observed a statistically significant dose-response relationship, with animals who ate the environmentally relevant doses of 10 ug/kg/day (0.12, 0.22, 0.172) or more exposed to 10 ng BPA/g/day compared with unexposed controls. Observed early disease result, absence of bacterial or viral infection, and lack of characteristic sexual dimorphism in tumor incidence support a nonclinical etiology. CONCLUSIONS: To our knowledge, this is the first report of a statistically significant association between BPA exposure and hepatic tumors in any organ. Our results link early life exposure to BPA with the development of hepatic tumors in rodents, and have potential implications for human health and disease.	Environ Health Perspect. 2014 May;122(5):485-91.	10.1289/ehp.1307449	24487385	動物	発がん(肝がん)	1	1	1	----------	3用量：1	Mice: 10ug, 10ug, 10mg/kg/day	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	-	-	-	-	-	-
統合_2554	Churchwell MI et al.	2014	Comparison of life-stage-dependent internal dosimetry for bisphenol A, ethinyl estradiol, a reference estrogen, and endogenous estradiol to test an estrogenic mode of action in Sprague Dawley rats	Bisphenol A (BPA) was administered by gavage (3.5-350,000 mug/kg body weight [bw]/day) to pregnant Sprague Dawley dams, newborn pups, and continuing into adulthood. Aglycone (i.e., unconjugated and active) and total (aglycone + conjugated) concentrations were measured in serum and tissues using ultra-sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS). Ethinyl estradiol (EE2; 0.3 and 3 mug/kg bw/day) and the endogenous hormone, 17beta-estradiol (E2) and testosterone, were similarly evaluated. Mean BPA aglycone levels in adults and naive neonates (≤PND 10) ingesting untreated sample processing artifact, consistent with literature reports of a propensity for postexposure blood contamination by BPA. Direct measurements of BPA glucuronide in vehicle and naive control serum (1-3 nM) indicated unintentional exposure and metabolism at levels similar to those produced by 0.3 mug/kg bw/day. Despite careful attention to potential BPA contamination, vehicle, sham, saphenectomy, and dead-end rigorous dosing solution sterilization and delivery. The source of this exposure could not be identified, but interpretation of the toxicological effects, observed only at the highest BPA doses, was not compromised. Internal exposures to BPA and E2 aglycones were highest in pups at birth. When resolved serum concentrations from the two highest BPA doses, and both EE2 doses, were compared with concurrent levels in endogenous E2, the ED₅₀like dosing equivalents were similar to or above those of endogenous E2 in male and female rats of all ages tested. Such evaluations of estrogenic internal dosimetry and comprehensive evaluation of contamination impact should aid in extrapolating risks from human BPA exposures.	Toxicol Sci. 2014 May;139(1):4-20	10.1093/toxsci/kfu021	24496641	動物	ADME	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-
統合_2555	Sriwattara S et al.	2019	Dose exposure of Bisphenol- A on female Wistar rats fertility	Background 2,2-Bis (4-hydroxyphenyl propane [bisphenol A (BPA)] is one of the major environmental pollutants and has the adverse effects on human health. BPA mimics the structure of estrogen and binds to estrogen receptors and alters the secretion of the hormone. It is ingested in humans through the regular use of plastic containers, bottles, and food cans. Materials and methods Female Wistar rats were exposed orally to 0, 50, 500, and 800 mg BPA/kg body weight (bw. wt.) twice-weed in olive oil and administered every 24h for 3 months continuously through the mating, gestation and lactation periods to perform fertility, reproductive organ weight and hormones (LH (luteinizing hormone), FSH (follicle-stimulating hormone), estradiol (E2), progesterone (PROG) and PRL (prolactin)) were evaluated. Results: The findings revealed that females exposed to BPA exhibited a significant decrease in the number of corpora lutea, implantation sites, and litter size. Moreover, the number of resorbed fetuses was significantly increased in the BPA-treated groups. However, no significant difference was found in fertility rate, reproductive organ weight and hormonal levels. Conclusion: These data indicate an increased sensitivity to BPA needs careful evaluation of the current level of exposure.	Horm Mol Biol Clin Investig. 2019 May;7;38(2):/j/hmbci.2019.38.issue-2/hmbci-2018-0061/hmbci-2018-0061.xml.	10.1515/hmbci-2018-0061	31063457	動物	ホルモンレベル	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	●	-	-	-	-	-
統合_2556	Luo S et al.	2017	Effects of bisphenol A on inflammation and Th17 cells in adipose tissue of high-fat fed mice[Article in Chinese]	OBJECTIVE: To study the effects of bisphenol A (BPA) on inflammation and Th17 cells in adipose tissue of high fat fed mice. METHODS: 8 weeks old male C57 BL/6mice were fed at high fat diet (HFD) and were administered 10, 100 and 1000 mol·L-1 BPA by drinking water. The normal diet (ND) and HFD control groups were set as well. Body weight of mice was recorded weekly. Mice were sacrificed at eighth and sixteenth week, and the epididymal adipose tissue was collected. The mRNA expression of TNF-α, IL-6, IL-17A and IL-23 in adipose tissue was detected by real-time quantitative PCR (RT-qPCR). The IL-17 level in epididymal adipose tissue was detected by ELISA. Flow cytometry (FCM) was used to detect the Th17 cell in epididymal adipose tissue. RESULTS: Compared with ND control groups, HFD increased body weight of mice, enhanced the mRNA expression of inflammatory cells and the expression of TNF-α in adipose tissue. Also, the proportion of Th17 cells and the expression of IL-17 in adipose tissue were elevated in a dose-dependent way. And the effects at sixteenth week was more obvious than that at eighth week. CONCLUSION: BPA exposure can promote inflammation in adipose tissue of high fat fed mice and elevate the proportion of Th17 cells and the expression of IL-17. Th17 cells may play an important role in the effects BPA on adipose tissue inflammation.	Wai Sheng Yan Jiu. 2017 Jan;46(1):7-12.	-	29903144	動物	免疫	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2557	Prins GS et al.	2018	Evaluation of Bisphenol A (BPA) Exposures on Prostate Stem Cell Homeostasis and Prostate Cancer Risk in the NCTR-Sprague-Dawley Rat: An NIEHS/FDA CLARITY-BPA Consortium Study	BACKGROUND: Previous work determined that early life exposure to low- dose Bisphenol A (BPA) increased rat prostate cancer risk with aging. Herein, we report on prostate-specific results from CLARITY-BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity), which aims to resolve uncertainties regarding BPA toxicity. OBJECTIVES: We sought to a) measure whether a range of BPA exposures dose-dependently altered prostate stem cell homeostasis and cancer risk; and b) determine whether BPA exposure altered the prostate transcriptome. METHODS: CLARITY-BPA Core 1 Sprague-Dawley rats were exposed daily via oral gavage to BPA (0, 2.5, 25, 250, 2500, 25000 ug/kg bw/day) or ethinyl estradiol (EE) or 5α-estradiol (5AE) or 5α-dihydrotestosterone (DHT) and were evaluated at 1 year of age. Core 2 rats were orally exposed to BPA (0, 25, 250, 2500 ug/kg bw/day) or EE and were euthanized at 6 months, and prostate pathology was assessed at one year. Core 3 rats were orally exposed to BPA (0, 25, 250, 2500 ug/kg bw/day) or EE and were given testosterone propionate (TP) to induce prostatic hyperplasia. Ventral prostate (VP) lobes were evaluated for pathology. Core 4 rats were orally exposed to BPA (0, 25, 250, 2500 ug/kg bw/day) or EE and were given testosterone propionate (TP) and were euthanized at 6 months. Prostate lobes were evaluated for pathology. HCS was used to detect the expression of IL-17 in epididymal adipose tissue. Flow cytometry (FCM) was used to detect the proportion of Th17 cells in epididymal adipose tissue. RESULTS: Compared with ND control groups, HFD increased body weight of mice, enhanced the mRNA expression of inflammatory cells and the expression of TNF- in adipose tissue. Also, the proportion of Th17 cells and the expression of IL-17 in adipose tissue were elevated in a dose-dependent way. And the effects at sixteenth week was more obvious than that at eighth week. CONCLUSION: BPA exposure can promote inflammation in adipose tissue of high fat fed mice and elevate the proportion of Th17 cells and the expression of IL-17. Th17 cells may play an important role in the effects BPA on adipose tissue inflammation.	Environ Health Perspect. 2018 Nov;126(11):117001.	10.1289/EHP3953	30387366	動物	前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	1	●	-	-	-	-	●	-	●
統合_2558	Liu Y et al.	2019	Food up-take and reproduction performance of Daphnia magna under the exposure of Bisphenols	Because the application of Bisphenol A (BPA) was restricted, many substitutes, such as Bisphenol F (BPF) and Bisphenol S (BPS), were developed as BPA substitutes. Therefore, environmental impacts of BPA and its substitutes on aquatic organisms should be concerned, especially their combined toxicity. In this study, the impacts of BPA, BPF, BPS and their mixture on the feeding behavior, reproduction and physiological function of daphnids were synthetically evaluated, involving the duration and mode of exposure. In short-term exposure tests, feeding rates of D. magna decreased after exposure to BPA, BPF, BPS and their mixture, while the inhibition occurred into stimulation in the recovery period. It may benefit from environmental toxicity of D. magna. In long-term exposure tests, the inhibition effect on the reproduction was more obvious in the exposed D. magna was difficult to recover, and only were experimental groups have a certain recovery. In conclusion, environmental risk of BPA, BPF, BPS and their mixture on the behavior of D. magna increased with prolonged exposure time. Moreover, the activities of superoxide dismutase (SOD), catalase (CAT), and acetylcholinesterase (AChE) and malondialdehyde (MDA) and superoxide dismutase (SOD) of the exposed daphnids also increased in the treatment groups, indicating the disorder of digestion, nervous and antioxidation system of D. magna. Interestingly, inhibition of enzymes activities decreased with the increase of the exposure time, which implied the tolerance may be occurred.	Ecotoxicology and environmental safety.2019;170:47-54	10.1016/j.ecoenv.2018.11.106	30522006	動物	胚中濃度（摩擦部）	0	1	1	1	1	胚中濃度（摩擦部）	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2559	Nagao T et al.	2014	Neurobehavioral evaluation of mouse newborns exposed prenatally to low-dose bisphenol A (出生前に低用量ビスフェノールAに暴露した新生仔マウスの神経行動学的評価)(英語)	There have been few neurobehavioral toxicology studies on newborn animals. Thus, we developed a mouse newborn behavioral testing method for evaluating the risk of neurotoxicity of environmental toxicants, by means of determining the newborn's motor activity applying the term function of an analytical balance. Motor activities including crawling, pivoting, righting or turnover of mouse newborns were evaluated. Tremors of newborns were also measured using a PVDF film sensor. Pregnant ICR mice were orally administered bisphenol A (BPA) at 0 (vehicle), 0.2 (tolerable daily intake), 2 (no-observed-adverse-effect-level), 20 (lowest-observed-adverse-effect-level), or 200 (guideline permissible) mg BPA/kg/day from gestation day (GD) 0 to postnatal day (PND) 21 and Formate ion (FI) exposure. FI is an inhibitor of mitochondrial respiratory chain enzyme, which is also a BPA metabolite. Pregnant mice were exposed to FI at 0 (control), 0.1 (no-observed-adverse-effect-level), or 1 (lowest-observed-adverse-effect-level) mg FI/kg/day from GD 0 to PND 21. Newborn mice were tested on PND 1, 3, 5, 7, 9, 11, 13, 15, 17, and 19. Crawling distance was significantly decreased in the 200 mg BPA/kg/day group on PND 1 and 3. Tremors were significantly increased in the 200 mg BPA/kg/day group on PND 1, 3, 5, 7, and 9. Crawling distance was significantly decreased in the 1 mg FI/kg/day group on PND 1. Tremors were significantly increased in the 1 mg FI/kg/day group on PND 1, 3, 5, 7, 9, 11, 13, 15, 17, and 19. Thus, the present study revealed that BPA and FI exposure via maternal transfer to newborns induced neurotoxicity, and that the present behavioral testing method was sensitive enough to detect the neurotoxicity. Next, we examined the effects of BPA and FI exposure via maternal transfer on the hippocampal neurogenesis of newborns. BPA and FI exposure via maternal transfer significantly decreased the number of BrdU-positive cells in the hippocampal dentate gyrus of 21-day-old newborns. Therefore, these results confirm and extend previous evidence using a rat model and human prostate epithelial cells that low-dose BPA augments prostate cancer susceptibility and alters adult prostate stem cell homeostasis. Therefore, we propose that BPA exposures may contribute to the increased carcinogenic risk in humans that occurs with aging. https://doi.org/10.1289/EHP1953.	J Toxicol Sci. 2014 Apr;39(2):231-5.	10.2131/jts.39.231	24646703	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	1	●	-	-	-	-	-	-	-
統合_2560	Dosoo AO et al.	2018	Six months exposure to a real life mixture of 13 chemicals' below individual NOAELs induced non monotonic sex-dependent biochemical and redox status changes in rats	This study assessed the potential adverse health effects of long-term low-dose exposure to chemical mixtures simulating complex real-life human exposures. Four groups of Sprague Dawley rats were administered mixtures containing arsenic, deltamethrin, glyphosate, methanol, methyl parathion, nickel chloride, oxytetracycline, paracetamol, propiconazole, sodium dichlorvos, sodium fluoride, tolylfluanid, bisphenol A, and acacia gum at doses of 0, 0.25, 1 or 5 times the respective Toxicological Reference Values (TRV) acceptable daily intake (ADI) or tolerable daily intake (TDI) in a 13 weeks toxicity study. Body weight gain, feed and water consumption, hematological, biochemical, oxidative stress, histopathological and organ weight parameters were evaluated. Results showed that the mixtures induced significant changes in some of the parameters such as the total bilirubin, alanine aminotransferase (ALT) and alkaline phosphatase (ALP), especially in low dose and fluctuating nearly mark rats. The low dose group showed increased oxidative activity both in females and males, whereas the high dose group exhibited decreased protein content and total antioxidant capacity (TAC) levels in both sex groups. Non-monotonic effects and adaptive responses on liver function tests and redox status, leading to non-linear dose-response curves, are probably produced by modulation of different mechanisms.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association.2018;115:470-481	10.1016/j.fct.2018.03.052	29621577	動物	胚中濃度（摩擦部）	-	1	1	0	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2561	Uchimann KS et al.	2019	Fetal bisphenol A and ethinylestradiol exposure alters male rat urogenital tract morphology at birth: Confirmation of prior low-dose findings in CLARITY-BPA	Bisphenol A (BPA) is a contaminant in virtually all Americans. To examine BPA's adverse effects, the FDA-NCTR, NIEHS, and 16 groups of academic scientists formed a consortium (CLARITY-BPA). The purpose of our study was to confirm and extend findings of fetal BPA effects on the urogenital tract (UGT) reported by vom Saal et al. (2007). Pregnant CLARITY-BPA Core 1 CD-1 mice were orally exposed to BPA (0, 2.5, 25, 250, 2500, 25000 EE2 ng/kg bw/day) or ethinyl estradiol (EE2) daily, via oral gavage, from gestational day 6 through parturition. Tissues were collected on postnatal day (PND) 1 and the UGT was analyzed using computer-assisted 3D morphometry. Unexpectedly, only low doses of BPA, as well as EE2, significantly changed birth weight and UGT morphology, including an increased size of the urethrae, and decreased size of the urethra, consistent with prior reported BPA and EE2 effects. Our findings provide further evidence that BPA mediates nonmonotonic developmental effects on the fetal urogenital sinus.	Reprod Toxicol. 2020 Jan;91:131-141.	10.1016/j.reprotox.2019.11.007	31756437	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	●	-	-	●	-	-	-	●
統合_2562	Witchey SK et al.	2019	Perinatal bisphenol A (BPA) exposure alters brain oxytocin receptor (OTR) expression in a sex- and region- specific manner: A CLARITY-BPA consortium follow-up study	Bisphenol A (BPA) is a well-characterized endocrine disrupting chemical (EDC) used in plastics, epoxy resins and other products. Neurodevelopmental effects of BPA exposure are a major concern with multiple rodent and human studies showing that early life BPA exposure may impact the developing brain and sexually dimorphic behaviors. The CLARITY-BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity) program was established to assess multiple endpoints, including neural, across a wide dose range. Studies from our labs are part of (and prior to) CLARITY-BPA have shown that BPA disrupts oxytocin receptor expression in the developing female, and some inhibition of oxytocin (OT) and oxytocin receptor (OTR) expression in the adult male. Oxytocin is a critical hormone for social behavior in both sexes and across species. Given the role of oxytocin in human function in both sexes, and the potential for BPA to disrupt oxytocin, we hypothesized that perinatal BPA exposure would alter OTR expression across the brain in a sex-specific manner. In this CLARITY-BPA follow-up study, we used immunofluorescence and quantitative analysis to examine OTR expression in the hypothalamus, hippocampus, and amygdala of juvenile and adult male and female rats exposed perinatally to BPA. Ethinyl estradiol (0.3mug/kg bw/day) was used as a reference estrogen. Animals of both sexes were sacrificed as juveniles and OTR expression assessed by receptor binding. Our results demonstrate perinatal exposure to BPA can alleviate sex differences in OTR expression in three hypothalamic regions, and that male OTR expression may be more susceptible. Our data also identify a sub-region of the BNST with sexually dimorphic OTR expression not previously reported in juvenile rats that is also susceptible to BPA.	Neurotoxicology. 2019 Sep;74:139-148.	10.1016/j.neuro.2019.06.007	31251963	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	●	-	-	●	-	-	-	●
統合_2563	Harley KG et al.	2013	Prenatal and early childhood bisphenol A concentrations and behavior in school-aged children	INTRODUCTION: Early life exposure to bisphenol A (BPA), an endocrine disrupting chemical used in some food and beverage containers, receipts, and dental sealants, has been associated with anxiety and hyperactivity in animal studies. OBJECTIVE: We evaluated associations between prenatal and childhood BPA exposure and behavior at age 7 years in a population-based cohort of mothers and children in the Salinas Valley, California. METHODS: We measured BPA in maternal urine samples collected during pregnancy and in urine collected from children at 1 and 3 years old (N=282). Child behavior was evaluated by mothers and teachers when children were 7 years old using the Behavior Assessment System for Children (BASC-2). Parental and child characteristics were collected via questionnaires. We used linear regression to examine associations between BPA and behavior scores. RESULTS: Prenatal urinary BPA concentrations were associated with increased internalizing problems in boys, including anxiety and depression, at age 7. In associations score were with prenatal BPA concentrations and behaviors in girls. Childhood urinary BPA concentrations were associated with increased externalizing behaviors, including conduct problems, in girls at age 7 and increased internalizing behaviors and inattention and hyperactivity behaviors in boys and girls at age 7. CONCLUSIONS: This study adds to the existing literature showing associations of early life BPA exposure with behavior problems, including anxiety, depression, and hyperactivity in children. Additional information about timing of exposures and sex differences in effects is still needed.	Environ Res. 2013 Oct;126:43-50.	10.1016/j.envres.2013.06.004	23870093	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	-	-	-	-	-	-	●	-	-	-	-	-
統合_2564	Hong SB et al.	2013	Bisphenol A in relation to behavior and learning of school-age children	BACKGROUND: Bisphenol A (BPA) has been shown to affect brain architecture in rodents and nonhuman primates, but there are few studies focusing on its relationship to human neurobehavior. We aimed to investigate the relationship between environmental exposure to BPA and childhood neurobehavior. METHODS: Urinary BPA concentrations and behavioral and learning characteristics were evaluated in a general population of 1,288 children aged 8-11 years. Behavioral characteristics were assessed using the Child Behavior Checklist (CBCL), Behavior Assessment System for Children (BASC), and Conners' Continuous Performance Test (CPT). Learning characteristics were assessed using the Wechsler Intelligence Scale for Children (WISC). Total problems score and negatively associated with the learning quotient from the CBCL. The linear association with the CBCL anxiety/depression score and the quadratic association with the CBCL learning score were significant after correction for multiple comparisons. CONCLUSIONS: Environmental exposure to BPA might be associated with childhood behavioral and learning development. The results suggest possible nonmonotonic relationships.	J Child Psychol Psychiatry 2013, 54(8):890-9.	10.1111/jcpp.12050	23445117	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で排除しない原則。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2565	Snijder CA et al.	2013	Fetal growth and prenatal exposure to bisphenol A: the generation R study	BACKGROUND: Prenatal exposure to bisphenol A (BPA) has been associated with adverse birth outcomes, but findings of previous studies have been inconsistent. OBJECTIVE: We investigated the relation of prenatal BPA exposure with intrauterine growth and evaluated the effect of the number of measurements per subject on observed associations. METHODS: This study was embedded in a Dutch population-based prospective cohort study (Generation R Study). Maternal urine samples (n = 7,938) collected during pregnancy were analyzed for BPA. Fetal growth was assessed by ultrasonography every trimester. Using linear mixed-effects models with repeated measurements, we studied associations of birth BPA and fetal growth rate and to estimate associations between urinary concentrations of creatinine-based BPA (BPACR) and intrauterine growth. RESULTS: The relationship between BPACR and fetal growth was sensitive to the number of measurements per subject. Associations were strongest in models including all three measurements (n = 4,311 mothers). Higher BPACR (> 4.01 mug/g creatinine) had lower growth rates for fetal weight and head circumference than did women with BPACR < 1.36 mug/g creatinine, estimated differences in mean values at birth of -185 g (95% CI: -341, -29) and -0.9 cm (-1.6, -0.1), respectively. When fewer measurements were available per women, the exposure-response relationship became progressively attenuated and statistically nonsignificant. CONCLUSION: Our findings suggest that maternal urinary BPA may impair fetal growth. Because previous studies have shown contradictory findings, further evidence is needed to corroborate these findings in the general population.	Environ Health Perspect. 2013 Mar;121(3):393-8.	10.1289/ehp.1205296	23459363	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	-	-	●	-	-
統合_2566	Lee et al.	2014	Prenatal bisphenol A and birth outcomes: MOCEH (Mothers and Children's Environmental Health) study	Bisphenol A (BPA) is used primarily in the production of polycarbonate plastics and epoxy resins. Widespread exposure to BPA has created a great deal of concern regarding its potential adverse effects on human health. This study examined the relationship between prenatal BPA exposure and birth outcomes, including birth weight, birth length, and gestational index considering gender difference. A multi-center birth cohort study, Mothers and Children's Environmental Health (MOCEH) has been established in Korea since 2006. Study subjects are 707 pregnant women from the original cohort, who had their urinary BPA level measured during the third trimester, as well as information on birth outcomes, prior medical history, psychosocial status, health behavior, environmental exposure as well as socio-demographic characteristics. Regression analysis was performed to estimate the effect of BPA exposure on birth outcomes. Urinary BPA concentrations were detected in 97.5% of the samples with a median (range) of 1.5 (<0.4 - 36.0) ng/mL. Urinary BPA concentrations were higher in women with a higher income level. Univariate regression analysis revealed a significant association between BPA levels and birth weight. In adjusted analysis, the second tertile of maternal BPA exposure established an increase in birth weight, relative to the first tertile (p=0.06). These relationships were more pronounced in male neonates. Also, prenatal exposure to BPA was associated with an increase of gestational index in total, and especially female neonates. This study shows that the accumulation of prenatal exposure to BPA with anthropometric measures, such as birth weight and birth length, differed by gender. Further study is required to more fully elaborate this relationship between prenatal BPA exposure and birth outcomes.	Int J Hyg Environ Health. 2014 Mar;217(2-3):328-34.	10.1016/j.ijheh.2013.07.005	23911140	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2567	Braun JM, Yolton K, Dietrich KN, Hornung R, Ye X, Calafat AM, et al.	2009	Prenatal bisphenol A exposure and early childhood behavior	BACKGROUND: Prenatal exposure to bisphenol A (BPA) increases offspring aggression and diminishes differences in sexually dimorphic behaviors in rodents. OBJECTIVE: We examined the association between prenatal BPA exposure and child behavior at 3 years of age, hypothesizing that higher BPA concentrations would be associated with more externalizing behaviors. METHODS: Maternal urine BPA concentrations were quantified using high-performance liquid chromatography/tandem mass spectrometry. Child behavior was assessed at 3 years of age using the second edition of the Behavior Assessment System for Children (BASC-2). The association between prenatal BPA concentrations and BASC-2 scores was analyzed using linear regression. RESULTS: Median BPA concentrations were 1.8 (10 weeks) and 1.7 (16 weeks), and 2.6 ng/mL (delivery). Mean (+/- SD) BASC-2 externalizing and internalizing scores were 47.8 (+/- 7.8) and 48.8 (+/- 7.3), respectively. After adjustment for confounders, a 10-fold transformed mean prenatal BPA concentrations were associated with externalizing scores, but only among females (beta = 4.8; 90% confidence interval [CI], 0.1-9.6). Compared with 36-week and birth concentrations, BPA concentrations collected around 16 weeks were more strongly associated with externalizing scores in females (beta = 5.9; 90% CI, 0.7-11.1), and the associations were stronger in females than in males. Among all children, measurements collected at our 16-weeks showed a stronger association (beta = 3.1; 90% CI, 0.4-5.8) with externalizing scores than did measurements taken at 27-31 weeks (beta = 0.6; 90% CI, -2.9 to 4.1). CONCLUSIONS: These results suggest that prenatal BPA exposure may be associated with externalizing behaviors in 3-year-old children, especially among female children.	Environ Health Perspect. 2009 Dec;117(12):1945-52.	10.1289/ehp.0900979	20049216	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	●	●	-	●	-
統合_2568	Braun JM, Kalkbrenner AE, Calafat AM, Yolton K, Ye X, Dietrich KN, et al.	2011	Impact of early-life bisphenol A exposure on behavior and executive function in children	OBJECTIVES: To estimate the impact of gestational and childhood bisphenol A (BPA) exposures on behavior and executive function at 3 years of age and to determine whether child gender modified these associations. METHODS: We used a prospective birth cohort of 244 mothers and their 3-year-old children from the greater Cincinnati, Ohio, area. We characterized gestational and childhood BPA exposures by using the mean BPA concentrations measured in 2 urine samples collected during pregnancy and 2 samples collected when the children were 1 and 2 years of age. We assessed behavior by using the Behavior Assessment System for Children-2 (BASC-2) and the Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P). RESULTS: The BPA urine detection frequency was 95% at the approximate 2.0-ng/mL limit of detection. A 5-mug/L urine sample, BPA adjustment for confounders, and 10-fold increase in gestational BPA concentrations was associated with more anxious and depressed behavior on the BASC-2 and poorer emotional control and inhibition on the BRIEF-P. The magnitude of the gestational BPA associations differed according to child gender. BASC-2 and BRIEF-P scores increased 9 to 12 points among girls, but changes were null or negative among boys. Associations between childhood BPA exposure and neurobehavior were largely null and not modified by child gender. CONCLUSIONS: In this study, gestational BPA exposure affected behavioral and emotional regulation domains at 3 years of age, especially among girls. Clinicians may advise concerned patients to reduce their exposure to certain consumer products, but the benefits of such reductions are unclear.	Pediatrics. 2011 Nov;128(5):873-82.	10.1542/peds.2011-1335	22025598	ヒト	発達神経	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	●	-	-	-	-
統合_2569	Chou WC et al.	2011	Biomonitoring of bisphenol A concentrations in maternal and umbilical cord blood in regard to birth outcomes and adipokine expression: a birth cohort study in Taiwan	BACKGROUND: Bisphenol A (BPA) is a potent and flux of plastic materials and has been determined to be an endocrine-disrupting chemical. Prenatal exposure to BPA can lead to substantial adverse effects on fetal growth and development. This study was conducted to assess BPA concentration in pregnant women and umbilical cord blood, and to investigate whether maternal BPA exposure affected fetal outcomes including term birth weight (BW), smaller size for gestational age (SGA), and high-density BPA protein adiponectin (APN) and leptin (LEP) concentrations in cord blood. METHODS: We recruited 109 mothers and their fetuses in this within-high performance liquid chromatography/UV detector. The protein secretion of leptin and adiponectin were separately determined using enzyme-linked immunosorbent assay. A logistic regression was performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of SGA and BW. RESULTS: The BPA concentrations in maternal urine and cord blood were 1.71 ng/mL (median) and 1.72 ng/mL, respectively. Elevated risks of LBW (OR 5.23, 95% confidence interval (CI) 1.77-15.46), SGA (OR 3.56, 95% CI 1.38-9.20), and adverse action of leptin (OR 5.67, 95% CI 1.52-21.19) and adiponectin (OR 3.26, 95% CI 1.02-10.47) were observed in male neonates in the highest quartile of maternal BPA exposure. CONCLUSIONS: Elevated prenatal BPA exposure increased the risk of LBW, SGA, and adverse actions of adipokines in neonates, especially in male infants. These results provide further evidence that maternal exposure is correlated with adverse birth outcomes.	Environ Health. 2011 Nov 3;10:94.	10.1186/1476-069X-10-94	22050967	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	-	-	-	●	-
統合_2570	Cobellis L. et al.	2009	Measurement of bisphenol A and bisphenol B levels in human blood sera from healthy and endometriotic women	A sensitive HPLC method with fluorescence detection was developed for the determination of bisphenol A (BPA) and bisphenol B (BPB) in human blood serum. The detection limits of the method were 0.18 and 0.20 ng/mL for BPA and BPB, respectively. A single-step liquid-liquid extraction was used for the pre-treatment of serum samples. The recoveries of BPA and BPB spiked to sera were 85.0 and 87.7%, respectively. The analyses of sera from both healthy and endometriotic women emphasized the absence of bisphenols in all the control cases (11 women), whereas BPA was found in 50 sera (61.7%) and BPB was found in 26 sera (37.0%) in the group of 81 women affected by endometriosis. The mean concentrations of BPA and BPB were 0.61 and 0.27 ng/mL, respectively, in the sera of women with endometriosis. The ranges were 0.18-3.73 ng/mL for BPA and 0.20-1.73 ng/mL for BPB. Therefore, the presence of at least one of the two bisphenols was verified in a percentage as high as 43.8% in the sera from endometriotic women, suggesting the existence of a relationship between endometriosis and BPA and/or BPB exposure. Indeed, it is well known that bisphenols can work as xenoestrogens, owing to their structural similarity to natural and synthetic estrogens (e.g. estradiol and diethylstilbestrol). However, further studies are necessary to confirm this hypothesis and to assess the actual dose at which exposure to bisphenols are able to increase the sensitivity of the endometriotic cells to estradiol.	Biomed Chromatogr. 2009 Nov;23(11):1186-90.	10.1002/bmc.1241	19444800	ヒト	子宮	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	-	●	-	-	-
統合_2571	Fujimoto VY et al.	2011	Serum unconjugated bisphenol A concentrations in women may adversely influence oocyte quality during in vitro fertilization	Bisphenol A (BPA) is an endocrine disruptor with estrogenic properties that can adversely affect meiotic spindle assemblies. Our data indicate that BPA exposure in female patients may interfere with oocyte quality during IVF, as suggested by the inverse association between serum unconjugated BPA concentration and normal fertilization.	Fertil Steril. 2011 Apr;95(5):1816-9.	10.1016/j.fertnstert.2010.11.008	21122836	ヒト	卵巣	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	●	-	-	●	-	-	-
統合_2572	Galloway T et al.	2010	Daily bisphenol A excretion and associations with sex hormone concentrations: results from the InCHIANTI adult population study	BACKGROUND: Bisphenol A (BPA) is a high production volume chemical widely used in packaging for food and beverages. Numerous studies have demonstrated that BPA can alter endocrine function in animals, yet human studies remain limited. OBJECTIVE: We estimated daily excretion of BPA among adults and examined hypothesized associations with serum estrogen and testosterone concentrations. METHODS: We conducted cross-sectional analyses using data from the InCHIANTI Study, a prospective population-based study of before adults. Our study included 715 adults between 20 and 74 years old. BPA concentrations were measured by liquid chromatography--mass spectrometry in 24 hr urine samples. The main outcome measures were serum concentrations of total testosterone (TT), free testosterone (FT), and sex hormone binding globulin (SHBG). RESULTS: The median BPA concentration was 3.96 ng/mL (95% confidence interval [CI], 3.43-4.72 ng/mL), and mean excretion was 3.63 microg/day (95 percentile = 11.2 microg/day; 95th percentile, 31.5 microg/day). We found higher BPA concentrations in women (p = 0.0001), those who were younger (p = 0.0001), and those who were premenopausal (p = 0.0001). In multivariate models, BPA concentrations were positively associated with TT concentrations in men. In models adjusted for age and study site (p < 0.0001), and in models additionally adjusted for smoking, measures of obesity, and urinary creatinine concentrations (beta = 0.006; 95% CI, 0.003-0.009; p < 0.0001). We found no associations with the other serum measures. We also found no associations with the primary outcomes among women, but we did find an association between BPA and SHBG concentrations in the 60 premenopausal women. CONCLUSION: Higher BPA exposure may be associated with endocrine changes in men. The mechanisms involved in the observed cross-sectional association with total testosterone concentrations need to be clarified.	Environmental Health Perspectives.2010;118:1603-1608	10.1289/ehp.1002367	20797929	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	●	-
統合_2573	Itoh H et al.	2007	Urinary bisphenol-A concentration in infertile Japanese women and its association with endometriosis: A cross-sectional study	OBJECTIVES: Bisphenol A (BPA), a raw material commonly used in the manufacture of resins such as polycarbonate and epoxy, is a possible xenoestrogen that is hypothesized to disrupt the human endocrine system. Fetuses are widely exposed to BPA. We investigated the urinary concentration of BPA in infertile Japanese women and its possible association with endometriosis. MATERIALS AND METHODS: We recruited 186 women (aged 20-45) who had complained of infertility and visited a university hospital in Tokyo. The subjects were interviewed and their urine samples were obtained. Laparoscopic diagnosis of endometriosis between January 2002 and December 2003. Urinary total BPA concentration in 183 eligible urine samples was then measured using enzyme-labeled fluorescence. RESULTS: The geometric mean of urinary BPA concentration was 1.3 ng/mL (95% confidence interval [CI], 1.2-1.5). Urinary BPA concentration was significantly higher in women with endometriosis (p = 0.0001). A significant monotonic association of endometriosis with urinary BPA concentration was observed. Median urinary BPA concentration in women with stage 0-1 endometriosis (0.71 ng/mL) was not significantly different from that in those with stage 2-4 endometriosis (0.91 ng/mL) (p = 0.0001). We found no associations with the other serum measures. We also found no associations with the primary outcomes among women, but we did find an association between BPA and SHBG concentrations in the 60 premenopausal women. CONCLUSION: Higher BPA exposure may be associated with endocrine changes in men. The mechanisms involved in the observed cross-sectional association with total testosterone concentrations need to be clarified.	Environ. Health Prev. Med.2007;12:258-264	10.1007/BF02898033	21432072	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	●	-
統合_2574	Li DK et al.	2011	Urine bisphenol-A (BPA) level in relation to semen quality	OBJECTIVE: To determine whether urine bisphenol-A (BPA) levels are associated with lower semen quality. DESIGN: Cohort study. SETTING: Four regions in China where high exposure to BPA in the workplace existed. PATIENTS: 218 men with and without BPA exposure in the workplace. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Semen parameters. RESULT(S): After adjustment for potential confounders using linear regression models, the urine BPA level was found to be significantly associated with lower sperm concentration, lower sperm motility, and lower percentage of normal sperm morphology. Compared with men who did not have detectable urine BPA levels, those with detectable urine BPA had more than three times the risk of lowered sperm concentration and lower sperm vitality, more than four times the risk of lower sperm count, and more than twice the risk of lower sperm motility. The urine BPA level was not associated with semen volume or abnormal sperm morphology. Similar dose-response associations were observed among men with environmental BPA exposure at levels comparable with those in the U.S. population. Despite a markedly reduced sample size, the inverse correlations between increased urine BPA levels and decreased sperm concentration and total sperm count remained statistically significant. CONCLUSION(S): These results provide the first epidemiologic evidence of an adverse effect of BPA on semen quality.	Fertil Steril. 2011 Feb;95(2):625-30.e1-4.	10.1016/j.fertnstert.2010.09.026	21035116	ヒト	精巣	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	-	-	-	-	-	-	●	-	-	●	-	●	-
統合_2575	Meeker JD et al.	2010	Urinary bisphenol a concentrations in relation to serum thyroid and reproductive hormone levels in men from an infertility clinic	Human exposure to bisphenol A (BPA) is a widespread. Animal studies have demonstrated that BPA can alter endocrine function, but human studies are limited. For the present study, we measured urinary BPA concentrations and serum thyroid and reproductive hormone levels in 167 men recruited through an infertility clinic. BPA was detected in 89% of urine samples with a median (range) of 2.5 (<0.4 - 36.0) ng/mL. In regression models, we found that BPA was significantly associated with serum follicle-stimulating hormone (FSH) and TSH. Men in the highest tertile of BPA exposure had 19% higher FSH and 33% higher TSH levels than men in the lowest tertile. Associations between BPA and free androgen index (FAI) were also significant. Men in the highest tertile of BPA exposure had a 17% higher mean FAI and 17% lower free testosterone than men in the lowest tertile. Associations between BPA and estradiol, sex hormone binding globulin, inhibin B, and total testosterone were not significant. Men in the highest tertile of BPA exposure had a 17% higher mean FAI and 17% lower free testosterone than men in the lowest tertile. Associations between BPA and estradiol, sex hormone binding globulin, inhibin B, and total testosterone were not significant. After further adjustment for urinary creatinine concentrations, associations between BPA and FSH, TSH, and FAI were no longer significant. Our results suggest that urinary BPA concentrations may be associated with altered hormone levels in men, but these findings need to be substantiated through further research.	Environmental Science and Technology 44, 1458-1463	10.1021/es9028292	20030380	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	-	-
統合_2576	Meeker JD et al.	2010	Semen quality and sperm DNA damage in relation to urinary bisphenol A among men from an infertility clinic	Bisphenol A (BPA) impairs spermatogenesis in animals, but human studies are lacking. We measured urinary BPA concentrations, semen quality, and sperm DNA damage (comet assay) in 190 men recruited through an infertility clinic. BPA was detected in 90% of samples, with a median (interquartile range) (IQR) concentration of 1.7 (0.8-3.5) ng/mL. Urinary BPA concentration was associated with significantly lower, odds for below reference sperm concentration, motility, and morphology. When modeled as continuous dependent variables, an IQR increase in urinary BPA concentration was associated with declines in sperm concentration, motility, and morphology of 15% (95%CI: -30%, 1.5%; 1.5%, 1.5%), and 5% (-18%, 8.1%), respectively, along with a 18% (0.03%, 37%) increase in sperm DNA damage measured as the percentage of DNA in comet tail. In conclusion, urinary BPA may be associated with declined semen quality and increased sperm DNA damage, but confirmatory studies are needed.	Reproductive Toxicology, 30(4):532-539	10.1016/j.reprotox.2010.07.005	20656017	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	-	-
統合_2577	Meeker D et al.	2010	Association of urinary bisphenol a concentration with heart diseases: evidence from NHANES 2003/06	BACKGROUND: Bisphenol A (BPA) is a high production volume chemical widely used in food and drinks packaging. Associations have previously been reported between urinary BPA concentrations and heart disease. Diabetes and liver enzymes in adult participants of the National Health and Nutrition Examination Survey (NHANES) 2003/06. We aimed to estimate associations between urinary BPA concentrations and health measures in NHANES 2003/06 which data pooled across collection years. METHODS AND FINDINGS: A cross-sectional analysis of NHANES subjects were n = 1,455 (2003/04) and n = 1,493 (2005/06) adults aged 18-74 years, representative of the general adult population of the United States. Regression models were adjusted for age, sex, race/ethnicity, education, income, smoking, BMI, waist circumference, and urinary creatinine concentrations. Urinary BPA concentrations were detected in 95% of participants. Geometric mean BPA concentrations were 2.66 ng/mL (95% CI 2.46, 2.87) in 2003/04 and 2.97 ng/mL (95% CI 2.77, 3.18) in 2005/06. Higher BPA concentrations were associated with coronary heart disease in 2003/06 (OR per 1 ng/mL increase in BPA = 1.23; 95%CI: 1.02 to 1.75, p = 0.032) and in pooled data (OR = 1.22; CI: 1.17 to 1.72, p = 0.001). Associations with diabetes did not reach significance in 2003/06, but pooled estimates remained significant (OR = 1.15; CI: 1.01 to 1.32, p = 0.001). There was no overall association with gamma glutamyl transferase concentrations, but pooled associations with alkaline phosphatase and bivariate dehydrogenase remained significant. CONCLUSIONS: Higher BPA exposure, reflected in higher urinary concentrations of BPA, is consistently associated with reported heart disease in the general adult population of the USA. Studies to clarify the mechanisms of these associations are urgently needed.	PLoS One 5, e8673	10.1371/journal.pone.0008673	20084273	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2578	Meiner D et al.	2012	Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women	BACKGROUND: The endocrine-disrupting chemical bisphenol A (BPA) is widely used in food and beverage packaging. Higher urinary BPA concentrations were cross-sectionally associated with heart disease in National Health and Nutrition Examination Survey (NHANES) 2003–2004 and NHANES 2005–2006. Interpretation of traditional risk factors. METHODS AND RESULTS: We included 758 incident coronary artery disease (CAD) cases and 861 controls, followed for 13.8 years from the European Prospective Investigation of Cancer-Norfolk UK. Respondents aged 40 to 79 years and free of CAD, stroke, or diabetes mellitus provided baseline spot urine samples. Urinary BPA concentrations were measured by high-performance liquid chromatography–tandem mass spectrometry. Cox proportional hazards models, stratified by age at recruitment and sex, were used to examine associations of BPA quartiles (Q) with CAD risk. Models 1 and 2 were sequentially adjusted for traditional and novel risk factors. In 2009, odds ratios (ORs) for CAD by BPA quartiles (Q1 to Q4) were 1.00 (reference), 1.07 (95% CI, 0.77–1.49), 1.39 (1.00–1.94), and 1.64 (1.17–2.31), respectively (P for trend = 0.002). After adjustment for traditional risk factors (adjusted model), including those with newly CAD (1–3 years follow-up), body mass index (BMI), waist-to-hip ratio, smoking, ethnicity, urinary creatinine concentration, time of sample collection, and duration of abstinence, BPA (Q2, Q3, and Q4) remained associated with CAD (OR, 1.00 [reference], 1.07 [95% CI, 0.77–1.49], 1.39 [1.00–1.94], and 1.64 [1.17–2.31], respectively; P for trend = 0.002). Additional adjustment for novel risk factors (fully adjusted model), including those with newly CAD (1–3 years follow-up), body mass index (BMI), waist-to-hip ratio, smoking, ethnicity, urinary creatinine concentration, time of sample collection, and duration of abstinence, BPA (Q2, Q3, and Q4) remained associated with CAD (OR, 1.00 [reference], 1.07 [95% CI, 0.77–1.49], 1.39 [1.00–1.94], and 1.64 [1.17–2.31], respectively; P for trend = 0.002). With CAD risk factor adjustment including education, occupational social class, leisure time category, systolic blood pressure, lipid concentrations, and exercise (not), the estimated rate ratio (similar but narrowly missed 2-sided significance (n=758); odds ratio (OR) 1.11; 95% confidence interval, 1.00–1.23; P = 0.060). Sensitivity analyses with the fully adjusted model, including those with newly CAD (1–3 year follow-up), body mass index (BMI), waist-to-hip ratio, smoking, ethnicity, urinary creatinine concentration, time of sample collection, and duration of abstinence, BPA (Q2, Q3, and Q4) remained associated with CAD (OR, 1.00 [reference], 1.07 [95% CI, 0.77–1.49], 1.39 [1.00–1.94], and 1.64 [1.17–2.31], respectively; P for trend = 0.002). With multivariate adjustment, we observed no significant associations between any urine parameter and urinary BPA concentration. However, a significant inverse association was found between urinary BPA concentration and FEV1 levels and the FVC/LV ratio, as well as a significant positive association between BPA and SHBG. CONCLUSIONS: Our results suggest that, in further men, exposure to low environmental levels of BPA may be associated with a modest reduction in markers of liver testosterone, but any effects on reproductive function are likely to be small, and of uncertain clinical significance.	Circulation. 2012 Mar 27;125(12):1482-90.	10.1161/CIRCULATIONAHA.111.069153	22354940	ヒト	心血管	-	-	-	-	-	-	-	-	-	-	nested case-control	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_2579	Mendiola J et al.	2010	Are Environmental Levels of Bisphenol A Associated with Reproductive Function in Fertile Men?	BACKGROUND: Rodent and in vitro studies have demonstrated the estrogenic by-of bisphenol A (BPA). However, few studies have examined the relationship between human exposure to BPA and male reproductive function. OBJECTIVES: We investigated the relationships between environmental BPA exposure and reproductive parameters, including semen quality and male reproductive hormones, in previously recruited fertile men. METHODS: Participants (n = 370) were partners of pregnant women who participated in the Study for Future Families in the U.S. cities, and all of them provided blood, semen, and urine samples. BPA was measured in urine. Serum samples were analyzed for reproductive hormones, including follicle-stimulating hormone, luteinizing hormone (LH), testosterone, inhibin B, estradiol, and sex hormone–binding globulin (SHBG). Semen samples were analyzed for sperm concentration, motility, and morphology. RESULTS: Median urinary BPA concentration was 2.5 ng/mL, and 93% of participants had detectable BPA concentrations. Multivariate linear regression models were used to examine associations controlling for age, body mass index, smoking, ethnicity, urinary creatinine concentration, time of sample collection, and duration of abstinence. RESULTS: After multivariate adjustment, we observed no significant associations between any semen parameter and urinary BPA concentration. However, a significant inverse association was found between urinary BPA concentration and FSH levels and the FSH/LH ratio, as well as a significant positive association between BPA and SHBG. CONCLUSIONS: Our results suggest that, in fertile men, exposure to low environmental levels of BPA may be associated with a modest reduction in markers of liver testosterone, but any effects on reproductive function are likely to be small, and of uncertain clinical significance.	Environ Health Perspect 118,1286-1291	10.1289/ehp.1002037	20494855	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	●	-	-	-	-
統合_2580	Miao M et al.	2011	In utero exposure to bisphenol-A and its effect on birth weight of offspring	To examine the effect of in utero BPA exposure on the birth weight of offspring, a total of 587 children from families in which parents(+&) or did not have occupational exposure to BPA were examined. Their birth weights were obtained by an in person interview of the mother. Parental BPA exposure level during the index pregnancy was determined through personal air sampling measurements and exposure history. After controlling for potential confounders, parental exposure to BPA in the index pregnancy was associated with decreased birth weight. The association was stronger for maternal exposure than for paternal exposure which is statistically significant (P=.022). A clear exposure–relationship was observed with increased BPA exposure levels in pregnancy associated with greater magnitude of decrease of birth weight in offspring (P=.0.001). Our findings provide the new epidemiologic evidence suggesting that in utero exposure to BPA during pregnancy may be associated with decreased birth weight in offspring.	Reprod Toxicol. 2011 Jul;32(1):64-8.	10.1016/j.reprotox.2011.03.002	21440056	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_2581	Miodovnik A et al.	2011	Endocrine disruptors and childhood social impairment	Prenatal exposure to endocrine disruptors has the potential to impact early brain development. Neurodevelopmental toxicity in utero may manifest as psychosocial deficits later in childhood. This study investigates prenatal exposure to two ubiquitous endocrine disruptors, the phthalate esters and bisphenol A (BPA), and social behavior in a sample of adolescent inner-city children. Third-trimester urines of women enrolled in the Mount Sinai Children's Environmental Health Study between 1998 and 2002 (n = 402) were analyzed for phthalate metabolites and BPA. Mother–child pairs were asked to return for a follow-up assessment when the child was between the ages of 7 and 9 years. At this visit, mothers completed the Social Responsiveness Scale (SRS). The SRS (n = 337), a quantitative scale measuring the severity of social impairment related to Autistic Spectrum Disorders (ASD) in the general population, is adjusted general linear models increasing log-transformed low molecular weight (LMW) phthalate metabolite concentrations were associated with greater social deficits (beta = 2.26; 95% CI: 0.12, 4.40; p = 0.038) and social communication problems (beta = 2.19; 95% CI: 0.03, 4.35; p = 0.047). Maternal BPA was not associated with SRS scores (beta = 0.26; 95% CI: −2.12, 2.64), but not for Autistic Mannerisms or Social Motivation. No significant association with BPA was found. Beta = 1.34; 95% CI: −0.79, 3.12). Prenatal phthalate exposure was associated with childhood social impairment in a multiethnic urban population. Even mild degrees of impaired social functioning in otherwise healthy individuals can have very important adverse effects over a child's lifetime. These results extend our previous finding of atypical neonatal and early childhood behaviors in relation to prenatal phthalate exposure.	Neurotoxicology. 2011 Mar;32(2):261-7.	10.1016/j.neuro.2010.12.009	21182865	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	-	-	●	-	●	-
統合_2582	Padmanabhan V et al.	2008	Maternal bisphenol-A levels at delivery: a looming problem?	OBJECTIVE: The objective was to determine whether bisphenol-A (BPA) is found in maternal circulation of pregnant women in the US population and is related to gestational length and birth weight. METHODS: Circulating levels of BPA were quantified by high-performance liquid chromatography–tandem mass spectrometry in 45 southeastern Michigan mothers and correlated with birth weight of offspring. RESULTS: Maternal levels of unconjugated BPA ranged between 0.5 and 22.3 ng/mL (1 in southeastern Michigan mothers. There was no correlation between BPA concentrations and gestational length or birth weight of offspring. CONCLUSION: This is the first reported measurable levels of BPA in maternal blood of the US population. Long-term follow-up studies of offspring are needed to address in vitro concerns over human fetal exposure to synthetic exogenous estrogens.	J. Perinatol. 2008; 28:258–63.	10.1038/sj.jp.7211913	18273031	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	-	-
統合_2583	Perera F et al.	2012	Prenatal bisphenol a exposure and child behavior in an inner-city cohort	BACKGROUND: Experimental laboratory evidence suggests that bisphenol A (BPA), an endocrine disruptor, is a neurodevelopmental toxicant. However, there have been limited and inconclusive results with respect to sex-specific BPA effects on child behavior. OBJECTIVE: We examined the association between prenatal BPA exposure and child behavior, adjusting for postnatal BPA exposure and maternal urinary cotinine as sex-specific effects. METHODS: We followed African American and Dominican women and their children from pregnancy to child's age 9 years, collecting spot urine samples from the mothers during pregnancy (24 weeks on average) and the children at ages 3, 5, and 7 years. We measured urinary BPA concentrations in 249 mothers and 244 children. We assessed behavior using the Child Behavior Checklist (CBCL). We used linear regression to examine associations between BPA exposure and child behavior, adjusting for potential confounders. RESULTS: The analysis was restricted to 196 children (82 boys and 112 girls). Among boys, high prenatal BPA exposure (highest quartile vs. the lowest three quartiles) was associated with significantly higher CBCL scores (more problems) on Emotionally Reactive (2.82 times greater; 95% confidence interval (CI): 1.31, 3.82) and Aggressive Behavior syndromes (2.29 times greater; 95% CI: 1.06, 3.52). Among girls, higher maternal urine was associated with lower scores on all syndromes, reaching statistical significance for Anxious/Depressed (0.76 times as high; 95% CI: 0.61, 0.99) and Aggressive Behavior (0.62 times as high; 95% CI: 0.35, 0.97). CONCLUSIONS: These results suggest that prenatal exposure to BPA may affect child behavior, and differently among boys and girls.	Environ Health Perspect. 2012 Aug;120(8):1190-4.	10.1289/ehp.1104492	22543054	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	●	-	-	-	-	-
統合_2584	Philippat C et al.	2012	Exposure to phthalates and phenols during pregnancy and offspring size at birth	BACKGROUND: Data concerning the effects of prenatal exposures to phthalates and phenols on fetal growth are limited in humans. Previous findings suggest possible effects of some phenols on male birth weight. OBJECTIVE: Our aim was to assess the relationships between prenatal exposures to phthalates and phenols and fetal growth among male newborns. METHODS: We conducted a case–control study on male malformations of the genitalia nested in a French mother–child cohort, with recruitment between 2002 and 2006. We measured, in maternal urinary samples collected between 5 and 19 gestational weeks, the concentrations of 11 phthalate metabolites, 4 parabens, triclosan, benzophenone-3, bisphenol A, and 2 chlorinated phenols. We used linear regression models to estimate associations between urinary biomarker concentrations and birth weight, birth length, and head circumference, controlling for the corresponding in utilitarianism score. RESULTS: Adjusted birth weight decreased by 77 g [95% confidence interval (CI): −134, −20] and by 89 g (95% CI: −146, −31) in association with a 1-unit increase in ln-transformed 2,4-dichlorophenol (2,4-DCP) and 2,5-DCP urinary concentrations, respectively. Benzophenone-3 (BP3) ln-transformed concentrations were positively associated with weight (38 g; 95% CI: −3, 79) and head circumference at birth (0.1 cm; 95% CI: 0.0, 0.3). Head circumference increased by 0.2 cm (95% CI: 0.0, 0.3) in association with a 1-unit increase in ln-transformed BP3 concentration. For phthalates, we found that there was no evidence of metabolic associations with birth weight. CONCLUSIONS: Consistent with findings of a previous study, our observed evidence of an inverse association of 2,5-DCP and a positive association of BP3 with male birth weight.	Environ Health Perspect. 2012 Mar;120(3):464-70.	21900077	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	1	-	-	-	●	-	-	-	-	-	-
統合_2585	Teeguarden JG et al.	2011	Twenty-Four Hour Human Urine and Serum Profiles of Bisphenol A during High-Dietary Exposure	By virtue of its binding to steroid hormone receptors, bisphenol A (BPA, the unconjugated bioactive monomer) is hypothesized to be estrogenic when present in sufficient quantities. In the body, raising concerns that widespread exposure to BPA may impact human health. To better understand the internal exposure of adult humans to BPA and the relationship between the serum and urinary pharmacokinetics of BPA, a clinical research unit study was conducted in which 20 adult volunteers consumed canned foods for five days and provided urine and serum samples for BPA analysis. Urine samples were collected in 3 h intervals and serum samples were collected at the end of each 24 h period. Deuterium-labeled BPA (D6-BPA) was administered orally in a dose of 0.5 μg/kg body weight (bw) to estimate non-oral exposures to BPA. The volunteers' average consumption of BPA, estimated from the concentration of total BPA (TOTBPA = unconjugated BPA + conjugated BPA) and 24 h urine volumes, was 0.81 (0.46) μg/kg bw/day (mean (SD)). Consistent with findings of a previous study, our observed evidence of an inverse association of 2,5-DCP and a positive association of BP3 with male birth weight.	Toxicological Sciences, 123, 48-57	10.1093/toxsci/kfr160	21705716	ヒト	臨床曝露試験	1	1	-	-	-	-	-	-	-	-	臨床曝露試験	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	●	-	-
統合_2586	Wolff MS et al. et al.	2010	Investigation of relationships between urinary biomarkers of phytoestrogens, phthalates, and phenols and pubertal stages in girls	BACKGROUND: Hormonally active environmental agents may alter the course of pubertal development in girls, which is controlled by steroids and gonadotropins. OBJECTIVES: We investigated associations of concurrent exposures from three chemical classes (phenols, phthalates, and phytoestrogens) with pubertal stages in a multiethnic longitudinal study of 1,151 girls from New York City, New York, greater Cincinnati, Ohio, and northern California who were 6–8 years of age at enrollment (2004–2007). METHODS: We measured urinary exposure biomarkers at visit 1 and examined associations with breast and pubic hair development (present or absent, assessed 1 year later) using multivariate adjusted prevalence ratios (PR) and 95% confidence intervals (CIs). Modification of biomarker associations by age-specific body mass index percentile (BMI%) was examined. RESULTS: Adjusted PR for breast development (advanced PR, 0.66 [95% CI, 0.46–0.95]) and pubic hair development (PR, 0.68 [95% CI, 0.49–0.94]) were lower among girls with higher urinary concentrations of genistein, a soy isoflavone. Urinary concentrations of some weakly associated estrogenic phthalates were weakly associated with pubic hair development (adjusted PR, 0.66 [95% CI, 0.48–1.00], fifth vs. first quintile). Small inverse associations were seen for daidzein and soy isoflavones and high BMI% in girls' public hair stage; a positive trend was observed for low molecular weight phthalate biomarkers with breast and pubic hair development. Associations attenuated BMI associations with breast development. In the first menstruation epochs, for the association of high BMI with sex development, the PR was 1.56 (95% CI, 1.25–1.95 vs. no BMI). There was no BMI association in the 10%, highest quintile of exterminators. CONCLUSIONS: Weak hormonally active xenobiotic agents investigated in this study had small associations with pubertal development, mainly among those agents detected at highest concentrations.	Environ Health Perspect. 2010 Jul;118(7):1039-46.	10.1289/ehp.0901690	20308033	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	-	-	-	●	-	-	●	-	●	-
統合_2587	Wolff MS et al.	2008	Environmental exposures and puberty in inner-city girls	BACKGROUND: Hormonally active environmental exposures are suspected to alter onset of puberty in girls, but research on this question has been very limited. OBJECTIVE: We investigated pubertal status in relation to hormonally active environmental exposures among a multiethnic group of 197 healthy 9-year-old girls residing in New York City. METHODS: Information was collected on breast and pubic hair stages, weight and height. Thyroid-gland intake was estimated from a food frequency questionnaire. Three phytoestrogens and the phenolic BPA were measured in urine. In a subset, 1,17-dihydroxy-2,3,7-tris(3-chloropropyl)cyclotetraphosphazane (OH7), polychlorinated biphenyls (PCBs) were measured in blood plasma and lipid (PL) in blood. Associations of exposures with pubertal stages (present versus 2 + in adjusted stage 2) were examined using t tests and Poisson regression models with robust variance. RESULTS: Adjusted prevalence ratios (PR) for breast development (PR, 0.66; 95% confidence interval [CI], 0.46–0.95) and pubic hair development (PR, 0.68; 95% CI, 0.49–0.94) were lower among girls with high urinary genistein (a soy isoflavone) concentrations associated with breast stage. Urinary phytoestrogen biomarker concentrations were lower among girls with greater development compared with no development. In relation to pubic hair stage, soy isoflavones, daidzein (PR 0.68 [0.48–1.00] for 5th vs. 1st quintile) and genistein (0.70 [0.48–1.02]). Body mass index (BMI) is a hormonally relevant, strong risk factor for breast development. Therefore, BMI-adjusted models were also examined. Associations of BMI with breast development were stronger in girls with higher concentrations of OH7 (PR 1.56 [1.25–1.95] for 4th vs. 1st quintile) and PCBs (1.60 [1.28–2.00]). Similar associations were seen with pubic hair development. CONCLUSIONS: Early pubertal development was more common among girls with high BMI, where breast development was delayed among those with high urinary concentrations (PR 0.63 [0.52–0.96] for the upper tertile vs. lower two combined). There was no main effect of PCBs on breast stage, but girls with below-median BMI and 4th vs. median PCB levels had reduced risk for breast development (very vs. none) compared with other BMI-PCB groups. No biomarkers were associated with hair development, which was present in 51% of girls. CONCLUSIONS: Phytoestrogens and PCBs, are environmental exposures that may delay breast development, especially in conjunction with BMI, which governs the endogenous hormonal milieu. Further research to confirm these findings may improve our understanding of the role of early life development in breast cancer risk and other chronic diseases related to obesity.	Environmental Research, 107, 393-400	10.1016/j.envres.2008.03.006	18479682	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	●	-	●	-
統合_2588	Yang Y J et al.	2009	Bisphenol A exposure is associated with oxidative stress and inflammation in postmenopausal women	Bisphenol A (BPA) is widely used in the production of polycarbonate plastics and epoxy resins. There is increasing health concerns regarding low level exposure to BPA among the general population. The aim of this study was to determine the association between BPA exposure with oxidative stress and inflammation in adult populations. A cross-sectional study was conducted. This study included 385 adults, 190 men, 92 premenopausal women, and 103 postmenopausal women, randomly recruited from the general population in Taichung City and Taichung County, Taiwan, from 2006 to 2007. Urinary concentrations of BPA and 8-hydroxy-2′-deoxyguanosine (8-OHdG) as a marker of DNA oxidative damage, and C-reactive protein (CRP) were measured. Multivariate analyses were applied to determine the associations of BPA exposure with oxidative stress and inflammation. The urinary concentrations of BPA in men, premenopausal women, and postmenopausal women were 3.92, 3.61, and 3.58 microg/g cr, respectively. The urinary BPA concentrations were positively associated with 8OHdG, R-CRP, and CRP levels in the postmenopausal women; however, such associations did not exist in men and premenopausal women. The findings of this study suggest that BPA exposure could promote oxidative stress and inflammation, in which postmenopausal women are likely to be more susceptible to BPA-induced health effects.	Environ. Res. 2009; 6:797-801.	10.1016/j.envres.2009.04.014	19464675	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_2589	Yolton K et al.	2011	Prenatal exposure to bisphenol A and phthalates and infant neurobehavior	OBJECTIVE: To examine the association of prenatal exposure to bisphenol A and select common phthalates, with infant neurobehavior measured at 5 weeks. METHODS: We compared the concentration of maternal urinary metabolites of bisphenol A and phthalates at two distinct time points in pregnancy (16w, 26w) with scores on the NICU Network Neurobehavioral Scale (NNNS) at 5 weeks of age in a cohort of 360 mother/infant pairs. RESULTS: Prenatal exposure to BPA was not significantly associated with neurobehavioral outcomes at 5 weeks. Significant associations between prenatal exposure to metabolites of several phthalates and infant neurobehavioral outcomes differed by type of phthalate and were only seen with exposure measured at 26 weeks. Higher level of butyl phthalate (BBP) metabolites at 26w were associated with improved behavioral organization evidenced by lower Regulation and Nonoptimal Reflexes factor scores. Higher level of diethyl phthalate (DEP) metabolites at 26w were associated with poorer performance on the Attention and Executive Function factor scores. CONCLUSIONS: The association between prenatal phthalate exposure and infant neurobehavior differed by type of phthalate and was evident only with exposure measured at 26w. Prenatal exposure to DBP was associated with improved behavioral organization in 5-week-old infants. Prenatal exposure to DEHP was associated with nonoptimal reflexes in male infants. There was no evidence of an association between prenatal BPA exposure and infant neurobehavior.	Neurotoxicol Teratol. 2011 Sep-Oct;33(5):558-66.	10.1016/j.ntt.2011.08.003	21854843	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	-	●	-	-	-	-
統合_2590	Meiner D et al.	2012	Urinary bisphenol a concentration and angiography-defined coronary artery stenosis	BACKGROUND: Bisphenol A is widely used in food and drink packaging. There is evidence of associations between raised urinary bisphenol A (uBPA) and increased incidence of reported cardiovascular diagnoses. We investigated the association between uBPA and angiographically defined coronary artery stenosis. METHODS AND RESULTS: We studied 1,439 participants undergoing coronary angiography at the Cambridge Coronary Artery Disease (CADET) study in Cambridge/the UK, comparing urinary BPA (uBPA) with grades of severity of coronary artery disease (CAD) at angiography. Linear models were adjusted for BMA, occupational social class and diabetes status. There (one in three vessel) CAD was present in 583 patients, 86 had intermediate disease (to 49) and 170 had normal coronary arteries. The (unadjusted) median uBPA concentration was 1.8 ng/mL with normal coronary arteries, and 2.05 ng/mL with normal CAD. Compared to those with normal coronary arteries, uBPA concentration was significantly higher in those with severe CAD (3.4 per uBPA (95% CI: 0.90 ng/mL) (-1.11, 1.33) to 1.66, p=0.033), and was significant for intermediate disease (50% (-0.39, 0.58) to 2.56, p=0.002). There was no significant uBPA difference between patients with severe CAD (treating surgery) and the remaining groups combined (CONCLUSIONS/CONFUSION): BPA exposure was significantly higher in those with severe coronary artery stenosis compared to those with no vessel disease. Larger studies are needed to exclude true dose-response relationships. The mechanisms underlying this association remain to be established.	PLoS One. 2012;7(8):e43378.	10.1371/journal.pone.0043378	22916252	ヒト	心血管	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	●	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2591	Mok-Lin E et al.	2010	Urinary bisphenol A concentrations and ovarian response among women undergoing IVF	Bisphenol A (BPA) is a synthetic chemical used in the manufacture of materials present in many common consumer products. In experimental animals, BPA caused oocyte aneuploidy and reduced production of oestradiol. In a prospective cohort study, we investigated the association between urinary BPA concentrations and ovarian response among women undergoing in vitro fertilization (IVF) at the Massachusetts General Hospital (MGH) Fertility Center. The gonadotropin dose of two specific gravity (SG)-adjusted urinary BPA concentrations, collected during each IVF cycle was used as the cycle-specific BPA exposure level. BPA concentrations were measured in 352 urine samples collected from 115 women undergoing 137 IVF cycles between 2004 and 2008. Ovarian response was assessed by the number of oocytes retrieved and by the number of oocytes classified as mature (metaphase II). Multivariable-adjusted effect models used Poisson regression models, adjusting for age, BMI and day 3 follicle-stimulating hormone (FSH) levels, a clinical measure of ovarian reserve. Urinary BPA concentrations were measured in 93 women (mean age 33.3 years) undergoing 122 IVF cycles; 35 women (37%) contributed more than one IVF cycle. BPA concentrations ranged from <0.4 to 29.5 microg/L (geometric mean 2.0; +/- SD 0.5). 10% of urine samples had concentrations <0.4 microg/L. Peak serum estradiol levels correlated with the total number of oocytes retrieved per cycle (r = 0.46, p < 0.001). For each log unit increase in SG-BPA, there was an average decrease of 13% (95% CI: 5, 21%; p = 0.007) in the number of oocytes retrieved and an average decrease of 23 (up to 95%) (5; -107, -25; p = 0.02) in peak estradiol. BPA was detected in the urine of the majority of women undergoing IVF, and was inversely associated with number of oocytes retrieved and peak estradiol levels.	Int J Androl. 2010 Apr;33(2):385-93.	10.1111/j.1365-2605.2009.01014.x	20002217	ヒト	生殖発生							横断研究	1	1				1	1	1						●			●					
統合_2592	Caserta D et al.	2013	Correlation of Endocrine Disrupting Chemicals Serum Levels and White Blood Cells Gene Expression of Nuclear Receptors in a Population of Infertile Women	Significant evidence supports that many endocrine disrupting chemicals could affect female reproductive health. Aim of this study was to compare the internal exposure to bisphenol A (BPA), perfluorooctane sulphonate (PFOS), perfluorooctanoic acid (PFOA), monoethylhexyl phthalate (MEHP), and 4,5'-dichlorodiphenyldichloroethylene (DDE) in serum samples of 111 infertile women and 106 fertile women and the expression of nuclear receptors (ER alpha, ER beta, AR, PXR, and PPAR gamma) genes also analyzed as biomarkers of effective dose. The percentage of women with BPA concentrations above the limit of detection was significantly higher in infertile women than in fertile women (respectively 75.7% and 50.9%; $P < 0.001$). Median BPA concentrations were 0.8 ng/mL (range 0.2–4.1 ng/mL) in infertile and 0.5 ng/mL (range 0.2–3.2 ng/mL) in fertile women ($P < 0.001$). PXR significantly higher than controls. In infertile women, a positive association was found between BPA and MEHP levels and ER alpha, ER beta, AR, PXR, and PPAR gene expression. PFOS levels negatively correlated with AHR expression. No correlation was found between DDEHP levels and all evaluated nuclear receptors. This study underlines the need to provide special attention to substances that are still widely present in the environment and to integrate exposure measurements with relevant indicators of biological effects.	Int J Endocrinol. 2013;2013:510703.	10.1155/2013/510703	23710174	ヒト	生殖発生							横断研究	1	1				1	1	1						●								
統合_2593	Chen MJ et al.	2013	Association of exposure to phenols and idiopathic male infertility	Widespread human exposure to phenols has been documented recently, and some phenols which are potential endocrine disruptors have demonstrated adverse effects on male reproduction in animal and in vitro studies. However, implications about exposure to phenols and male infertility are scarce in humans. Case-control study of 327 idiopathic infertile men and 173 fertile controls was conducted. Urinary levels of bisphenol A (BPA), benzophenone-3 (BP-3), 2,2,4,4-tetrahydroxybenzophenone (BP-2), triclosan (TCS), and 2,5-dichlorophenol (2,5-DCP) were measured by high-performance liquid chromatography-tandem mass spectrometry. Men in the highest tertile of BPA concentration had at least two-fold higher odds ratio (OR) of idiopathic male infertility (in which the OR = 1 for the lowest tertile) than those in the lowest tertile (OR = 2.58, 95% confidence interval (CI) = 1.45–4.59, $P = 0.001$). After adjusting for potential confounders, the ORs of the second and third tertiles of BPA exposure were also significantly associated with idiopathic male infertility (in which the ORs = 2.06 and 2.51, respectively). Aside from these associations, the ORs of the highest tertile of 2,5-DCP exposure were also associated with idiopathic male infertility (in which the OR = 2.11). Increased urinary levels of BPA, benzophenone-3 (BP-3), 2,2,4,4-tetrahydroxybenzophenone (2,2,4,4-THBP), 2,5-dichlorophenol (2,5-DCP), and 2,4,5-trichlorophenol (2,4,5-TCP), were also associated with idiopathic male infertility. There were no relationships between exposure to other phenols and idiopathic male infertility in the present study. Our study provides the first evidence that exposure to 4%–5.1% of BPA or DCP and/or TCP is associated with idiopathic male infertility.	J Hazard Mater. 2013 Apr 15:250-251:115-21.	10.1016/j.jhazmat.2013.01.061	23435201	ヒト	精巣							症例対照研究	1	1				1	1	1														
統合_2594	Chen XJ et al.	2013	Parental phenols exposure and spontaneous abortion in Chinese population residing in the middle and lower reaches of the Yangtze River	Widespread use of phenols has led to ubiquitous exposure to phenols. In experimental animals, phenols increased resorptions, reduced fetal/litter size and fetal body weights. However, there are limited epidemiological evidences of the relationships between exposure to phenols and pregnancy outcomes. We evaluated the associations between parental urinary levels of various phenols and spontaneous abortion in a Chinese population residing in the middle and lower reaches of the Yangtze River. A hospital-based case-control study was conducted between 2010 and 2011. Cases were women with spontaneous abortion (SAB) (n=1,120) who had a history of two or more consecutive abortion and had at least one living child. Both parental urinary phenols were measured by high-performance liquid chromatography-tandem mass spectrometry, including bisphenol A (BPA), benzophenone-3 (BP-3), 2,2,4,4-tetrahydroxybenzophenone (2,2,4,4- TCP), pentachlorophenol (PCP), 2,4,6-trichlorophenol (2,4,6- TCP), 2,4-dichlorophenol (2,4-DCP), and 4-n-nonylphenol (4-n-NP). Compared with the low exposure group, there was an increased risk of spontaneous abortion with high parental urinary PCP concentration (odds ratio (OR)=2.06, 95% Confidence Interval (CI): 1.39-3.13), and maternal exposure to 4-n-NP and alkylphenols also significantly increased the risk of spontaneous abortion (OR=2.21, 95% CI: 1.52-3.60; OR=2.81, 95% CI: 1.39-5.66, respectively). Our study firstly provides the evidence that paternal PCP exposure, maternal 4-n-OP and alkylphenols exposure are associated with spontaneous abortion in humans.	Chemosphere. 2013 Sep;93(2):217-22.	10.1016/j.chemosphere.2013.04.067	23714150	ヒト	生殖発生							横断研究	1	1				1	1	1						●								
統合_2595	Ehrlich S et al.	2013	Urinary bisphenol A concentrations and cytochrome P450 19 A1 (Cyp19) gene expression in ovarian granulosa cells: An in vivo human study	BACKGROUND: Exposure to bisphenol A (BPA), a chemical widely used in consumer products, has been associated in in vitro Cyp19 gene expression. OBJECTIVE: To evaluate an in vivo human model of Cyp19 gene expression in granulosa cells. STUDY DESIGN: A cohort of an ongoing prospective cohort study of women undergoing in vitro fertilization (IVF) at the Massachusetts General Hospital (MGH) Fertility Center. METHODS: Mixed effect models were used to evaluate the association of urinary BPA concentrations with granulosa cell Cyp19 mRNA expression. RESULTS: In 42 women undergoing 70 IVF cycles, adjusted changes in mean Cyp19 expression (beta and 95% CI) for quartiles 2-4 were (as compared to the lowest quartile were: -0.47 (-2.2-1.28); -3.97 (-5.58-2.35) and -0.38 (-1.98-1.18). CONCLUSIONS: An in vivo model for evaluation of Cyp19 gene expression was developed for use in epidemiologic studies. In this pilot study, we found no statistically significant linear association between urinary BPA concentrations and Cyp19 expression.	Reprod Toxicol. 2013 Dec;42:18-23.	10.1016/j.reprotox.2013.06.071	23850856	ヒト	生殖発生							横断研究	1	1				1	1	1						●								
統合_2596	Louis GMB et al.	2013	Bisphenol A and phthalates and endometriosis: the Endometriosis: Natural History, Diagnosis and Outcomes Study	OBJECTIVE: To explore the relation between bisphenol A and 11 phthalate metabolites and endometriosis. DESIGN: Matched cohort design. SETTING: Fourteen clinical centers. PATIENTS: The operative cohort comprised 656 women undergoing laparoscopy/hysteroscopy, whereas the population cohort comprised 231 women matched on age and residence. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Surgically visualized or pelvic magnetic resonance imaging diagnosed endometriosis in the two cohorts, respectively. RESULT(S): Odds ratios (OR) and 95% confidence intervals (CIs) were estimated using logistic regression models. In the operative cohort, when restricting to visualized and histologic endometriosis (stages I–IV), the OR (95% CI) for 1 ng/mL increase in urinary BPA was 1.01 (0.99–1.03). Urinary concentrations of 2-methyl-6-phenylphenol, mono-(2-ethyl)-phthalate, mono-(2-ethyl-5-hydroxyhexyl)-phthalate, and mono-(2-ethyl-5-oxohexyl)-phthalate were significantly associated with an approximately twofold increase in the odds of an endometriosis diagnosis. Two phthalates were associated with endometriosis in the operative cohort when restricting to visualized and histologic endometriosis (women/all phthalates OR 1.38, 95% CI 1.10–1.71) or when restricting comparison women to those with a postoperative diagnosis of a normal pelvis (mono-(2-ethylhexyl)-phthalate OR 1.39, 95% CI 1.03–1.90; CONCLUSION(S): Select phthalates were associated with higher odds of an endometriosis diagnosis for women with magnetic resonance imaging–diagnosed endometriosis. The lack of consistency of findings across cohorts underscores the impact of methodology on findings.	Fertil SFertil Steril. 2013 Jul;100(1):162-9.e1-2.Seril	10.1016/j.fertnstert.2013.03.026	23579005	ヒト	子宮							横断研究	1	1				1	1	1						●								
統合_2597	Donohue KM et al.	2013	Prenatal and postnatal bisphenol a exposure and asthma development among inner-city children	BACKGROUND: Bisphenol A (BPA) is used widely to manufacture food container linings. Mouse models suggest exposure to BPA might increase allergic inflammation. OBJECTIVES: We hypothesized that BPA exposure as measured based on urinary BPA concentrations, could be associated with increased odds of a former and asthma and increased incident of wheeze/ skin-prick test (SPT) responses in children. METHODS: The Columbia Center for Children's Environmental Health recruited pregnant women for a prospective birth cohort study in ~1560. Mothers during the third trimester and children at ages 3, 5, and 7 years provided spot urine samples. Urinary BPA concentrations were measured in 568 mothers and 404 children. Asthma and wheeze were ascertained annually by questionnaire. SPT to 10 allergens was performed at age 7 years. Associations between BPA and asthma/wheeze at ages 3, 5, and 7 years, lifetime wheeze, lifetime asthma, and recent (12 months) asthma/wheeze were significantly associated with an approximately twofold increase in the odds of an endometriosis diagnosis. Two phthalates were associated with endometriosis in the operative cohort when restricting to visualized and histologic endometriosis (women/all phthalates OR 1.38, 95% CI 1.10–1.71) or when restricting comparison women to those with a postoperative diagnosis of a normal pelvis (mono-(2-ethylhexyl)-phthalate OR 1.39, 95% CI 1.03–1.90; CONCLUSION(S): Select phthalates were associated with higher odds of an endometriosis diagnosis for women with magnetic resonance imaging–diagnosed endometriosis. The lack of consistency of findings across cohorts underscores the impact of methodology on findings.	J Allergy Clin Immunol. 2013 Mar;131(3):736-42.	10.1016/j.jaci.2012.12.1573	23452902	ヒト	免疫							コホート研究	1	1				1	1	1		1				●		●						
統合_2598	Sprague BL et al.	2013	Circulating serum xenoestrogens and mammographic breast density	INTRODUCTION: Humans are widely exposed to the exogenously active phthalates, parabens, and phenols, raising concerns about potential effects on breast tissue and breast cancer risk. We sought to determine the association of circulating serum levels of these chemicals, hypothesizing recent exposure with mammographic breast density (a marker of breast cancer risk). METHODS: We recruited premenopausal women aged 18 to 75 years from mammography clinics in Madison, Wisconsin (N = 360). Subjects completed a questionnaire and provided a blood sample that was analyzed for seven ethyl phthalate, seven butyl phthalate, seven benzyl phthalate, butyl paraben, propyl paraben, butylphenol, and butylphenol diethanol (B-PH). Percentage breast density was measured from mammograms by using a computer-assisted thresholding method. RESULTS: 70% (range 0% to 90%) of women had detectable levels of at least one of the xenoestrogens measured. Women with detectable butyl paraben had 4.6% greater breast density (95% CI, 0.9% to 8.4%; $P = 0.02$) than women with undetectable butyl paraben. Women in the highest tertile of B-PH had 4.3% greater breast density (95% CI, 0.3% to 8.3%; $P = 0.04$) than women in the lowest tertile. Women with detectable butyl, ethyl, or benzyl phthalate had 3.6% greater breast density (95% CI, −0.1% to 7.3%; $P = 0.06$) than women without detectable phthalate. Women in the highest tertile of ethyl phthalate had 4.2% greater breast density (95% CI, −0.1% to 8.5%; $P = 0.06$) than women in the lowest tertile. Women with detectable butyl phthalate had 3.6% greater breast density (95% CI, −0.1% to 7.3%; $P = 0.06$) than women without detectable butyl phthalate. Women in the highest tertile of butyl phthalate had 3.6% greater breast density (95% CI, −0.1% to 7.3

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2604	Sripradipong C et al.	2013	Association between bisphenol A and abnormal free thyroxine level in men	Bisphenol A (BPA) is a chemical that is used in a variety of consumer products, and exposure to BPA is widespread among the general population. Recent studies have suggested that BPA may affect the thyroid and related pathways. However, human studies are still limited. The aim of this study was to determine the relationship between BPA exposure and thyroid function. We obtained survey data and blood samples from The Third National Health and Nutrition Survey (NHANES III) conducted between 1991 and 1994 by the National Center for Health Statistics (NCHS). Data from 1,326 men aged 20 to 80 years were used in the present study. Serum BPA, TSH, FT4, and related covariates were measured. BPA levels were log-transformed prior to analysis. BPA was detected in 62.6% of human samples with a median concentration of 0.28 (range 0.08-50.5) ng/ml. We included subjects who tested positive for thyroid autoantibody and then stratified the remaining subjects by gender. Bayesian analysis showed a significantly negative correlation between serum BPA and FT4 levels in males (r = -0.12, P = 0.02). In contrast, no association was observed in females. BPA was not associated with TSH in either gender. This gender-related discrepancy is possibly related to estrogen-related differences in the metabolism of BPA. Our preliminary results provide evidence of a negative association between BPA and FT4 levels. Additional detailed studies are needed to investigate the temporal relationship and potential public health implications of such an association.	Endocrine.2013;44(2):441-447	10.1007/s12020-013-9889-y Full text linksCite	23377699	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	●	-	-	-	-	-	-
統合_2605	Wang TG et al.	2013	Urinary Bisphenol A Concentration and Thyroid Function in Chinese Adults	BACKGROUND: Bisphenol A (BPA) is an endocrine disruptor that in animal studies can bind to the thyroid hormone receptor and affect thyroid function. Relevant epidemiologic studies are limited and results are inconsistent. OBJECTIVE: We investigated the association between urinary BPA and thyroid function in Chinese adults. METHODS: We conducted a cross-sectional study in a general population-based study from Shanghai Community Shenkang District, Shanghai, China, from June through August 2009. We analyzed the association between urinary BPA and thyroid function using multivariate linear regression models. Participants were further divided according to thyroid function status, and logistic regression was applied to determine the relationship between urinary BPA and thyroid function. RESULTS: Each one-quartile increase in BPA was related to an increase of 0.088 μIU/ml (95% confidence interval: 0.088-0.0872) in free triiodothyronine and a 0.081 μ/dl fall decline (-0.09 to -0.072) in TSH. High urinary BPA level was associated with increased thyroid function (adjusted odds ratio = 1.39; 95% confidence interval: 1.04-1.86) in comparison with the lowest quartile. In stratified analysis, the association between BPA and thyroid function was significant in women, there was a 0.23-μmol/l (0.09 to 0.21) increase in free triiodothyronine and a 0.21 μU/ml decline (-0.32 to -0.11

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統合_2630	Gascon M et al.	2015	Prenatal exposure to bisphenol A and phthalates and childhood respiratory tract infections and allergy	BACKGROUND: There is growing concern that prenatal exposure to bisphenol A (BPA) and phthalates, which are widely used in consumer products, might affect susceptibility to infections and the development of allergy and asthma in children, but there are currently very few prospective studies. OBJECTIVE: We sought to evaluate whether prenatal exposure to BPA and phthalates increases the risk of respiratory and allergic outcomes in children at various ages from birth to 7 years. METHODS: We measured BPA and metabolites of high-molecular-weight phthalates, 4-(2-(2-ethoxy)ethoxy) (DEHP) metabolites (Σ(prod)DEHP) and mono-benzyl phthalate (MBzP) in urine samples collected during pregnancy from 2,644 women participating in the Spanish INMA-Sabadell birth cohort study. The occurrence of chest infections, bronchitis, wheeze, and eczema in children was assessed at ages 6 and 14 months and 4 and 7 years through questionnaires given to the mothers. Atopy (specific IgE measurement) and asthma (questionnaire) were assessed at ages 4 and 7 years, respectively. RESULTS: The relative risks (RRs) of wheeze (RR, 1.26; 95% CI, 1.01-1.56; P = .041), chest infections (RR, 1.16; 95% CI, 1.00-1.35; P = .05), and bronchitis (RR, 1.18; 95% CI, 1.01-1.37; P = .03) at any age increased for each doubling in concentration of maternal urinary BPA. Σ(prod)DEHP metabolites were associated with the same outcomes (wheeze: RR, 1.29; 95% CI, 1.02-1.62; P = .03; chest infections: RR, 1.19; 95% CI, 0.97-1.39; P = .11; bronchitis: RR, 1.26; 95% CI, 1.02-1.55; P = .03). MBzP was associated with higher risk of wheeze (RR, 1.31; 95% CI, 1.00-1.70; P = .05). The risk of asthma at age 7 years was also increased with increasing prenatal BPA, Σ(prod)DEHP, and MBzP exposure. There were no other exposure-outcome associations. CONCLUSIONS: Prenatal exposure to BPA and high molecular-weight phthalates might increase the risk of asthma symptoms and respiratory tract infections throughout childhood.	J Allergy Clin Immunol. 2015 Feb;135(2):370-8.	10.1016/j.jaci.2014.09.030	25445825	ヒト	免疫毒性	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-
統合_2631	Gu J et al.	2018	Urinary concentration of personal care products and polycystic ovary syndrome: A case-control study	Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorder among females of reproductive age. Many emerging contaminants in personal care products have been confirmed with endocrine disruptive effects. We performed a case-control study to explore the associations between the urine levels of six common emerging contaminants (parabens (Σ4Paras), bisphenol A, and 2,5-dichlorophenol) and the risk of PCOS. Urine samples were collected from 83 women with PCOS (case group) and 83 healthy women (control group). No significant differences were found in detection rate or total concentrations of analytes in women with PCOS and controls (p > 0.05). In addition, no association was found between certain emerging contaminants and PCOS either in an unadjusted binary logistic regression model or in a model adjusted for potential confounders. However, with stratification according to body mass index, one organic UV filter - isoamyl p-MeO cinnamic(IMC) was significantly associated with PCOS in women with BMI <= 24 (adjusted OR = 1.923, 95% CI: 1.160, 3.187). It is the first time to investigate the associations between exposure of organic UV filters and PCOS risk. We conclude that there is positive association between IC and PCOS risk in obese and overweight women.	Environ Res. 2019 Jan;168:48-53.	10.1016/j.envres.2018.09.014	30265948	ヒト	卵巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2632	Gu Ida M et al.	2015	Bisphenol A and congenital developmental defects in humans	Over 50% of the causes of fetal malformations in humans are still unknown. Recent evidence suggests the relationship between environmental exposure to endocrine disruptors and fetal malformations. Our study aims to establish the role of Bisphenol A (BPA), if any, in altering human reproduction. We enrolled 261 pregnant women who were divided into two groups: case group (CA, n=101), women with established diagnosis of malformations in their fetuses, and control group (CO, n=160), women with normal pregnancies. BPA was measured in maternal urine samples collected at 11-13 weeks of gestation. The study shows a correlation between environmental exposure to BPA and the genesis of fetal malformations. Compared BPA, which was higher in the CA, cases, light on the hypothesis that a reduced detoxification by the mother is at the root of the mother-conceiver to the occurrence of malformation. In a more detailed manner, in case of chromosomal malformations, the average value of free BPA appears to be nearly three times greater than that of the controls. Similarly, in case of central and peripheral nervous system non-chromosomal malformations, the value of free BPA is nearly two times greater than that of the controls.	Mutat Res. 2015 Apr;774:33-9.	10.1016/j.mrfmmm.2015.02.007	25796969	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2633	Hao LX et al.	2016	Effect of bisphenol a on occurrence and progression of prolactinoma and its underlying mechanisms	OBJECTIVE: To investigate the effects of Bisphenol A (BPA) on prolactin (PRL) release, pituitary cell proliferation, prolactinoma formation in estrogen-sensitive Fischer 344 (F344) rats. MATERIALS AND METHODS: Four-week-old female F344 rats were orally administered with different concentrations of BPA or intraperitoneal injection of estradiol benzoate (estradiolbenzoate, EB) for 12 weeks. Bodyweight, blood BPA, level and serum PRL level were measured. Pituitary cell proliferation was detected by immunohistochemistry. Pituitary tumor formation was observed by hematoxylin and eosin (HE) staining. Pituitary cell estrogen receptor subtype (ERα/β), and also tumor transforming gene (FGF2/4) and its relevant receptor (FGFR-1/4) mRNA. The level and BPA concentration in patients with prolactinoma and the healthy controls were measured as well. RESULTS: Body weights of the rats treated with BPA were significantly decreased compared with those in the control group. The plasma PRL level and the pituitary weights of the rats were higher than those in the control group after BPA treatment. Compared with the control group, the pituitary mRNA and protein expression levels of FGF4/4 and FTF1 were significantly increased after BPA treatment. Moreover, ERα' expression level was enhancedby the treatment of BPA in comparison with that of the control group. Finally, the plasma BPA concentration in the prolactin tumor patients was significantly higher than that in the healthy participants. CONCLUSIONS: BPA may significantly promote pituitary cell proliferation and prolactin secretion in F344 rats, which may have impact on the proliferation and secretion of pituitary cell function through the FFGr pathway.	Am J Transl Res. 2016 Oct 15;8(10):4195-4204. eCollection 2016.	-	27830003	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2634	Hoyo SM et al.	2015	Variation in Urinary Flow Rates According to Demographic Characteristics and Body Mass Index in NHANES: Potential Confounding of Associations between Health Outcomes and Urinary Biomarker Concentrations	BACKGROUND: Urinary analyte concentrations are affected both by exposure level and by urinary flow rate (UFR). Systematic variations in UFR with demographic characteristics or body mass index (BMI) could confound assessment of associations between health outcomes and biomarker concentrations. OBJECTIVES: We assessed patterns of UFR (milliliters per hour) and body weight–adjusted UFR (UFRBW; milliliters per kilogram per hour) in relation to demographic characteristics and BMI. METHODS: We analyzed 24-h urine collections from 1,338 participants in the National Health and Nutrition Examination Survey 2009–2010 (ages stratified 6–11, 12–19, 20–39, 40–59, and ≥ 60 years; subgroups: low, mean/ideal, and BMI-dependent). Patterns of UFR and UFRBW were identified in linear and multivariate regression models. RESULTS: Urine volume increased from ages 6 to 40 years, and then declined with increasing age. UFRBW varied inversely with age category and was 1.6 times greater in children ages 6–11 years than in adults ages 40–59 years. Urine volume also increased with increasing BMI. Compared with the mean/ideal BMI category, UFRBW, but not UFR, varied inversely with BMI category and was 1.4 times greater in underweight children (BMI < 18.5 kg/m2) than in obese children (BMI ≥ 30 kg/m2). Urine volume and UFRBW were significantly greater in Mexican-American children than in non-Hispanic white children. Urine volume increased from 1 to 4 p.m. and then declined. Urine volume was 1.3 times greater in the afternoon than in the morning. Compared with fasting urine samples, urine volume was 1.2 times greater in samples collected 2–4 h after a meal. Urine volume was 1.2 times greater in samples collected in the summer than in samples collected in the winter. CONCLUSIONS: Urine volume and UFRBW vary substantially with age, sex, race/ethnicity, and BMI category. These variables should be considered in analyses of potential exposure–health outcome associations based on urinary concentration. Analyte-creatinine ratios are valuable exposure metrics in such assessments.	Environmental Health Perspectives.2015;123(4):293-300	10.1289/ehp.1408944	25625328	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2635	Hu WY et al.	2016	Gene-gene and gene-environment interactions on risk of male infertility: Focus on the metabolites	Infertility affects about 15% couples, and males contribute to half of the cases. Compared to20 independent effects of genetic and environmental factors, interactions between them help in the understanding of the susceptibility to male infertility. Thus, we genotyped 26 polymorphisms, measured 12 urinary chemical concentrations, and explored interactions between gene-gene and gene-environment in 1089 Han Chinese using metabolomic analysis. We first observed that GSTT1 might interact with GSTM1 (Pinteraction=0.0132). Furthermore, an interaction between GSTM1 and it is polymorphism (I- vs. del) was identified (Pinteraction=1.08x10-3), as well as a 2-way interaction among GSTT1, GSTM1 and 4-OP (Pinteraction=0.0002). Subjects with GSTT1-present and GSTM1-null genotypes were susceptible to male infertility when exposed to it (P=OR=1.828, 95% CI=1.178-90.23, P=1.94x10-10). Nine metabolites identified were involved in the tricarboxylic acid cycle. In conclusion, it is a novel study of the interaction on male infertility from the aspect of metabolomics.	Environment International.2016;91:188-195	10.1016/j.envint.2016.02.025	26970590	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2636	Hu s WQ et al.	2015	Maternal urinary bisphenol A levels and infant low birth weight: A nested case-control study of the Health Baby Cohort in China	BACKGROUND: Exposure to bisphenol A (BPA), a known endocrine disruptor, has been demonstrated to affect fetal development in animal studies, but findings in human studies have been inconsistent. OBJECTIVES: We investigated whether maternal exposure to BPA during pregnancy is associated with an increased risk of intrauterine growth restriction (IUGR) and low birth weight (LBW). METHODS: A total 302 mother-infant pairs (151 LBW cases and 151 matched controls) were selected from the participants enrolled in the prospective Health Baby Cohort (HBC) in Wuhan city, China, during 2012-2013. BPA concentrations were measured in maternal urine samples collected at delivery, and the information of birth outcomes was retrieved from the medical records. A conditional logistic regression was used to evaluate the relationship between urinary BPA levels and LBW. RESULTS: Mothers with LBW infants had significantly higher urinary BPA levels (median: 4.72ng/L) than the control mothers (median:2.76ng/L) (p<0.05). Increased risk of LBW was associated with higher maternal urinary levels of BPA (OR=1.69, 95% CI=1.08-2.65) after adjusting for potential confounders. Compared to the lowest BPA quartile, the highest quartile had an OR of 3.06 (95% CI=1.36-6.89). The associations were also assessed among female infants, male infants, and in a stratified analysis of heterogeneity in risk by GDD. CONCLUSIONS: Prenatal exposure to higher levels of BPA may potentially increase the risk of delivering LBW infants, especially for female infants. This is the first case-control study to examine the association in China.	Environ Int. 2015 Dec;85:96-103.	10.1016/j.envint.2015.09.005	26382648	ヒト	生殖(低出生体重)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2637	Ince T et al.	2018	Urinary bisphenol-A levels in children with type 1 diabetes mellitus	BACKGROUND: Bisphenol-A (BPA) is one of the most abundantly produced chemicals globally. Concerns have been raised about BPA's possible role in the pathogenesis of type 1 diabetes mellitus (T1DM). The main aim of the current study was to evaluate the possible association between BPA exposure and T1DM. The second aim was to investigate children's possible BPA exposure route. In Turkey. METHODS: A total of 100 children aged between 5 and 18 years, including 50 children with T1DM and 50 healthy children were included. Urinary BPA levels of all children were measured using high performance liquid chromatography. Mothers of children enrolled in the study were also requested to complete a survey that included questions on the sociodemographic characteristics, medical history and possible BPA exposure routes of their children. RESULTS: In the T1DM group, 76% of the children were female, and the mean age was 11.5 ± 3.8 years. In the control group, 64% of the children were female, and the mean age was 11.2 ± 3.6 years. The urinary BPA levels were not significantly different between the two groups. It was found that the use of plastic bottles and the consumption of daily products in plastic boxes significantly increased the urinary BPA concentrations in all children (p < 0.05). CONCLUSIONS: Although there was no significant association between urinary BPA levels and T1DM, we found an inverse relationship between current urinary BPA levels and birth weight. This finding might be important for prenatal exposure, and further prospective research must be conducted. Also, the use of plastic bottles, which has not been mentioned much in the literature before, was found to be an important exposure route for BPA.	J Pediatr Endocrinol Metab. 2018 Aug 28;31(8):829-836.	10.1515/jpem-2018-0141	29975667	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2638	Jeong EH et al.	2013	The Relationship between Uterine Myoma Growth and the Endocrine Disruptor in Postmenopausal Women	OBJECTIVES: To investigate the number of leiomyoma patients exposed to bisphenol A (BPA) and to observe whether the serum concentration of BPA is related to leiomyoma growth. METHODS: A total of 198 patients who underwent hysterectomy or myomectomy were enrolled in this study from March 2011 to February 2012. Serum BPA concentrations were measured by enzyme-linked immunosorbent assay. RESULTS: BPA was detected in 85.9% out of a total of 198 samples, and in 88.0% out of 108 leiomyoma patients. In detail, the detection rates of serum BPA were 88.0% in the control group, 77.3% in the mid group, 90.9% in the moderate group and 96% in the severe group. The mean BPA concentration in the control group was 0.018 +/- 0.007 ng/mL. the leiomyoma groups, the mean BPA concentrations were 0.176 +/- 0.068 ng/mL (mid), 0.169 +/- 0.082 ng/mL (moderate) and 0.437 +/- 0.338 ng/mL (severe) (P = 0.0003). Values represent the mean +/- standard error. CONCLUSIONS: The detection rates of serum BPA in the control and leiomyoma groups were 88.0% and 96.0%, respectively. However, there was no significant difference in the serum BPA concentrations between the control and leiomyoma groups. To verify the effect of BPA on leiomyoma growth, a clear and sequential mechanism is recommended for people who are at risk for uterine leiomyoma.	J Menopausal Med.2013;19(3):130-134	10.6118/jmm.2013.19.3.130	25371878	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2639	Jia J et al.	2013	Interactive Effect of Bisphenol A (BPA) Exposure with-22G/C Polymorphism in LOX Gene on the Risk of Osteosarcoma	BACKGROUND: Osteosarcomas have many established risk factors, both genetic and environmental, but by themselves these explain only part of the total cancer incidence. Bisphenol A (BPA) is an environmental estrogen associated with risk of several kinds of cancer. The lysyl oxidase gene (LOX) may also contribute to risk of tumours including osteosarcoma. Here, we investigated possible interactions of BPA and a LOX polymorphism on the risk of osteosarcoma. METHODS: The present hospital-based case–control study included 286 cancer patients and 212 controls from a Chinese population. Internal burdens of BPA exposure was measured by urinary BPA concentrations, and the LOX-22G/C polymorphism was genotyped by PCR-RFLP. RESULTS: Urinary BPA concentrations were significantly higher in osteosarcoma cases than in controls. Compared to subjects with BPA-free (limit of detection) urine, subjects with BPA more than or equal to median value had significantly increased risk of osteosarcoma among subjects who carried C at LOX genotypes. A significant interaction between BPA and the -22 G/C polymorphism was observed for osteosarcoma overall, osteosarcomas affecting knee and osteosarcomas affecting hip, as P(interaction) = 0.0036 for osteosarcoma overall, P(interaction) = 0.0016 for osteosarcoma affecting knee and P(interaction) = 0.0017 for osteosarcoma affecting hip. CONCLUSIONS: The results suggest that BPA exposure interacts with the -22 G/C polymorphism of the LOX gene to increase the risk of osteosarcoma.	Asian Pac J Cancer Prev. 2013;14(6):3805-8.	10.7314/apjcp.2013.14.6.3805	23886186	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2640	Kardas F et al.	2016	Increased Serum Phthalates (MEHP, DEHP) and Bisphenol A Concentrations in Children With Autism Spectrum Disorder: The Role of Endocrine Disruptors in Autism Etiopathogenesis	The aim of this study was to investigate the relationship between autism spectrum disorders development and exposure to mono (2-ethylhexyl) phthalate (MEHP), di (2-ethylhexyl) phthalate (DEHP), and bisphenol A (BPA), 3 of the endocrine disruptors, among adolescents. The study included 80 children with autism spectrum disorder (27 girls, 53 boys) and 80 healthy subjects (30 girls, 50 boys) as controls. Serum MEHP, DEHP, and BPA levels were measured by using high-performance liquid chromatography. Children with autism spectrum disorder had significantly increased serum MEHP, DEHP, and BPA concentrations (2.47 +/- 0.12 ng/mg ml, 0.74 +/- 0.08 ng/mg ml, 3.2 +/- 0.18 ng/ml) compared to healthy control subjects (0.91 +/- 0.05 ng/mg ml, 0.42 +/- 0.06 ng/mg ml, 0.88 +/- 0.14 ng/ml) respectively (P < .001). The fact that higher serum MEHP, DEHP, and BPA were found levels in the autism spectrum disorder group compared to healthy controls suggests that endocrine disruptors may have a role in the pathogenesis of autism spectrum disorders.	J Child Neurol. 2016 Apr;31(5):629-35.	10.1177/0883073815609150	26450281	ヒト	発達神経	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	●	-	-
統合_2641	Komarowska MD et al.	2015	Serum Bisphenol A Level in Boys with Cryptorchidism: A Step to Male Infertility?	Cryptorchidism is the most common congenital birth defect in boys and affects about 2-3% full term male neonates. Its etiology is multifactorial. Purpose. To evaluate the concentrationof A (BPA) levels in boys with cryptorchidism and to assess the relationship between BPA concentration and the degree of testicular maldescent. Material and methods. The study group consisted of 30 boys with cryptorchidism (mean age 1.5 ± 1.1 years). The control group consisted of 30 healthy boys (mean age 1.7 ± 1.2 years). The exclusion criteria were: prematurity, other abnormalities of the urinary tract, endocrinopathy, chromosomal abnormalities and the coexistence of other congenital defects. Parents or legal guardians were interviewed by a questionnaire on the risks of exposure to BPA in everyday life. Results. The testes, in both groups were similar in size. The largest of the undescended testis in the group of boys with cryptorchidism was decreased. Free serum BPA level in cryptorchid boys and in the control group was not statistically significant (p > 0.05). The conjugated serum BPA level in cryptorchid boys and in the control group was statistically significant (p < 0.05). Total serum BPA level in cryptorchid boys and in the control group was statistically significant (p < 0.05). Serum total BPA level was related with a positive answer about problems with conception (p < 0.03). Conclusion. Our study indicated that high serum BPA was associated with cryptorchidism.	Int J Endocrinol. 2015;2015:973154.	10.1155/2015/973154	26491444	ヒト	精巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-	-
統合_2642	Kondoh M et al.	2016	Plasma phthalate and bisphenol a levels and oxidant-antioxidant status in autistic children	Phthalates and bisphenol A (BPA) are endocrine disrupting chemicals (EDCs) that are suggested to exert neurotoxic effects. This study aimed to determine plasma phthalates and BPA levels along with oxidant/antioxidant status in autistic children (n=31), including 13 children pre-diagnosed with 'Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS)'. Plasma levels of BPA, di (2-ethylhexyl) phthalate (DEHP) and its primary metabolite mono (2-ethylhexyl) phthalate (MEHP) were measured by high performance liquid chromatography (HPLC). Oxidant/antioxidant status was assessed by measuring plasma thiobarbituric acid reactive substances (TBARS), superoxide dismutase (SOD) and glutathione reductase (GR) activities and glutathione (GSH) and cysteine levels were measured. Plasma BPA levels, of children with PDD-NOS were significantly higher than both typical autistic children and controls (t=-3.0, P<0.01). Carbonyl, cysteine concentrations and GPx1, SOD and GR activities were higher (p<0.05). CAT activity was markedly lower in study group. BPA exposure might be associated with PDD-NOS. Intracellular imbalance between oxidant and antioxidant status might facilitate its neurotoxicity.	Environmental Toxicology and Pharmacology.2016;43:149-158	10.1016/j.etap.2016.03.006	26991849	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-	-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と2用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2643	Kosieczna A et al.	2018	Serum bisphenol A concentrations correlate with serum testosterone levels in women with polycystic ovary syndrome	The aim of this study was to determine serum bisphenol A (BPA) concentrations using high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) in women with polycystic ovary syndrome (PCOS) (n = 58, age range 18-35 yrs) and to evaluate its potential impact on their hormonal and metabolic profile. The control group consisted of age- and BMI-matched 58 women from women with no clinical or biochemical hyperandrogenism. Our results showed that women with PCOS had significantly higher serum BPA concentrations than healthy controls (geometric mean and 95% CI: 0.302 ng/mL [0.260; 0.350] vs. 0.156 ng/mL [0.138; 0.181], P < 0.001), which correlated positively with serum total testosterone (r = 0.277; 95% CI [0.086; 0.452], P = 0.003) and the free androgen index (FAI; r = 0.286, P = 0.029). There were no significant correlations between serum BPA and BMI, waist circumference, serum glucose, insulin and lipids. These results point to the potential role of BPA in the pathogenesis of the ovarian hyperandrogenism in women with PCOS.	Reprod Toxicol. 2018 Dec;82:32-37.	10.1016/j.reprotox.2018.09.006	30266220	ヒト	卵巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2644	La Rocca C et al.	2015	Exposure to Endocrine Disruptors and Nuclear Receptors Gene Expression in Infertile and Fertile Men from Italian Areas with Different Environmental Features	Internal levels of selected endocrine disruptors (EDs) (i.e., perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), 4-2 ethylhexyl phthalate (DEHP), mono (2-ethylhexyl) phthalate (MEHP), and bisphenol A (BPA)) were assessed in blood/serum of infertile and fertile men from central Italian areas and characterized by different environmental features. PFOS and PFOA levels were also measured in seminal plasma of the same subjects, gene expression levels of a panel of nuclear receptors (NRs), namely androgen receptor alpha (ERalpha) estrogen receptor beta (ERbeta), androgen receptor (AR), and hydrocarbon receptor (AhR), were evaluated in spermatozoa. Results showed that PFOS and PFOA were the most prevalent pollutants detected in the blood of the enrolled subjects. Specifically, the concentrations of all EDs, except PFOA/plasma, compared to subjects from other areas. Subjects from urban areas had significantly higher levels of MEHP, whereas subjects from rural areas had higher levels of PFOA in both blood and seminal plasma. Interestingly, ERalpha, ERbeta, AR, PXR and AhR expression is directly correlated with BPA and inversely correlated with PFOA serum levels. Our study indicates the relevance of the living environment when investigating the exposure to specific EDs. Moreover, the NRs panel in PBMCs, demonstrated to be a potential biomarker of effect to assess the EDs impact on reproductive health.	International Journal of Environmental Research and Public Health.2015;12(10):12426-12445	10.3390/ijerph121012426	26445054	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2645	La Rocca C et al.	2014	Exposure to Endocrine Disruptors and Nuclear Receptor Gene Expression in Infertile and Fertile Women from Different Italian Areas	Within the PRIVATA project, infertile and fertile women were enrolled from metropolitan, urban and rural Italian areas. Blood/serum levels of several endocrine disruptors (EDs) (perfluorooctane sulfonate, PFOS; perfluorooctanoic acid, PFOA; di-2-ethylhexyl phthalate, DEHP; mono (2-ethylhexyl) phthalate, MEHP; bisphenol A, BPA) were evaluated concurrently with nuclear receptors, (NRs) gene expression levels (ERα, ERβ, AR, PXR, AhR) in spermatozoa. Results showed that women from metropolitan areas (PRIMA) - infertile women from the metropolitan area displayed significantly higher levels of BPA as well as lower (0.05 vs. 0.1 ng/mL, p=0.0001) and MEHP compared to infertile women from urban and rural areas, increased expression levels of NRs, except PPARβ. Infertile women from urban and rural areas had PXR levels significantly higher than those from metropolitan areas. Our study indicates the relevance of the living environment when investigating the exposure to EDs and the modulation of the NR panel in PBMC as a suitable biomarker of the effects in assess the EDs impact on reproductive health.	International Journal of Environmental Research and Public Health.2014;11(10):10146-10164	10.3390/ijerph111010146	25268510	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2646	Landolfi A et al.	2017	Bisphenol A glucuronidation in patients with Parkinson's disease	BACKGROUND: Bisphenol A (BPA) is a widely distributed estrogen-mimetic molecule, with well-established effects on the dopaminergic system. It can be found in canned food, dental sealants, thermal paper, etc. BPA undergoes liver conjugation with glucuronic acid and is subsequently excreted in the urine. OBJECTIVES: In the present study we quantified the concentration of free and conjugated Bisphenol A in blood of patients with Parkinson's disease (PD) and healthy controls. METHODS: Urinary BPA concentration was measured by isotope dilution-TurboFlow-liquid chromatography-tandem mass spectrometry. We used multiple linear regression analysis to estimate associations between BPA-glucuronidation and molecular hormones and motor ability, adjusting for confounding factors. RESULTS: Parkinson's Disease patients carried a significantly lower amount of conjugated Bisphenol A and a correlation between BPA-glucuronidation and motor ability. Conversely, the control group was mostly homogeneous in terms of exposure to possible Bisphenol A sources. The only exceptions were exposure to corrections and carried females. PD patients consumed significantly more of both (p<0.05). Moreover, no difference in Bisphenol A glucuronidation was found after stratification by typology of anti-Parkinson's drugs taken and either conversion to the Levodopa Equivalent Daily Dose. CONCLUSIONS: BPA glucuronidation was decreased in patients with Parkinson disease. The possible unique mechanisms underlying Bisphenol A metabolism in PD patients deserve further elucidation. Moreover, further study is needed to assess a possible BPA role in Parkinson's Disease pathogenesis, due to its documented dopaminergic toxicity.	Neurotoxicology. 2017 Dec;63:90-96.	10.1016/j.neuro.2017.09.008	28939238	ヒト	発達神経	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2647	Lassen TH et al.	2014	Urinary Bisphenol A Levels in Young Men: Association with Reproductive Hormones and Semen Quality	BACKGROUND: Few human studies have examined bisphenol A (BPA) exposure in relation to semen quality and reproductive hormones in men, and results are divergent. OBJECTIVES: We examined associations between urinary BPA concentration and reproductive hormones, as well as semen quality, in young men from the general population. METHODS: Our study population consisted of 308 young men from the general population. Urinary BPA concentration was measured by isotope dilution-TurboFlow-liquid chromatography-tandem mass spectrometry. We used multiple linear regression analysis to estimate associations between BPA concentration and reproductive hormones and semen quality, adjusting for confounding factors. RESULTS: Median BPA concentration was 2.9 ng/mL. We found that 95% of the men had detectable urinary BPA concentrations. BPA concentration was 1.29 ng/mL (34.9–1,189 ng/mL). Men in the 90% concentration, above the lowest quartile had higher concentrations of serum testosterone, luteinizing hormone (LH), estradiol, and free testosterone (adjusted 95% CI: 0.1, 18.8; 95% CI: 0.1, 19.0;

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2656	Metwally FM et al.	2018	Study of the Effect of Bisphenol A on Oxidative Stress in Children with Autism Spectrum Disorders	The role of bisphenol A (BPA) in autism was investigated in 85 children (mean age ± SHM +/- 1.961) years) with autism spectrum disorders (ASDs) and 85 comparable age and sex-matched children used as controls. Urinary BPA levels and the activities of the oxidative stress markers glutathione peroxidase (GPX) and catalase (CAT) in erythrocytes were measured. The mean urinary BPA and GPX levels were significantly higher in children with autism than those of control children (p-values = 0.005 and 0.001, respectively). There was a positive correlation between BPA and B-cadil ratio (ASD, p-value = 0.000 and 0.005, respectively); these correlations were highly significant (p-values < 0.000 and 0.001, respectively). There was a significant positive correlation between BPA and GPX, but the correlation between BPA and B-cadil was not significant in children with autism. The observed results revealed that BPA may increase oxidative stress resulting in mitochondrial dysfunction that affecting the behavior and functioning of ASDs children.	Indian J Clin Biochem. 2018 Apr;33(2):196-201.	10.1007/s12291-017-0667-0	29651211	ヒト	発達神経	-	-	-	-	-	-	-	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-	-	-
統合_2657	Mínguez-Alarcón L, Gaskins AJ, Chiu YH, Souter I, Williams PL, Calafat AM, Hauser R, Chavarro JE	2016	Dietary folate intake and modification of the association of urinary bisphenol A concentrations with in vitro fertilization outcomes among women from a fertility clinic	Experimental data in rodents suggest that the effects of bisphenol A (BPA) on oocyte development may be modified by dietary methyl donors. Whether the same interaction exists in humans is unknown. We evaluated whether intake of methyl donors modified the associations between urinary BPA concentrations and treatment outcomes among 176 women who underwent 180 IVF cycles at a fertility center in Boston between 2007 and 2013. Participants completed a validated food frequency questionnaire and provided up to two urine samples per treatment cycle. High urinary BPA concentrations were associated with a 66% lower probability of implantation (n = 180 cycles; adjusted RR: 0.34; 95% CI: 0.13, 0.89) among women who consumed <800 mcg/day of total folate, but not among women consuming >/=800 mcg/day (n = 175 cycles; adjusted RR: 0.73; 95% CI: 0.46, 1.16; P-interaction = 0.03). A similar pattern was observed for probability of clinical pregnancy (p-interaction=0.07) and live birth (p-interaction=0.04). These results are consistent with previous animal data but further evaluation in other human populations is needed.	Reprod Toxicol. 2016 Oct;65:104-112.	10.1016/j.reprotox.2016.07.012	27423903	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	1	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-
統合_2658	Nahar MS et al.	2014	Bisphenol A-associated alterations in the expression and epigenetic regulation of genes encoding xenobiotic metabolizing enzymes in human fetal liver	Alterations in xenobiotic metabolizing enzyme (XME) expression across the life course, along with genetic, nutritional, and environmental regulation, can influence how organisms respond to toxic insults. In this study, we investigated the effects of bisphenol A (BPA) exposure on the expression and epigenetic regulation of genes encoding XMEs in human fetal liver. Quantitative RT-PCR was used to measure mRNA levels in 54 female human fetal liver specimens quantified for maternal BPA levels. we examined XME gene expression using PCR-Array in 15 and PCR sequencing in ~120 platforms. Of the genes that 160 XME genes assayed, Cytochrome P450 family 1 subfamily A member 2 (CYP1A2), CYP2A6, CYP2A7, CYP2B6, CYP2C8, CYP2C18, CYP2D6, CYP2E1, CYP3A4, CYP3A5, CYP3A7, CYP4A11, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4X1, CYP4Z1, CYP4Z2P, CYP4Z2P, CYP4B1, CYP4V2, CYP27A1, CYP20A1, NAD(P)H dehydrogenase, quinone 1 (NQO1), sulfotransferase family 1A member 1 (SULT1A1), SULT1A2, SULT1B1, SULT1E1, SULT2A1, SULT2B1, UDP glucuronosyltransferase family 1 member A1 (UGT1A1), UGT1A3, UGT1A4, UGT1A6, UGT1A9, UGT2A1, UGT2A2, UGT2B4, UGT2B7, UGT2B10, UGT2B11, UGT2B15, UGT2B17, UGT2B28, aldehyde dehydrogenase 1 family member A1 (ALDH1A1), ALDH1A2, ALDH1A3, ALDH1B1, ALDH2, ALDH3A1, ALDH3A2, ALDH3B1, ALDH3B2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, ALDH8A1, ALDH9A1, ALDH16A1, ALDH18A1, ALDH1L1, ALDH1L2, glutathione S-transferase alpha 1 (GSTA1), GSTA2, GSTA3, GSTA4, GSTA5, glutathione S-transferase mu 1 (GSTM1), GSTM2, GSTM3, GSTM4, GSTM5, glutathione S-transferase theta 1 (GSTT1), GSTT2, GSTT2B, glutathione S-transferase omega 1 (GSTO1), GSTO2, glutathione S-transferase pi 1 (GSTP1), glutathione S-transferase zeta 1 (GSTZ1), glutathione S-transferase kappa 1 (GSTK1), glutathione S-transferase MAPEG, glutathione peroxidase 1 (GPX1), GPX2, GPX3, GPX4, GPX5, GPX6, GPX7, GPX8, glutathione peroxidase 3 (plasma) (GPX3), glutathione peroxidase 4 (phospholipid hydroperoxidase) (GPX4), glutathione peroxidase 5 (epididymal androgen-related protein) (GPX5), glutathione peroxidase 6 (olfactory) (GPX6), glutathione peroxidase 7 (GPX7), glutathione peroxidase 8 (putative) (GPX8), epoxide hydrolase 1, microsomal (xenobiotic) (EPHX1), EPHX2, EPHX3, EPHX4, microsomal glutathione S-transferase 1 (MGST1), MGST2, MGST3, prostaglandin E synthase (PTGES), PTGES2, PTGES3, glutathione S-transferase zeta 1 (GSTZ1), glutathione S-transferase theta 1 (GSTT1), glutathione S-transferase theta 2 (GSTT2), glutathione S-transferase theta 2B (GSTT2B), glutathione S-transferase omega 1 (GSTO1), glutathione S-transferase omega 2 (GSTO2), glutathione S-transferase A1 (GSTA1), glutathione S-transferase A2 (GSTA2), glutathione S-transferase A3 (GSTA3), glutathione S-transferase A4 (GSTA4), glutathione S-transferase A5 (GSTA5), glutathione S-transferase mu 1 (GSTM1), glutathione S-transferase mu 2 (GSTM2), glutathione S-transferase mu 3 (GSTM3), glutathione S-transferase mu 4 (GSTM4), glutathione S-transferase mu 5 (GSTM5), glutathione S-transferase pi 1 (GSTP

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通毒性評価（動物）1：該当、0：該当しない　　通毒性評価（疫学）1：該当、0：該当しない　　通毒性評価（in vitro）1：該当、0：該当しない　　通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるものは作成根拠評価への進め、当該時点評価段階で原則として精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2669	Reeves KW et al.	2018	Bisphenol-A in breast adipose tissue of breast cancer cases and controls	We evaluated whether bisphenol A (BPA) could be quantified in breast adipose tissue samples provided by 20 breast cancer mastectomy patients and 11 reduction mammoplasty patients. Samples of breast adipose tissue were collected and BPA concentration was quantified using HPLC-ESI-MS/MS. BPA was detectable above the limit of quantitation of 0.38 ng/g in 30.4% of samples. BPA concentrations varied within- and between-breasts and were similar between cases and controls (0.39 vs. 0.51 ng/g, p = 0.74).	Environ Res. 2018 Nov;167:735-738.	10.1016/j.envres.2018.08.033	30236518	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-
統合_2670	Robledo C et al.	2013	Is bisphenol-A exposure during pregnancy associated with blood glucose levels or diagnosis of gestational diabetes?	Recent epidemiological studies indicate bisphenol A (BPA), an estrogenic chemical used in production of epoxy and polycarbonate, and plastic may increase risk of insulin resistance and type 2 diabetes. Exposure to BPA during pregnancy may also increase risk of gestational diabetes mellitus (GDM). We examined the association between BPA exposure during pregnancy and maternal glucose levels, HOMA-IR, and GDM diagnosis during pregnancy. Random urine samples from 2 visits of 2,350 and 1,744 women were analyzed for total (free BPA + conjugated BPA) urinary BPA concentrations. Data were obtained from 1 fasting glucose and 2 oral glucose tolerance tests (OGTT) that women underwent for routine GDM screening (mean gestational age = 26.6 weeks, SD = 3.8). Those with an initial screening value (>/= 135 mg/dl challenge 1-h 130 g oral OGTT, GDM diagnosis were made when the initial screening value was >/= 200 mg/dl or when values at >/= 2 time points exceeded 3 h oral OGTT thresholds. Among controls, median FBG levels (mg/dL) did not differ across exposure tertiles, defined according to the distribution of total specific-gravity adjusted urinary BPA concentrations. Logistic regression models controlling for race/ethnicity did not provide evidence of an association between BPA exposure and GDM (adjusted odds ratio (OR) for 3rd vs. 1st tertile = 0.9; 95% confidence interval (CI) = 0.6, 1.4; p-trend = 0.513). Findings do not support a relationship between total urinary BPA concentrations and altered glucose metabolism during pregnancy. However, due to study limitations, findings need to be interpreted with caution.	J Toxicol Environ Health A. 2013;76(14):865-73.	10.1080/15287394.2013.824395	24053363	ヒト	生殖(妊娠糖尿病)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	1	●	-	-	-	-	-	-	-	-	-
統合_2671	Shen Y et al.	2016	Phenolic environmental estrogens in urine and blood plasma from women with uterine leiomyoma: Epidemiological survey	AIM: To explore the effect of phenolic environmental estrogens (EE) on women with uterine leiomyoma (UL). METHODS: Urine and blood plasma samples were collected from 300 patients diagnosed with UL at the Affiliated Zhongda Hospital of Southeast University between December 2013 and December 2015. Control urine and blood plasma samples were collected from 300 women without uterine leiomyoma or other conditions at the UL or healthy volunteers presenting to the same hospital for physical examination during the same period. Bisphenol A (BPA), nonylphenol (NP), and octylphenol (OP) concentrations in these samples were measured using solid phase extraction (SPE) coupled with liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). RESULTS: Phenolic EE concentrations in urine and blood plasma were determined by solid-phase extraction (SPE) coupled with liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). RESULTS: The urine BPA concentration was significantly different between the UL group and the control group (t = 3.009, P = 0.003). There was also no statistically significant difference in urine NP concentration between the two groups (t = -0.870, P = 0.418). On logistic regression, exposure concentration of urine BPA (OR, 1.139; 95%CI: 1.040-1.278) and NP (OR, 1.165; 95%CI: 1.029-1.302) was associated with UL genesis (P < 0.05). Nonetheless, there was no significant difference in blood plasma concentrations of BPA, OP, and NP between the two groups (P > 0.05). CONCLUSIONS: Urine and blood plasma EE exposure levels in women, especially the urine level, was related to the incidence of UL.	J Obstet Gynaecol Res. 2016 Apr;42(4):440-5.	10.1111/jog.12928	26842765	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2672	Shen Y et al.	2013	Measurement of Phenolic Environmental Estrogens in Women with Uterine Leiomyoma	OBJECTIVES: To investigate the effect of phenolic environmental estrogens on uterine leiomyoma from the perspective of clinical epidemiology. METHODS: Urine and blood samples were collected from two women with uterine leiomyoma and women without uterine leiomyoma, living in Nanjing, China, between September 2012 and February 2013. A total of 256 urine samples and 213 blood samples were collected from the uterine leiomyoma group and 226 urine samples and 178 blood plasma samples from the control group. Bisphenol A (BPA), nonylphenol (NP) and octylphenol (OP) concentrations were determined by solid-phase extraction (SPE) coupled with liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). RESULTS: The Phenolic environmental estrogens in the uterine leiomyoma and control groups were compared by t-test. (1) In participants with grades 0, urine BPI concentration was significantly (P<0.05) higher in the uterine leiomyoma group than in the control group. In participants with grades >/= 1, urine NP concentration was significantly (P<0.05) higher in the uterine leiomyoma group than in the control group. (2) The urine BPA concentration was significantly different between grades 0 and grades >/= 1 (P<0.05). The urine NP concentration was significantly different between grades 0 and grades >/= 2 (P<0.05). (3) The urine BPA concentration was not significantly (P>0.05) different between grades 0 and grades >/= 1 (P>0.05). (4) The urine BPA concentration was not significantly (P>0.05) different between grades 0 and grades >/= 2 (P>0.05). (5) The urine BPA concentration was not significantly (P>0.05) different between grades 1 and grades >/= 2 (P>0.05). CONCLUSIONS: Exposure level of phenolic environmental estrogens in human was related with leiomyoma tumorigenesis.	PLoS One. 2013 Nov 8;8(11):e79838.	10.1371/journal.pone.0079838	24255718	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2673	Shen YP et al.	2015	Higher Urinary Bisphenol A Concentration Is Associated with Unexplained Recurrent Miscarriage Risk: Evidence from a Case-Control Study in Eastern China	BACKGROUND: Evidence about the association between Bisphenol A (BPA) and the risk of recurrent miscarriage (RM) in human being is still limited. OBJECTIVE: We evaluated the association of urinary BPA concentrations with RM in human being. METHODS: A hospital-based 1:2 matched case-control study on RM was carried out in Suzhou and Kunshan in Jiangsu Province in China between August 2008 and November 2012. Urinary BPA concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). RESULTS: The median urinary BPA concentrations were 1.61 ng/mL for 214 RM cases and 1.30 ng/mL for 428 controls. Conditional logistic regression was used to estimate the difference between the cases and controls. RM was associated with BPA (unadjusted odds ratio (OR), 1.27; 95% confidence interval (CI), 1.02-1.58; P-trend = 0.032). Compared to the groups with urinary BPA levels less than 0.34 mug/g Cr, the women with levels of 0.34-0.91 mug/g Cr and 0.91 mug/g Cr or above had a significantly higher risk of RM (OR = 1.91; 95% CI, 1.20-3.04 and OR = 1.93; 95% CI, 1.12-3.32). After adjusted after adjusting for confounding factors. The time from recently RM date to recruitment does not significantly influence the urinary BPA level (P = 0.382). CONCLUSIONS: Exposure to BPA may be associated with RM risk.	PLoS One. 2015 May 5;10(5):e0127886.	10.1371/journal.pone.0127886	26011304	ヒト	生殖(流早産)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2674	Shu X et al.	2018	Bisphenol A is not associated with a 5-year incidence of type 2 diabetes: a prospective nested case-control study	AIMS: The relationship between bisphenol A (BPA) and diabetes remains controversial. This study aims to investigate whether serum BPA level could predict the 5-year incidence of type 2 diabetes (T2D). METHODS: A nested case-control study was conducted among participants from the Tianjin Chronic Low-grade Systemic Inflammation and Health Cohort Study. Cases were defined as participants who developed diabetes during the 5-year follow-up. Cases and controls were matched for age and gender by a ratio of 1:1. Homeostasis model assessment was used to estimate basal pancreatic beta cell function (HOMA-β) and insulin resistance (HOMA-IR). Participants were stratified into tertiles based on low, median and high baseline serum BPA levels. Regression models were used to analyze the relationship between serum BPA concentration and the incidence of T2D. RESULTS: At baseline, no significant difference in serum BPA concentration was observed between patients with T2D and controls (1.1 (0.3, 3.7) vs. 1.4 (0.6, 3.9) ng/mL, P = 0.199). serum BPA concentration was positively associated with fasting plasma glucose (r = 0.27, P < 0.001); however, neither HOMA-β nor HOMA-IR correlated with serum BPA concentration. During the follow-up, 214 incident cases of T2D were identified. The OR (95% CI) for T2D comparing the highest with the lowest tertile of serum BPA was 1.08 (0.68, 1.72) in the crude model and 1.05 (0.65, 1.70) in the fully adjusted model. CONCLUSIONS: Serum BPA was not associated with a 5-year T2D incidence. These data do not support previous cross-sectional study that BPA exerted a detrimental effect on glucose metabolism.	Acta Diabetol. 2018 Apr;55(4):369-375.	10.1007/s00592-018-1104-4	29387940	ヒト	代謝	-	-	-	-	-	-	nested case-control	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2675	Simonelli A et al.	2017	Environmental and occupational exposure to bisphenol A and endometriosis: urinary and peritoneal fluid concentration levels	OBJECTIVES: The study aimed to give a first data-set of bisphenol A (BPA) levels in the peritoneal fluid of patients suffering from endometriosis and to investigate the relationship between BPA exposure and endometriosis. METHODS: Urine and peritoneal fluid samples were collected and analyzed by ELC-MS/MS in BPA dosage. RESULTS: Some of the investigated environmental/lifestyle risk factors (occupation, exposure to industries/activities at risk) were associated with an increase in endometriosis; smoking resulted as protective factor others. Use of food plastic items (-ib) did not seem to influence the onset of pathology. The association between the occupational exposure summarizing all scientific factors (working activity, personal protective equipment, controls) and endometriosis was statistically significant (p < 10 -) = 0.012, p < 0.05). Contrasting results were obtained when specific activities were examined. Detectable urinary BPA levels were found in all analyzed samples (patients: 1.77-12.68 µg/g/cr, mean = 3.5; 6.51 ± 3.56 µg/g/cr; control group: 1.28-2.36 µg/g/cr, mean = 3D, 1.61 ± 0.46 µg/g/cr). Peritoneal fluid BPA concentrations were found in all analyzed samples (patients: 0.27-12.68 µg/g/cr, mean = 3.5; 6.51 ± 3.56 µg/g/cr; control group: 0.27-2.36 µg/g/cr, mean = 3D, 1.61 ± 0.46 µg/g/cr). Urinary and peritoneal fluid BPA concentrations were not correlated. Multivariate analysis showed that urinary BPA was significantly higher in controlled peritoneal fluid; hence, in comparison two with patients (range 0.38-3.48 µg/g) mean = 1.32; 0.67 ± 0.36 µg/g) median. 0.66 µg/g) are cases carried out. CONCLUSIONS: Results highlight the potential association between BPA exposure and endometriosis, as well as the current lack of knowledge regarding occupational exposure to BPA and the need of epidemiological studies focused on single activities/occupations, such as housewives, cleaners, cashiers.	Int Arch Occup Environ Health. 2017 Jan;90(1):49-61.	10.1007/s00420-016-1171-1	27718009	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2676	Song Y et al.	2014	Urinary concentrations of bisphenol A and phthalate metabolites and weight change: a prospective investigation in US women	OBJECTIVE: Both bisphenol A (BPA) and phthalates are known endocrine-disrupting chemicals for which there is widespread general population exposure. Human exposure occurs through dietary and non-dietary routes. Although animal studies have suggested a potential role of these chemicals in obesity, evidence from human studies is sparse and inconsistent, and prospective evidence is lacking. This study evaluated urinary concentrations of BPA and major phthalate metabolites in relation to prospective weight change. METHODS: The study population was from the controls in a prospective case–control study of type 2 diabetes in the Nurses' Health Study (NHS) and NHS2. A total of 877 participants provided first-morning void urine samples in 1999–2000. Urinary concentrations of BPA and nine phthalate metabolites were measured using liquid chromatography–mass spectrometry. Body weights were self-reported at baseline and updated biennially through 2011 for 21 years. RESULTS: On average, the women gained 2.83 kg (95% confidence interval (CI), -2.27 to 8.18) during 10 years of follow-up. Urinary BPA concentrations were not associated with weight change. Urinary concentrations of monoethyl phthalate (MEP) were positively associated with weight change: women in the highest quartile of MEP gained 1.19 kg per year (95% CI: 0.97, 1.41) more per year (P-trend = 0.02) than women in the lowest quartile. Several phthalate metabolites, including phthalic acid (MPA)* and monobutyl phthalates, were also associated with faster prospective weight gain in a dose–response fashion (P-trend <0.01), whereas other phthalates metabolites, including MEP and monoethylhexyl phthalate, were not monotonically associated with body weight change. CONCLUSIONS: These data suggest urinary concentrations of BPA and certain individual phthalate metabolites that were associated with modestly greater weight gain in a dose–response fashion. These data are consistent with a potential role of BPA and phthalates in obesity, although more prospective data are needed to corroborate these observations.	Int J Obes (Lond). 2014 Dec;38(12):1532-7.	10.1038/ijo.2014.63	24722546	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2677	Stein TP et al.	2015	Bisphenol A Exposure in Children With Autism Spectrum Disorders	The etiology of autism spectrum disorders (ASD) is believed to involve genetic and environmental components. This study focused on the plasticizer, Bisphenol-A (BPA). The major pathway for BPA metabolism and excretion is via glucuronidation. To determine whether there was a relationship between BPA exposure and ASD, urine specimens were collected from 60 children with ASD and 52 controls. Free and total BPA concentrations were determined by mass spectrometry. The fraction glucuronidated was calculated from the difference. A metabolomics study was done to investigate metabolite distribution in the urine. (1) Most of the BPA in the urine was glucuronidated. (2) Total BPA was significantly higher in the ASD group than in the controls (P = 0.0004). (3) Free BPA was not significantly different between the groups. (4) Whitney U tests and multiple regression analysis found significant differences (P < 0.05) between the groups in total and % bound BPA and for the metabolomics analysis showed the extent of abnormal partial correlations. (5) Between metabolite concentrations and total BPA was approximately 3 times greater within the ASD group than the controls (P = 0.0001), and the number of absolute partial correlations > 0.50 for % bound BPA was approximately 25 times higher with ASD (P = 0.0001). The results suggest there is an association between BPA and ASD.	Autism Res. 2015 Jun;8(3):272-83.	10.1002/aur.1444	25641946	ヒト	発達神経	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2678	Sun Q et al.	2014	Association of Urinary Concentrations of Bisphenol A and Phthalate Metabolites with Risk of Type 2 Diabetes: A Prospective Investigation in the Nurses' Health Study (NHS) and NHSII Cohorts	BACKGROUND: Prospective evidence regarding associations for exposures to bisphenol A (BPA) and phthalates, with type 2 diabetes (T2D) is lacking. OBJECTIVE: We prospectively examined urinary concentrations of BPA and phthalate metabolites with T2D risk. METHODS: We measured BPA and eight major phthalate metabolites among 671 incident T2D cases matched to 671 non-case control pairs from the Nurses' Health Study (NHS) (mean age, 63.0 years) and NHSII (mean age, 35.8 years). RESULTS: In the NHS, BPA levels were not associated with incident T2D in multivariate adjusted analysis; and body mass index was adjusted; odds ratio (OR) comparing extreme BPA quintiles was 1.00 (95% confidence interval (CI): 0.72, 1.39; p-trend = 0.98). Urinary concentrations of monoethyl phthalate (MEP) were positively associated with T2D risk (OR = 1.00, 0.77, 0.85, 1.08, 1.35; p-trend = 0.03). Likewise, urinary concentrations of total phthalate metabolites were associated with T2D in the NHSII comparing extreme quartiles (OR = 1.0, 95% CI: 1.01, 3.09; p-trend = 0.02), but not in the NHS (OR = 0.87, 95% CI: 0.58, 1.31; p-trend = 0.29). Summed metabolites of butyl phthalates or di (2-ethylhexyl) phthalates were significantly associated with T2D only in the NHSII. ORs comparing extreme quartiles were 1.31 (95% CI: 0.88, 1.95; p-trend = 0.082) and 1.91 (95% CI: 1.26, 2.89; p-trend = 0.01), respectively. CONCLUSIONS: These results suggest that BPA and phthalate exposures may be associated with the risk of T2D among middle-aged, but not older, women. The divergent findings between the two cohorts might be explained by menopausal status, or simply by chance. Clearly, these results need to be interpreted with caution and should be evaluated in future studies. Ideally with multiple urine samples collected prospectively to improve the measurement of these exposures with short half lives.	Environ Health Perspect. 2014 Jun;122(6):616-23.	10.1289/ehp.1307201	24633239	ヒト	代謝	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-
統合_2679	Trabert B et al.	2014	Urinary bisphenol A-glucuronide and postmenopausal breast cancer in Poland	PURPOSE: Concerns regarding a possible link between bisphenol A (BPA) and breast cancer have been mounting, but studies in human populations are lacking. We evaluated the association between the major urinary BPA metabolite BPA-glucuronide (BPA-G) and postmenopausal breast cancer risk in a large population-based case–control study conducted in two cities in Poland (2000-2003), and further explored the association of BPA-G with breast cancer risk factors. METHODS: Urinary BPA-G was measured in 1,455 postmenopausal women (730 cases and 725 controls) using high-performance liquid chromatography–tandem mass spectrometry (HPLC-MS/MS). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression models. RESULTS: Urinary BPA-G was detected in 99.7% of controls without breast cancer using a newly established assay. Cells with an 85.7% coefficient of variation were used to estimate the association between BPA-G level and breast cancer using conditional logistic regression. Among controls, geometric mean BPA-G levels were comparable across categories of breast cancer risk factors using linear regression models. RESULTS: There was no indication that increased BPA-G was associated with postmenopausal breast cancer (p-trend = 0.59). Among controls, mean BPA-G was higher among women reporting extended use of menopausal hormone, cyclic screening mammogram, and residence in Warsaw. Other comparisons across strata of postmenopausal breast cancer risk factors were not related to differences in BPA-G. CONCLUSIONS: Urinary BPA-G, measured at the time of diagnosis, is not linked to postmenopausal breast cancer.	Cancer Causes Control. 2014 Dec;25(12):1587-93.	10.1007/s10552-014-0461-8	25189422	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2680	Troisi J et al.	2014	Placental concentrations of bisphenol A and birth weight from births in the Southeastern US	INTRODUCTION: Bisphenol A (BPA) is a widely estrogenic compound that has been detected in a wide variety of food products and biological matrices (saliva, blood, urine, etc.) Despite the potential risk of human exposure to BPA, few studies have investigated placental concentrations of BPA. METHODS: Placental tissue samples were collected from 1,000 mother-infant pairs at delivery. Placental BPA concentrations were evaluated in relation to birth weight z-scores, and several other maternal and infant characteristics collected from medical charts and semi-parental variables with placental BPA levels. RESULTS: Placental BPA concentrations ranged from 0.2 ng/g to 2724 ng/g (a more skewed tissue (range: 653.4 +/- 63.8 ng/g). There was a significant negative correlation between calculated birth weight-specific and levels of placental BPA (p < 0.05). Low birth weight and small for gestational age infants also had significantly greater placental BPA concentrations, as compared to normal weight infants and average/appr for gestational age infants. Infants born to African American mothers also had greater placental BPA concentrations as compared to infants born to Hispanic mothers. DISCUSSION: Placental BPA concentrations are correlated with the growth potential of the fetus and may play a role in reduced fetal growth.	Placenta.2014;35(11):947-952	10.1016/j.placenta.2014.08.091	25227326	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2681	Tse LA et al.	2017	Bisphenol A and other environmental risk factors for prostate cancer in Hong Kong	BACKGROUND: Environmental exposures are contributing factors to prostate cancer etiology, but these remain unclear. We aimed to document the associations between environmental risk factors and prostate cancer in Hong Kong Chinese men. METHODS: A case-control study of 1,204 cases and 1,204 controls was conducted in Hong Kong between 2011 and 2015. Urinary bisphenol A (BPA) was measured by high-performance liquid chromatography-tandem mass spectrometry. Information on cases' and controls' clinical data and epidemiological information on chronic BPA exposure and other environmental risk factors (e.g., dietary habits, occupation and birth cohort) using a standard questionnaire. A new assessment tool of environmental BPA exposure was developed and replicated. Multiple logistic regression analysis was performed to examine odds ratio (OR) and 95% confidence interval (95%CI) for the association of prostate cancer with a most-contacted BPA exposure index (CBPAI) and other environmental risk factors. RESULTS: Weekly consumption of deep-fried food (OR=1.38, 95% CI: 1.16-1.64) and pickled vegetable (OR=1.87, 95% CI: 1.57-2.24) was significantly associated with excessive prostate cancer risk. Prostate cancer was positively associated with eighteenth-term (OR=1.75, 95% CI: 1.37-2.09) and it was negatively associated with green tea consumption (OR=0.77, 95% CI: 0.61-0.97). Significant associations were also found between prostate cancer and family history of cancer (OR=1.49, 95% CI: 1.16-1.92), BMI (OR=1.22, 95% CI: 1.12-1.32), CCDC1 (OR=1.18, 95% CI: 1.02-1.37), and CBPAI (OR=1.21, 95% CI: 1.05-1.39). CONCLUSIONS: Frequent consumption of deep-fried food and pickled vegetable, non-habitual green tea drinking and eighteenth rank are the contributing risk factors to prostate cancer in Hong Kong Chinese. More importantly, this study provides the first epidemiological evidence on carcinogenicity of BPA on the human prostate.	Environ Int. 2017 Oct;107:1-7.	10.1016/j.envint.2017.06.012	28644961	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、当該時点評価段階で原則として除外。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2682	Upson K et al.	2014	A population-based case-control study of urinary bisphenol A concentrations and risk of endometriosis	STUDY QUESTION: Is bisphenol A (BPA) exposure associated with the risk of endometriosis, an estrogen-driven disease of women of reproductive age? SUMMARY ANSWER: Our study suggests that increased urinary BPA is associated with an increased risk of non-ovarian pelvic endometriosis, but not ovarian endometriosis. WHAT IS KNOWN ALREADY: BPA, a high-volume chemical used in the polymer industry, has been the focus of much attention because of its estrogenic activity and its ubiquitous presence in the environment. Exposure to BPA is widespread in the general population. STUDY DESIGN, SIZE, DURATION: We used data from the Women's Risk of Endometriosis study, a population-based case-control study of endometriosis, conducted among female enrollees of a large healthcare system in the US Pacific Northwest. Cases were women laparoscopically confirmed to have endometriosis (n = 248) and controls were women undergoing laparoscopy for benign gynecologic conditions other than endometriosis (n = 352). Diagnosis of endometriosis. PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Total urinary BPA concentrations were measured in 24 h urine samples and BPA exposure-based urinary intake was estimated. Data were collected after disease diagnosis. In cases, Total urinary BPA concentration (free and conjugated species) was quantified using a high-performance liquid chromatography-mass spectrometry method. We estimated odds ratios (ORs) and 95% confidence intervals (CIs) using unconditional logistic regression, adjusting for urinary creatinine concentrations, age and reference year. We also evaluated the association by disease subtypes, ovarian and non-ovarian pelvic endometriosis, that may be etiologically distinct. MAIN RESULTS AND THE ROLE OF CHANCE: We did not observe a statistically significant association between total urinary BPA concentrations and risk of endometriosis (OR 1.0, 95% CI 0.7, 1.4 for the highest quartile compared with the lowest quartile; p-trend = 0.9). However, we observed a positive association with non-ovarian disease (OR 2.0, 95% CI 1.2, 3.3 for the highest quartile; p-trend = 0.01). We found no evidence of an association between urinary BPA and ovarian endometriosis (OR 0.8, 95% CI 0.5, 1.3; p-trend = 0.3). LIMITATIONS, REASONS FOR CAUTION: Given the short elimination half-life of BPA, our study was limited by the timing of collection of the single urine sample, that occurred after case diagnosis. Thus, our BPA measurements may not accurately represent the participants' levels during the etiologically relevant time period for endometriosis development. In addition, since it was not feasible in this population-based study to surgically confirm the absence of disease, it is possible that some controls may have had undiagnosed endometriosis. WIDER IMPLICATIONS OF THE FINDINGS: By using population-based data, it is more likely that the controls represented the underlying frequency of BPA exposure in contrast to prior studies. Our findings suggest that BPA exposure may be associated with non-ovarian endometriosis, but not ovarian endometriosis. Further research is warranted to confirm or refute BPA may affect the normal dynamic structural changes of hormonally responsive endometrial tissue during the menstrual cycle, potentially the establishment and persistence of ectopic endometrial tissue in cases with non-ovarian pelvic endometriosis. Further research is warranted to confirm or refute BPA may affect the normal dynamic structural changes of hormonally responsive endometrial tissue during the menstrual cycle, potentially the establishment and persistence of ectopic endometrial tissue in cases with non-ovarian pelvic endometriosis. Further research is warranted to confirm or refute our novel findings. Endometriosis's subtypes that may be etiologically distinct. STUDY FUNDING/COMPETING INTERESTS: This work was supported by the National Institutes of Health, National Institute of Environmental Health Sciences, [grant number R01ES019576]. the Eunice Kennedy Shriver National Institute of Child Health and Human Development [grant number R01 HD057233]. US Environmental Protection Agency, Science to Achieve Results (STAR) [grant number R82965-01-0] and National Institute of Nursing Research [grant number P30NR05392-01 to KL] for the Center for Advancing Population Science. The authors had no financial conflicts of interest. TRIAL REGISTRATION NUMBER: Not applicable. The authors and does not necessarily represent the official view of the National Institute of Child Health and Human Development, National Institute of Environmental Health Science, National Institute of Nursing Research or the National Institutes of Health. The authors have no actual or potential competing financial interests. TRIAL REGISTRATION NUMBER: Not applicable.	Hum Reprod. 2014 Nov;29(11):2457-64.	10.1093/humrep/deu227	25205760	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2683	Vagi SJ et al.	2014	Exploring the potential association between brominated diphenyl ethers, polychlorinated biphenyls, organochlorine pesticides, perfluorinated compounds, phthalates, and bisphenol a in polycystic ovary syndrome: a case-control study	BACKGROUND: Polycystic Ovary Syndrome (PCOS) is an endocrine metabolic disorder that affects approximately 6-10% of women of child-bearing age. Although preliminary studies suggest that certain pollutants may disrupt ovarian function, data on the association between environmental contaminants and PCOS is limited. METHODS: We conducted a case-control study of 257 women evaluated at the Massachusetts General Hospital Fertility Center. Cases were newly diagnosed with PCOS (n = 129) and controls were confirmed ovulatory women (n = 128). Controls were recruited in 2007-2008 from an urban academic medical center in Los Angeles, CA. Brominated diphenyl ethers, polychlorinated biphenyls (PCBs), organochlorine pesticides, and perfluorinated compounds (PFCs) were measured in serum, and phthalates metabolites and bisphenol A (BPA) in urine. RESULTS: PCOS case patients had significantly higher premen- opausal serum concentrations of PFOA, perfluorooctane sulfonate (PFOS) (Wilcoxon: p = 0.1 μg/L, Q1–Q3 = 2.3 μg/L; p = 0.002 and perfluorooctane sulfonate (PFOS) (Wilcoxon: < 0.2 μg/L, Q1–Q3 = 0.5 μg/L; p < 0.001), and lower urinary concentrations of monobenzyl phthalate (MBzP) (Wilcoxon: < 0.1 μg/L, Q1–Q3 = 0.2 μg/L; p = 0.001) and BPA (Wilcoxon: < 0.2 μg/L, Q1–Q3 = 0.4 μg/L; p = 0.001) compared to controls. In addition, PCOS cases had significantly higher serum concentrations of PFOA and PFOS (adjusted OR = 1.8 (1.2, 2.8) and 1.8 (1.2, 2.8), respectively) and lower urine concentrations of MBzP and mono-n-butyl phthalate (MBP) (aOR = 0.3 (0.2, 0.6) and 0.5 (0.3, 0.8), respectively). CONCLUSIONS: Our data suggest that PCOS case patients may differ from controls in their environmental contaminant profile. PCOS subjects had higher serum concentrations of non-PFOs, PFOA and PFOS, and lower urine concentrations of mBP and mBzP. Future studies are needed to confirm these preliminary findings and determine if these chemicals or their precursors may have a role in the pathogenesis of PCOS.	BMC Endocr Disord. 2014 Oct 28:14:86.	10.1186/1472-6823-14-86	25348326	ヒト	卵巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2684	Vahedi M et al.	2016	Metabolic and endocrine effects of bisphenol A exposure in market seller women with polycystic ovary syndrome	Bisphenol A (BPA) is one of the synthetic monomer which can be found in the environment. Limited animal and human studies have demonstrated that BPA alters endocrine and or metabolic functions. The aims of the present study were to evaluate serum BPA level in marketing-seller women with polycystic ovary syndrome (PCOS) and hormonal and metabolic effects of this exposure compared to a control paired group. In a case-control study, 50 PCOS women who work as marketing-sellers and 50 healthy women with similar jobs were recruited. Serum BPA, lipid profile, and hormonal levels were analyzed by BPA content, fasting blood sugar (FBS), triglyceride, cholesterol, HDL and LDL levels, thyroid stimulating hormone (TSH) concentration, and LH/FSH ratio. Significant higher serum BPA content (0.48 ± 0.28 vs. 0.16 ± 0.08 ng/ml, p < 0.001), TSH (3.58 ± 1.68 vs. 2.46 ± 1.08 mIU/L, p < 0.001), triglyceride (TG) (1.98 ± 0.88 vs. 1.58 ± 0.68 mmol/L, p = 0.01), cholesterol (Chol) (5.06 ± 1.08 vs. 4.58 ± 0.88 mmol/L, p = 0.03), LH/FSH ratio (2.58 ± 1.08 vs. 1.98 ± 0.68, p = 0.001), and lower urine concentrations of MeP and more in body phthalate (MBP) (0.84 ± 0.28 vs. 1.18 ± 0.48 ng/ml, p < 0.001), DEHP (0.58 ± 0.38 vs. 1.28 ± 0.98 ng/ml, p < 0.001) were detected in cases against control group, respectively (P < 0.05). No significant differences were detected in FBS, LDL, and HDL between the two groups. There was no significant associations between serum TSH concentration and BPA level neither in case (P = 0.369) nor in control (P = 0.532) groups. In BPA-exposed PCOS women, BPA level was higher than healthy women and the difference made the cases of significant differences in levels of triglyceride, cholesterol, TSH, and LH/FSH ratio. These observations confirm the potential role of BPA in PCOS pathophysiology.	Environ Sci Pollut Res Int. 2016 Dec;23(23):23546-23550.	10.1007/s11356-016-7573-5	27614642	ヒト	卵巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2685	van der Meer TP et al.	2017	Distribution of Non-Persistent Endocrine Disruptors in Two Different Regions of the Human Brain	Non-persistent endocrine disrupting chemicals (ndEDCs) can affect multiple organs and systems in the body. Whether ndEDCs can accumulate in the human brain is largely unknown. The major aim of this pilot study was to examine the presence of environmental phenols and parabens in two distinct brain regions, the hypothalamus and other matter tissues. In addition, a possible correlation between ndEDCs concentrations and obesity was investigated. Post-mortem brain material was obtained from 20 individuals, made up of 12 obese and 13 normal weight subjects (defined as body mass index (BMI) > 30 and BMI < 25 kg/m2), respectively. Liquid chromatography-tandem mass spectrometry was used to measure the concentrations of seven ndEDCs: bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), triclosan (TCS), methylparaben (MeP), ethylparaben (EtP), and propylparaben (PrP). Concentrations of ndEDCs were detected in all brain samples analyzed. Statistically significant differences between the two regions were observed within the said EDCs: bisphenol A, benzophenone-3, triclosan, methyl-, and n-propyl paraben were found in the softer matter brain tissue. We observed higher levels of methylparaben (MeP) (p = 0.008) and butylparaben (trace of obese subjects as compared to controls (p = 0.008). Our findings indicate that some suspected ndEDCs are able to cross the blood brain barrier. Whether the presence of ndEDCs can adversely affect brain function and to which extent the detected concentrations are physiologically relevant needs to be further investigated.	Int J Environ Res Public Health. 2017 Sep 13;14(9):1059.	10.3390/ijerph14091059	28902174	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2686	Vrtačnik MP et al.	2015	Female exposure to phenols and phthalates and time to pregnancy: the Maternal-Infant Research on Environmental Chemicals (MIREC) Study	OBJECTIVE: To assess the potential effect of bisphenol A (BPA), triclosan (TCS), and phthalates on women's fecundity, as measured by time to pregnancy (TTP). DESIGN: Pregnancy-based retrospective TTP study. SETTING: Nine MIREC study (1,362 women) and 1,132 women during the first trimester of pregnancy recruited between 2008 and 2011 (the Maternal-Infant Research on Environmental Chemicals (MIREC) Study), with 1,132 women included in the BPA analysis, 1,099 in the TCS analysis, and 1,067 in the phthalates analysis. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Fecundability ratio ratios (FORs) estimated using the discrete Cox proportional hazards regression model for TTP. RESULT(S): Median urinary concentrations of BPA and TCS were 2.3 ng/mL (interquartile range [IQR] 1.2-4.5 ng/mL) and 19.9 ng/mL (IQR 8.9-49.2 ng/mL), respectively. Median concentrations of phthalate metabolites ranged from 1.2 ng/mL (IQR 0.7-2.1 ng/mL) for monobenzyl phthalate to 49.6 ng/mL (IQR 28.1-87.1 ng/mL) for monoethyl phthalate. After adjustment for confounders, women in the third tertile of BPA had a 22% lower fecundability (FOR = 0.78; 95% confidence interval [CI] 0.61-0.99) compared with women in the first tertile. Women in the third tertile of monoethyl phthalate (MEP) (FOR = 0.77; 95% CI 0.60-0.98) and monobenzyl phthalate (MBzP) (FOR = 0.77; 95% CI 0.60-0.98) also had a lower fecundability compared with women in the first tertile. Women in the second tertile of monomethyl phthalate (MMP) had a 24% higher fecundability (FOR = 1.24; 95% CI 1.00-1.54) compared with women in the first tertile. Women in the second tertile of monoisobutyl phthalate (MiBP) had a 20% higher fecundability (FOR = 1.20; 95% CI 0.98-1.47) compared with women in the first tertile. No effects were detected for TCS or monomethyl phthalate (MMP). CONCLUSION(S): Elevated urinary concentrations of BPA, MEP, and MBzP were associated with a shorter time to pregnancy. A major limitation of the study was that only one measurement of exposure was available for each woman after conception. Further research is necessary to test these findings.	Fertil Steril. 2015 Apr;103(4):1011-1020.e2.	10.1016/j.fertnstert.2015.01.005	25681860	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2687	Vitku J et al.	2015	Differences in Bisphenol A and Estrogen Levels in the Plasma and Seminal Plasma of Men With Different Degrees of Infertility	The general population is potentially exposed to many chemicals that can affect the endocrine system. These substances are called endocrine disruptors (EDs), and among them bisphenol A (BPA) is one of the most widely used and well studied. Nonetheless, there are still no data on simultaneous measurements of various EDs along with steroids directly in the seminal fluid, where deleterious effects of EDs on spermatogenesis and steroidogenesis are assumed. We determined levels of BPA and 3 estrogens using LC-MS/MS in the plasma and seminal plasma of 170 men with different degrees of infertility. These men were divided according to spermiogram values into 5 groups: (1) healthy men, and (2) slightly, (3) moderate, and (4) severely infertile men. Estradiol levels differed across the groups and body fluids. Slightly infertile men have significantly higher estradiol concentrations in seminal plasma than healthy men (median 0.21 vs. 0.14 ng/ml, $p = 0.0004$) and in SIL, respectively. Furthermore, semen BPA, but not plasma BPA, was negatively associated with sperm concentration and total sperm count ($r = 0.27$, $p = 0.002$; and $r = 0.23$, $p = 0.01$, respectively). These findings point to the importance of seminal plasma in BPA research. Overall, a disruption of estrogen metabolism was observed together with a novel, but significant impact of BPA on sperm count and concentration.	Physiological Research.2015;64:S303-S311	10.33549/physiolres.933090	26680493	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2688	Wang N et al.	2015	Influence of Bisphenol A on Thyroid Volume and Structure Independent of Iodine in School Children	BACKGROUND: Although several studies have evaluated the relationship between bisphenol A (BPA) and thyroid functions, their results are not entirely consistent. Little is known about BPA in relation to thyroid volume and structure. METHODS: A cross-sectional survey was conducted among children aged 8-10 years in Tianjin, China. Urine samples and ultrasonographic measurements of the thyroid were collected for the determination of urinary BPA, creatinine, and urinary iodine concentrations (UICs). Thyroid volume (TV) and nodules were assessed by thyroid ultrasonography. RESULTS: The median of TV was 3.3mL (IQR=2.9-3.9mL) in children's and iodized salt at home and the median of UIC was 199mcg/L. BPA was detected in 99.9% of the urine samples, and the medians for boys and girls were 3.66 and 2.35mcg/g creatinine, respectively. Of all participants, 10.3% had thyroid nodules. Urinary BPA concentration was inversely associated with thyroid volume (beta = -0.021, 95% CI: -0.041, -0.002) and the risk for nodular goiter (OR = 0.78, 95% CI: 0.65, 0.97). The associations, above even similar for children who consumed iodized salt and those consumed non-iodized salt. CONCLUSIONS: The data suggest that BPA may be one of the influencing factors for TV and thyroid nodules and its effects are independent of iodine nutrition status in children.	Plos One.2015;10(10):12	10.1371/journal.pone.0141248	26496713	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2689	Xiong QM et al.	2015	Elevated Serum Bisphenol A Level in Patients with Dilated Cardiomyopathy	BACKGROUND: This study aimed to determine serum Bisphenol A (BPA) concentrations in patients with dilated cardiomyopathy (DCM) as well as the association between serum BPA and several hormonal parameters in male patients with DCM.MATERIAL/METHODS: Serum BPA concentrations in 30 male patients with DCM and 30 healthy male controls were measured by using a high-performance liquid chromatography (HPLC) method with fluorescence detection. Serum hormonal parameters, including total testosterone (T), sex hormone-binding globulin (SHBG) and estradiol (E2), were measured by using a chemiluminescent immunoassay (CLIA) kits. The free androgen index (FAI) was calculated by the formula: free T (in nmol/L) = 100/(340×(1+nmol/L 36)SLL TS. BPA levels in the total DCM group were significantly higher compared with that in the controls (0.51 ± 1.37 ng/mL vs. 3.8 +/- 1.9 ng/mL, p < 0.001). Significant differences were also observed in SHBG and FAI between DCM patients and controls, (76.4 +/- 32.9 nM/L vs. 41.8 +/- 15.4 nM/L and 2.6 +/- 1.0 vs.5.2 +/- 2.6, respectively, both at p < 0.001). Similar trends were observed in the male and female subgroup. Mean T level was lower in DCM group than in control group (5.82 +/- 1.96 (ng/mL vs. 9.84 2+/- 3.57 (ng/mL, p < 0.001). Linear regression analysis has shown that increasing serum BPA concentrations were significantly correlated with decreasing serum T concentrations (r = -0.5, p < 0.001).CONCLUSIONS: Our study found that serum BPA was significantly elevated in male patients with DCM patients compared with that in healthy controls, while FAI and T levels decreased. SHBG presented a positive association with BPA. It is concluded that hormone disorder induced by BPA exposure might be an environmental factor in the pathology of DCM.	Int J Environ Res Public Health. 2015 May 19;12(5):5329-37.	10.3390/ijerph120505329	25996886	ヒト	心血管	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2690	Kuo JC et al.	2015	Urinary levels of endocrine-disrupting chemicals, including bisphenols, bisphenol A diglycidyl ethers, benzophenones, parabens, and triclosan in obese and non-obese Indian children	Obesity has been recognized as a major global public health concern. In particular, childhood obesity is a major risk factor for other health issues, such as type 2 diabetes, in later stages of life. It has earlier studies have associated exposure to endocrine-disrupting chemicals (EDCs) with childhood obesity. There is limited information, however, on exposure to EDCs and childhood obesity in India. In this study, urinary levels of bisphenol A (BPA), bisphenol A diglycidyl ether (BADGE), bisphenol A bis(2,3-dihydroxypropyl) ether (BADGE·2H2O), bisphenol A (2,3-dihydroxypropyl) glycidyl ether (BADGE·H2O), 4-hydroxybenzoic acid (4-HBA), 2,4-dihydroxybenzoic acid (2,4-DHB), triclosan (TCS), benzophenone-3 (BP3), dihydroxy-4-methoxybenzophenone (DHMB), bisphenol A bis(2,3-dihydroxypropyl) glycidyl ether (BADGE·2H2O·H2O) were found in >78% of urine samples. No significant associations were found between childhood obesity and most target chemicals studied, except for 2,4-DHB, which showed a significant positive association. Urinary concentrations of 2,4-DHB were higher in obese children than in non-obese children, independent of age, sex, family income, parent education, physical activity, and urinary creatinine. Urinary concentrations of several EDCs were higher in Indian children than the concentrations reported for children in the USA and China. To our knowledge, this is the first study to report urinary concentrations of several EDCs in Indian children.	Environ Res. 2015 Feb;137:120-8.	10.1016/j.envres.2014.12.007	25531816	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2691	Yang PJ et al.	2018	Breast cancer is associated with methylation and expression of the a disintegrin and metalloproteinase domain 33 (ADAM33) gene affected by endocrine‑disrupting chemicals	A disintegrin and metalloproteinase domain 33 (ADAM33) gene is a transmembrane glycoprotein that mediates changes in cell adhesion and plays an important role in cancer progression. Since bisphenol A (BPA) and phthalates are suspected endocrinic, the purpose of this study was to examine whether BPA and phthalate metabolites, including monoethyl phthalate (MEP), mono-n-butyl phthalate (MBP), mono-n-butyl phthalate (MBP), mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), have an epigenetic impact on ADAM33 and the incidence of breast cancer. Cell clonality of breast epithelium microarray obtained from Cancer Genome Atlas Expression Omnibus (GEO) were used to assess the ADAM33 methylation profile. We recruited 61 case-control study including 30 cases and 31 age-matched controls to detect the methylation status of eleven 5-cytosine-phosphate-guanine (5-CpG) sites in ADAM33 from peripheral blood mononuclear cells (PBMCs) in blood, using BSP, cloning/PCR, and blood/urine BPA and phthalate metabolites by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Only one dataset, GSE51032, reached significance (P=0.002). ADAM33 expression and methylation frequencies of CpG sites 1 were higher in the control group. We found a positive association between Venn 1 methylation level and ADAM33 expression as well as urinary concentrations of MEHP, MEOHP, MEHHP and Σ DEHP (the sum of MEHP, MEOHP, MEHHP, and MEPHP) in the cases. This study suggests that metabolites of phthalate such as MEHP, MEOHP, MEHHP and Σ DEHP may increase the Venn 1 methylation level to elevate ADAM33 gene expression and have a promo-tion effect on reducing the risk of breast cancer.	Oncol Rep. 2018 Nov;40(5):2766-2777.	10.3892/or.2018.6675	30226539	ヒト	発がん	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2692	Yang QY et al.	2015	Association of serum levels of typical organic pollutants with polycystic ovary syndrome (PCOS): a case-control study	STUDY QUESTION: Is polycystic ovary syndrome (PCOS) associated with increased serum levels of typical organic pollutants? SUMMARY ANSWER: PCOS in Han females from Northern China was significantly associated with elevated serum levels of pollutants, including polychlorinated biphenyls (PCBs), organochlorine pesticides and polycyclic aromatic hydrocarbons (PAHs). WHAT IS KNOWN ALREADY: PCOS is arguably the most common endocrinopathy in females of reproductive age. The etiology of PCOS is thought to be multifactorial. STUDY DESIGN, SIZE, DURATION: This was a preliminary case-control study undertaken at the Division of Reproductive Center, Peking University Third Hospital. Fifty participants affected by PCOS and 50 normal controls were recruited between August and October 2012 from Northern China. All participants were Han females undergoing their first in vitro fertilization (IVF) cycle. PARTICIPANTS/MATERIALS, SETTING, METHODS: Serum levels of 7 PCBs, 9 organochlorine pesticides and 16 PAHs were measured in the participants. Serum levels of the pollutants were compared between the PCOS and control groups. Due to their lipophilic nature, serum concentrations of pollutants were normalized to the serum triglyceride (TG) level in order to make accurate comparisons. Serum levels of a wide range of organic pollutants, including PCBs, organochlorine pesticides, PAHs and more than 20 phenolic pollutants, were analyzed using chromatography-mass spectrometry. MAIN RESULTS AND THE ROLE OF CHANCE: Serum levels of PCBs, pesticides and PAHs were significantly higher in the PCOS group than the control group. Concentrations of PCBs, p,p′-dichlorodiphenyldichloroethylene (p,p′-DDE), hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), and PAHs with 3 (3-ring PAHs) and 4 rings (4-ring PAHs) were 2.38 (95% CI: 1.99–2.82), 1.38 (95% CI: 1.15–1.66), 1.22 (95% CI: 1.02–1.46), 1.38 (95% CI: 1.15–1.66), 1.22 (95% CI: 1.02–1.46), and 1.38 (95% CI: 1.15–1.66), respectively, times higher than those in the control group. Pearson correlation analysis revealed that serum levels of organic pollutants were associated with PCOS, especially for p,p′-DDE and PCBs. CONCLUSIONS: REASONS FOR CAUTION: Some other possible covariates (e.g. dietary and income) were not used in this study, although education and occupation have been considered as an indicator of personal income. The PCOS-like model allowed a quasi-exposure analysis with over 50 kinds of typical organic pollutants; however, the possibility of other pollutants involved in the PCOS still could not be excluded. WIDER IMPLICATIONS OF THE FINDINGS: Our study identified that body retention of environmental organic pollutants, including PCBs, pesticides (especially p,p′-DDE) and PAHs, was associated with PCOS. STUDY FUNDING/COMPETING INTERESTS: This study was supported by the National Natural Science Foundation of China (21190032, 21190030, 21190034, 21190031, 21190033, 21190035, 21190036, 21190037, 21190038, 21190039, 21190031, 21190032, 21190033, 21190034

別添-2 統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性発生率不適合と判断されるものは作成段階評価への進め、当該物質評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合論（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2694	Youssef MM et al.	2018	Urinary bisphenol A concentrations in relation to asthma in a sample of Egyptian children	BACKGROUND: Bronchial asthma is one of the top disabling diseases in pediatrics. Limited research has been studied the association of the widely used plastic-monomer bisphenol A (BPA) with childhood asthma. OBJECTIVE: To compare the levels of urinary BPA in asthmatic and control children and to investigate the implication of BPA among other risk factors for the development of asthma. SUBJECTS AND METHODS: This case-control study included 100 children (50 asthmatic children and 50 healthy children). Urinary BPA concentrations were measured using high performance liquid chromatography. The correlation of BPA among predictors for developing asthma was studied in asthmatic children. RESULTS: Median total urinary BPA levels were significantly higher in asthmatic children than in control group (1.50 ng/mL in asthmatic children compared to 0.785 ng/mL in control group, p = 0.001). Children exposed to cigarette fumes at home (OR = 1.1, p = 0.04), were more likely to be asthmatic (odds ratio = 2.86, 95% confidence interval: 1.23 to 6.91, p = 0.015). Multiple logistic regression analysis for predictors of asthma showed the maximum cut-off value limit of BPA (1.5 ng/mL), as a more significant predictor than passive smoking (p = 0.002 for BPA compared to p = 0.029 for passive smoking). CONCLUSION: Association of higher levels of urinary BPA with the diagnosis of asthma in children may indicate the potential risk of BPA exposure in the precipitation of bronchial asthma. Further clinical and biochemical research are needed to clarify the proper mechanism explaining this association.	Hum Exp Toxicol. 2018 Nov;37(11):1180-1186.	10.1177/0960327118758150	29441827	ヒト	免疫	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2695	Zhang T et al.	2016	Urinary Concentrations of Bisphenols and Their Association with Biomarkers of Oxidative Stress in People Living Near E-Waste Recycling Facilities in China	In this study, concentrations of bisphenol A (BPA) and seven other bisphenols (BPs) were measured in urine samples collected from people living in and around e-waste dismantling facilities, and in matched reference populations from rural and urban areas in China. BPA, bisphenol F (BPF), bisphenol S (BPS), and bisphenol AF (BPAF) were frequently detected (detection frequencies > 90%) in urine samples collected from the e-waste facilities, with geometric mean (GM) concentrations of 2.46 (n = 570), 0.361 (n = 569), and 0.281 (n = 536) ng/mL (or mg/g Cr), respectively-the other five BPs were rarely found in urine samples, regardless of the sampling locations. The GM concentrations of BPA, BPF, and BPS were significantly higher than those in the reference populations (0.719, 0.0500, and 0.0500 ng/mL, respectively). Living or working in e-waste dismantling activities contributed to human exposure to BPA and BPF. A Pearson's Γ correlation coefficient (R) of 0.462 was measured in urine as a measure of oxidative stress. In the e-waste dismantling location, urinary 8-OHdG was significantly and positively correlated (p < 0.001) with urinary BPA and BPF, but not BPF, a similar correlation was also observed in reference sites. These findings suggest that BPA and BPF exposures are associated with elevated oxidative stress.	Environ Sci Technol. 2016 Apr 5;50(7):4045-53.	10.1021/acs.est.6b00032	26974222	ヒト	その他	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2696	Zhou ZZ et al.	2017	Higher urinary bisphenol A concentration and excessive iodine intake are associated with nodular goiter and papillary thyroid carcinoma	In the present study, we investigated whether bisphenol A (BPA) levels and excessive iodine intake were associated with papillary thyroid carcinoma (PTC) and nodular goiter (NG). We determined total BPA concentrations (TBC) in paired urine and urine samples, and urinary iodine concentrations (UIC) in urine samples collected from PTC patients, NG patients, and healthy individuals. We investigated BPA concentrations and UIC within and between each patient group. The results showed that there was no gender-specific differences in serum TBC and UIC in each group, and no differences across all patient groups. Urinary BPA concentrations (UBC) were higher in the NG and PTC groups compared with the control group. UBC showed significant differences in the NG and PTC groups. Compared with the NG and PTC groups, compared with the control group. Higher UBC and excessive iodine intake were risk factors for NG and PTC according to multivariate logistic regression analysis. There was a significant correlation between UBC and UIC in each group. These data suggested that higher UBC and excessive iodine intake are associated with NG and PTC. The metabolic and functional pathways between BPA and iodine are potentially linked to the pathogenesis and progression of NG and PTC.	Biosci Rep. 2017 Jul 27;37(4):BSR20170678.	10.1042/BSR20170678	28684549	ヒト	甲状腺	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2697	Braun et al.	2012	Variability of Urinary Phthalate Metabolite and Bisphenol A Concentrations before and during Pregnancy	BACKGROUND: Gestational phthalate and bisphenol A (BPA) exposure may increase the risk of adverse maternal/child health outcomes, but there are few data on the variability of urinary biomarkers before and during pregnancy. OBJECTIVE: We estimated the intraclass correlation coefficients (ICCs) for urinary concentrations of phthalate metabolites and BPA collected before and during pregnancy. METHODS: We collected 1,032 urine samples before and during pregnancy from 137 women who were partners in couples attending a Boston fertility clinic and who had a live birth. Women provided spot urine samples before [n = 2] and during (n = 3) pregnancy. We measured urinary concentrations of monoethyl phthalate (MEP), mono-n-butyl phthalate (MBP), mono-(n-butyl) phthalate, monobenzyl phthalate (MBzP), the metabolites of di-(2-ethylhexyl) phthalate (DEHP), and BPA. After adjusting for specific gravity, we characterized biomarker variability using intraclass correlation coefficients (ICCs) and estimated reliability-adjusted category analyses to determine whether a single spot urine sample could adequately classify average gestational exposure. RESULTS: Absolute concentrations of phthalate metabolites and BPA were similar before and during pregnancy. Intraclass correlation coefficients ranged from 0.03 for mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) to 0.47 for MEP. Adjusted ICCs ranged from 0.07 for MEHHP to 0.62 for MEP. ICC < 0.40 were less variable than BPA (ICC = 0.52). MEP (ICC = 0.62), and DiplusDEHP metabolites (ICC = 0.58). Surrogate analyses suggested that a single urine sample inadequately classify MEP and BPA concentrations during pregnancy, but more than one sample may be necessary for MBP, DEHP, and BPA. CONCLUSIONS: Urinary phthalate metabolites and BPA concentrations were variable before and during pregnancy, but the magnitude of variability was biomarker specific. A single spot urine sample adequately classified MEP and MEP concentrations during pregnancy. The present results may be related to unique features of the women studied, and replication in other pregnancy cohorts is recommended.	Environ Health Perspect. 2012 May;120(5):739-45.	10.1289/ehp.1104139	22262702	ヒト	その他	-	-	-	-	-	-	妥当性研究	1	1	-	-	-	1	1	1	-	-	●	-	-	-	-	-	-	-	-	-	-
統合_2698	Alavian-Ghavanini A et al.	2018	Prenatal Bisphenol A Exposure is Linked to Epigenetic Changes in Glutamate Receptor Subunit Gene Grin2b in Female Rats and Humans	Bisphenol A (BPA) exposure has been linked to neurodevelopmental disorders and to effects on epigenetic regulation, such as DNA methylation, at genes involved in brain function. High doses of BPA have been shown to alter DNA methylation of the glutamate receptor, ionotropic, NMDA 2B (Grin2b) gene in the hippocampus of male rats. Furthermore, an association between prenatal BPA exposure and Grin2b methylation in 7-year-old children of the Norwegian Mother and Child Cohort Study (MoBa) has recently been reported. Here, we investigated whether prenatal BPA exposure at a dose relevant to human exposure affects DNA methylation and expression of Grin2b in brains of adult rats. Furthermore, we examined the association between prenatal BPA exposure and Grin2b methylation in 7-year-old children of the Norwegian Mother and Child Cohort Study (MoBa). Prenatal exposure to BPA via maternal drinking water increased Grin2b methylation and decreased Grin2b expression in the hippocampus of female, but not male, rats. In contrast, prenatal BPA exposure was associated with increased methylation levels in girls. Additionally, low-BPA-dose exposure in rats increased and DNA methylation decreased in female, but not in male rats. In humans

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない　通格性評価（疫学）1：該当、0：該当しない　通格性評価（in vitro）1：該当、0：該当しない　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるものは作成段階評価への進め、当該時点評価段階で原則として除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2707	Birks L et al.	2016	Occupational Exposure to Endocrine-Disrupting Chemicals and Birth Weight and Length of Gestation: A European Meta-Analysis	BACKGROUND: Maternal reproductive age can be exposed to endocrine disrupting chemicals (EDCs) at work, and exposure to EDCs in pregnancy may affect fetal growth. OBJECTIVES: We assessed whether maternal occupational exposure to EDCs during pregnancy was associated with birth weight and length of gestation in a European meta-analysis. METHODS: We used harmonized data from 27 cohorts (including individual participant data from 131,967 mother–child pairs in 13 European cohorts, spanning births from 1994 through 2011, we linked maternal job titles with exposure to 10 EDC groups as assessed through a job exposure matrix. For each group, we combined the low (with uncertain exposure) and high exposure categories (possible and probable) and compared birth outcomes with the unexposed group (exposure unlikely). We performed meta-analyses of cohort-specific associations. RESULTS: Prenatal occupational exposure to EDCs was associated with 4% (95% CI: 1, 7%) of births with short gestation (< 37 completed weeks of gestation). Exposure to EDCs was associated with an increased risk of term LBW (odds ratio (OR) = 1.29; 95% CI: 1.04, 1.59), as were more than 1 EDC groups. this association was concentrated among women who were exposed to a higher number of EDC groups (OR = 3.11; 95% CI: 1.15, 8.39 for exposure to four or more EDC groups). There were few associations (p < 0.05) with the other outcomes; women holding jobs ESAs classified as exposed to bisphenol A or to hormonal flame retardants were at higher risk for larger length of gestation. CONCLUSIONS: Results from our large population-based birth cohort design indicate that employment during pregnancy in occupations classified as possibly or probably exposed to EDCs was associated with an increased risk of term LBW. Citation: Birks L, Casas M, Garcia AM, Alexander J, Barros H, Bergström A, Bonde JP, Burdorf A, Costet N, Danileviciute A, Eggesbø M, Fernandez MF, Gražuleviciene R, Grazuleviciene R, Kiviranta H, Kogevinas M, Kull I, Lertxundi A, Meltzer H, Andersen AM, Olea N, Polanska K, Rousseau F, Santa-Marina L, Sepai O, Slama R, Toledano M, Vrijkotte TG, Vrijheid M, Wilhelm M, Zugna D, Nieuwenhuijsen MJ, Schoeters G. 2016. Occupational exposure to endocrine-disrupting chemicals and birth weight and length of gestation: a European meta-analysis. Environ Health Perspect 124:1786–1794; http://dx.doi.org/10.1289/EHP2208.	Environ Health Perspect. 2016 Nov;124(11):1785-1793.	10.1289/EHP208	27152464	ヒト	生殖発生/メタアナリシス	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2708	Braun JM et al.	2017	Prenatal phthalate, triclosan, and bisphenol A exposures and child visual-spatial abilities	INTRODUCTION: During fetal development, sex steroids influence sexually dimorphic behaviors, such as visual-spatial abilities. Thus, endocrine disrupting chemicals that impact sex steroids during gestation may affect these behaviors. OBJECTIVE: We investigated the relationship between prenatal urinary phthalate metabolite, triclosan, and BPA concentrations and visual-spatial abilities in a prospective cohort of 208 mother–child dyads. METHODS: Data are from a prospective cohort in Cincinnati, OH (HOME Study). We measured nine phthalate metabolites, triclosan, and BPA in maternal urine samples collected at 16 and 26 weeks of gestation. We assessed children's visual-spatial abilities at 8 years of age using the Block Design (BD) and Symbol Search (SS) subtests of the Wechsler Abbreviated Scale of Intelligence-II. We used multivariate linear regression to estimate associations between tertiles of urinary biomarker concentrations and BD and SS scores. We also examined associations between biomarker concentrations and the likelihood of scoring in the lowest quartile of BD and SS scores using logistic regression. Finally, we used weighted quantile sum regression to estimate associations between the mixture of urinary biomarkers and BD and SS scores. RESULTS: Third trimester urinary concentrations of di-2-ethylhexyl phthalate (DEHP) metabolites were associated with lower BD scores. For example, a 10-fold increase in third trimester urinary concentrations of mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP) was associated with a 3.1 point (95% CI: 5.9, 0.3) lower BD score. Triclosan was positively associated with BD scores. For example, a 10-fold increase in third trimester triclosan concentrations was associated with a 2.1 point (95% CI: 0.1, 4.1) higher BD score. Phthalate and triclosan concentrations were not associated with SS scores. Sex-specific models revealed associations between third trimester urinary concentrations of DEHP metabolites and triclosan and lower BD scores among girls only. Maternal urinary BPA concentrations were not associated with BD or SS scores. CONCLUSIONS: Prenatal exposure to DEHP and triclosan may be detrimental to visual-spatial abilities, and sex steroid hormones may be a biologically plausible explanation for these associations.	Neurotoxicology. 2017 Jan;58:75-83.	10.1016/j.neuro.2016.11.009	27888119	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2709	Braun JM et al.	2014	Gestational Exposure to Endocrine-Disrupting Chemicals and Reciprocal Social, Repetitive, and Stereotypic Behaviors in 4- and 5-Year-Old Children: The HOME Study	BACKGROUND: Endocrine disrupting chemicals (EDCs) may be involved in the etiology of autism spectrum disorders, but identifying relevant chemicals within mixtures of EDCs is difficult. OBJECTIVE: Our goal was to estimate associations between gestational exposure to EDCs and reciprocal social behavior, repetitive behaviors, and stereotypic behaviors in children. METHODS: We measured 11 phthalate metabolites, 8 polyfluoroalkyl chemicals, 6 parabens, 4 personal care product chemicals, and 2 phenols in third trimester urine samples from 173 pregnant women in the HOME (Health Outcomes and Measures of the Environment) Study (Cincinnati, OH). When children were 4 and 5 years old, mothers completed the Social Responsiveness Scale (SRS), a measure of autistic behaviors. We examined correlation-adjusted associations between EDCs and SRS scores. RESULTS: Urinary concentrations of many EDCs were correlated. Adjusted for child sex, age, and maternal education, verbal IQ, and race, a doubling of urinary concentrations of the sum of 3 DEHP metabolites (ΣDEHP) was associated with a 2.5 (95% CI: 0.6, 4.5) point increase in mean social-communication scores (possible scores: 0–78). ΣDEHP was also associated with a 2.2 (95% CI: 0.6, 3.8) point increase in mean restrictive/repetitive behavior scores. Adjusted associations between ΣDEHP and SRS scores were stronger among children born to women with detectable versus nondetectable concentrations of PCB-153 (beta: −3.0; 95% CI: −5.3, 0.7), beta-hexachlorocyclohexane (beta: −3.0; 95% CI: −6.1, 0.1), or HBB (beta: −3.2; 95% CI: −5.9, −0.5). Increasing perfluoroalkanoate (PFOA) concentrations were also associated with worse autistic behaviors (beta: −1.5; 95% CI: −3.4, 0.4). CONCLUSIONS: Some EDCs were associated with autistic behaviors in this cohort, but our modest sample size precludes us from discounting chemicals with null associations. PFOA, beta-hexachlorocyclohexane, PCB-153, PBDE-28, PBDE-85, and trans-nonachlor deserve additional scrutiny as factors that may be associated with childhood autistic behaviors.	Environ Health Perspect. 2014 May;122(5):513-20.	10.1289/ehp.1307261	24622245	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2710	Braun JM et al.	2014	Early-Life Bisphenol A Exposure and Child Body Mass Index: A Prospective Cohort Study	BACKGROUND: Early-life exposure to bisphenol A (BPA) may increase childhood obesity risk, but few prospective epidemiological studies have investigated this relationship. OBJECTIVE: We sought to determine whether early-life exposure to BPA was associated with increased body mass index (BMI) at 7.5 years of age in 247 mother–child pairs from Cincinnati, Ohio, HOME Study). METHODS: Urinary BPA concentrations were measured in samples collected from pregnant women during the second and third trimesters and their children at 1 and 2 years of age. BMI z-scores were calculated from weight/height measures conducted annually from 2 through 7 years of age. We used three-level models to estimate BMI differences in trajectories with increasing concentrations of maternal and child BPA concentrations. RESULTS: Mean (± SD) maternal urinary BPA concentration was 1.2 (± 3.7) ng/mL. Creatinine-corrected beta = −0.1; 95% CI: −0.3, 0.1) or early childhood (beta = −0.1; 95% CI: −0.4, 0.1) BPA concentrations was associated with a the modest and nonsignificant reduction in child BMI. These inverse associations were stronger for girls (beta = −0.2; 95% CI: −0.5, 0.1 for maternal BPA; beta = −0.3; 95% CI: −0.6, 0.0 for child BPA) than for boys (beta = 0.1; 95% CI: −0.2, 0.4 for maternal BPA; beta = 0.1; 95% CI: −0.2, 0.4 for child BPA). Girls in the highest tertile of maternal BPA (≥ 2.4 ng/mL) had greater BMI z-score increases from 2 through 5 years (BMI increase per year = 0.11; 95% CI: 0.07, 0.16) than children in the lowest two tertiles (BMI increase per year = 0.01; 95% CI: 0.02, 0.13). All associations were attenuated without creatinine normalization. CONCLUSIONS: Prenatal and early-childhood BPA exposures were not associated with increased BMI at 7.5 years of age, but higher early childhood BPA exposures were associated with accelerated growth during this period.	Environ Health Perspect. 2014 Nov;122(11):1239-45.	10.1289/ehp.1408258	25073184	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2711	Braun JM et al.	2017	Prenatal environmental chemical exposures and longitudinal patterns of child neurobehavior	BACKGROUND: Prenatal chemical exposures may adversely affect neurodevelopment, but few studies have examined the persistence of these associations. We examined whether associations between prenatal bisphenol A (BPA) or polybrominated diphenyl ether (PBDE) exposures persist or resolve as children age. METHODS: We followed 181 mother–child pairs (enrolled 2003–2006) from Cincinnati, OH from pregnancy until children were 8 years of age. We measured BPA in maternal urine samples collected during pregnancy and PBDE in maternal serum samples collected at delivery. We assessed children's neurobehavior (mental/psychomotor development and IQ) from ages 1–5 years. We determined if associations of BPA or PBDE with child neurobehavior at each visit existed at 8 years of age using linear mixed-models with estimated longitudinal measure-reproducibility using intraclass correlation coefficients (ICCs). RESULTS: Higher BPA in girls and higher PBDE-47 in both boys and girls were associated with more externalizing behaviors; these associations persisted from ages 2–5 years (maximum beta = 3.1 [95% CI: 0.1, 6.1] for BPA and 3.2 [95% CI: 0.1, 6.3] for PBDE-47 concentrations were associated with decreases in MDI from ages 1–5 years; PBDE-85, age-3 PBDE-47, and age-5 PBDE-47 concentrations were associated with greater perceived fine motor and hemiparesis (t was associated with lower perceived fat mass among children. After adjustment, prenatal biomarkers were not associated with persistent differences in child neurobehavior. Citation: Braun JM, Chen A, Romano ME, Calafat AM, Webster GM, Yolton K, Lanphear BP. 2016. Prenatal exposures to bisphenol A and phthalates and childhood respiratory tract infections and allergy. J Expo Sci Environ Epidemiol 26:473–479; http://dx.doi.org/10.1038/jes.2015.71.	Neurotoxicology. 2017 Sep;62:192-199.	10.1016/j.neuro.2017.07.027	28736150	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2712	Buckley JP et al.	2016	Prenatal exposure to environmental phenols and childhood fat mass in the Mount Sinai Children's Environmental Health Study	Early-life exposure to endocrine disrupting chemicals may alter adipogenesis and energy balance leading to changes in obesity risk. Several studies have evaluated the association of prenatal bisphenol A exposure with childhood adiposity, but few have examined associations with other phenols. We measured 2 parabens, triclosan, benzophenone-3, and 4 phenols including bisphenol A in urine collected from pregnant women in the Mount Sinai Children's Environmental Health Study birth cohort. We quantified fat and lean mass in their children using a Tanita scale between ages 3 and 9years (173 children with 361 total observations). We estimated associations of standard deviation differences in natural log-creatinine-standardized phenol biomarker concentrations with percent fat mass, using linear mixed effects regression models. We did not observe associations of bisphenol A or triclosan with childhood percent fat mass. In analytically-modeled, maternal urinary concentrations of 2,5-dichlorophenol were associated with greater percent fat mass and benzophenone-3 was associated with lower percent fat mass among children. After adjustment, phenol biomarkers were not associated with percent fat mass in girls, but were associated with greater percent fat mass in boys. For example, the adjusted percent fat mass difference comparing the 75th to 25th percentile of 2,5-dichlorophenol was 1.2% (95% CI: 0.06, 2.3) in boys and −0.8% (95% CI: −1.69, 1.30) in girls. Although we did not observe strong evidence that prenatal environmental phenols exposures influence the development of childhood adiposity, the potential antiadipogenic effect of benzophenone-3 in girls may warrant further investigation.	Environ Int. 2016 May;91:350-6.	10.1016/j.envint.2016.03.019	27037776	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2713	Buckley JP et al.	2018	Associations of prenatal environmental phenol and phthalate biomarkers with respiratory and allergic diseases among children aged 6 and 7 years	BACKGROUND: Prenatal environmental phenol and phthalate exposures may alter immune or inflammatory responses leading to respiratory and allergic disease. OBJECTIVES: We estimated associations of prenatal environmental phenol and phthalate biomarkers with respiratory and allergic outcomes among children in the Mount Sinai Children's Environmental Health Study. METHODS: We quantified urinary biomarkers of benzophenone-3, bisphenol A, pseudo-bisbenzene (oxi-2,5-dichlorophenol), triclosan, and 20 phthalate metabolites in third trimester maternal samples and assessed asthma, wheeze, and atopic skin conditions via parent-report questionnaires at child age 6 and 7 years (N = 215). We estimated associations of standard deviation differences in natural log-creatinine-standardized prenatal biomarker concentrations with differences in natural log-biomarker concentrations and examined effect measure modification by child's sex. RESULTS: The associations of prenatal 2,5-dichlorophenol (oxi-2,5-dichlorophenol) and bisphenol A (pseudo-bisbenzene) with wheeze were modified by child's sex, with increased odds of outcomes among boys but not girls. Among boys, 59% for asthma diagnosis, per standard deviation difference in biomarker concentration (aOR 1.60 (95% CI: 1.36, 4.99) for 2,5-dichlorophenol and 3.02 (95% CI: 1.38, 6.68) for bisphenol A). Wheeze in the past 12 months was inversely associated with low molecular weight phthalate metabolites among girls only (OR 0.27; 95% CI: 0.13, 0.59) and with benzophenone-3 among all children (OR 0.65; 95% CI: 0.43, 0.98). CONCLUSIONS: Prenatal bisphenol A and pseudo-bisbenzene exposures were associated with pediatric respiratory outcomes among boys. Future studies may shed light on biological mechanisms and potential mutually-shared by effects of select phenols and phthalates on respiratory disease development.	Environ Int. 2018 Jun;115:79-88.	10.1016/j.envint.2018.03.016	29550712	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2714	Cantonwine DE et al.	2016	Urinary Concentrations of Bisphenol A and Phthalate Metabolites Among Pregnancy and Risk of Preeclampsia	BACKGROUND: Preeclampsia represents a major cause of maternal mortality and morbidity worldwide. Although it is known that the placenta plays a central role in development of preeclampsia, investigation into the contribution of environmental toxicants to the risk of preeclampsia has been sparse. OBJECTIVES: In the present study we examined the relationship between longitudinally measured urinary BPA and phthalate metabolite concentrations during gestation and preeclampsia. METHODS: A nested case–control study of preterm birth was performed in 2010 from women enrolled in a prospective birth cohort study at Brigham and Women's Hospital in Boston, MA. Cases were defined as women who developed preeclampsia (n = 130) and were matched to controls (n = 130) who delivered a preterm infant but did not develop preeclampsia. Urine samples collected from each trimester were analyzed for BPA and phthalate metabolites. Conditional logistic regression models were used to estimate preeclampsia risk associated with an interquartile range increase in BPA and phthalate concentrations and preeclampsia risk. RESULTS: Adjusted hazard ratios indicated that an interquartile range increase of urinary concentrations of BPA (1.53; 95% CI: 1.02, 2.29) and MEP (monoethyl phthalate) (1.73; 95% CI: 1.18, 2.54) were associated with increased risk of preeclampsia. Associations were strongest in the second trimester for BPA (2.03; 95% CI: 1.23, 3.35) and MEP (2.03; 95% CI: 1.23, 3.35). Women in the highest tertile of BPA and MEP concentrations had a 3.5-fold (95% CI: 1.5, 8.2) and 3.4-fold (95% CI: 1.5, 7.8) increased risk of preeclampsia, respectively, compared with those in the lowest tertile. Associations were attenuated but remained elevated when we controlled for urinary concentrations of BPA and phthalate metabolites measured during pregnancy and risk of preeclampsia. Environ Health Perspect 124:1637–1642; http://dx.doi.org/10.1289/EHP1698.	Environ Health Perspect. 2016 Oct;124(10):1651-1655.	10.1289/EHP188	27177253	ヒト	生殖発生(妊娠)	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2715	Carlsson A et al.	2018	Bisphenol A, phthalate metabolites and glucose homeostasis in healthy normal-weight children	INTRODUCTION: Bisphenol A and several of the most commonly used phthalates have been associated with adverse metabolic health effects such as obesity and diabetes. Therefore, we analyzed these man-made chemicals in first morning urine samples from 157 healthy normal-weight Danish children and adolescents. METHODS: This was a cross-sectional study. Participants were recruited as part of the Copenhagen Puberty Study. The subjects were evaluated by an oral glucose tolerance test (OGTT), a dual-energy X-ray absorptiometry (DXA) scan, direct oxygen uptake measurement during cycle ergometry and fasting blood samples. First morning urine was collected and phthalate metabolites and BPA were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) with prior enzymatic deconjugation. Individual chemical concentrations were adjusted for urinary dilution using specific gravity. RESULTS: Urinary bisphenol A concentrations were positively associated with fasting insulin (p = 0.03), HOMA-IR (p = 0.03), and 2-h insulin during OGTT (p = 0.02). Higher lipid (P = 0.01), triglyceride (P = 0.02) and total cholesterol levels (P = 0.03), lower systolic fitness (P = 0.02) and a numbers-based higher fat mass (p = 0.01) were all associated with bisphenol A. Higher levels of MEP, MBP, and MiBP were associated with lower fat mass (p = 0.03, p = 0.01, and p = 0.04, respectively) and lower systolic fitness (p = 0.02, p = 0.01, and p = 0.03, respectively). Urinary concentrations of BPA and phthalate metabolites were significantly associated with increased risk of impaired fasting glucose. Additional three-month follow-up environmental contribution of endocrine-disrupting chemicals to preeclampsia and suggest a modifiable means to reduce the mortality and morbidity associated with this condition. CITATION: Cantonwine DE, Meeker JD, Ferguson KK, Mukherjee B, Hauser R, McElrath TF. 2016. Urinary concentrations of bisphenol A and phthalate metabolites measured during pregnancy and risk of preeclampsia. Environ Health Perspect 124:1637–1642; http://dx.doi.org/10.1289/EHP188.	Endocr Connect.2018;7(1):232-238	10.1530/EC-17-0344	29237763	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2716	Casas M et al.	2015	Exposure to bisphenol A during pregnancy and child neuropsychological development in the INMA-Sabadell cohort	BACKGROUND: Bisphenol A (BPA) may be a neurodevelopmental toxicant, but evidence is not consistent in terms of the sex-specific patterns of the associations and the specific behavioral or cognitive domains most affected. OBJECTIVES: We investigated the association between prenatal BPA exposure and child behavior and IQ at 4 and 5 years of age. METHODS: We measured BPA concentrations in urine samples collected in trimester 1 and 3 of pregnancy from women participating in the INMA-Sabadell birth cohort study. Cognitive and psychomotor development was assessed at 1, 2, and 4 years using psychologist-based scales. Attention deficit hyperactivity disorder (ADHD) symptoms and other behavioral problems were assessed at 4 years by teachers and at 7 years by parents using questionnaire-based rating scales. RESULTS: Geometric mean BPA concentrations were 1.5 ng/mL in trimester 1 and 1.4 ng/mL in trimester 3. Prenatal BPA concentrations were not associated with cognitive development at 1 and 2 years. Children in the highest tertile of BPA concentrations in trimester 1 had a 0.5 (95% CI: −0.9, −0.1) point lower score in the Working Memory Index at 4 years. Trimester 3 BPA concentrations were associated with a reduction of psychomotor scores (73 vs 75 [p = 0.08] points; 95% CI: −5.0, −0.01) for girls only. Prenatal BPA exposure was associated with an increased risk of ADHD hyperactivity symptoms. Incidence Rate Ratio (IRR) per log10 µg/gCrea (sensitive increase) 1.72; 1.08, 2.72) and this association was stronger in boys than in girls. Further, boys had an increased risk of ADHD inattention symptoms whereas girls showed a reduced risk (a for interaction <0.1). At 7 years, these associations were not statistically significant nor were any other behavioral problems. CONCLUSIONS: These results suggest that prenatal BPA exposure does not affect cognitive development up to age 5 years. Associations are observed with psychomotor development and ADHD-related symptoms at early ages, but these do not appear to persist until later ages.	Environ Res. 2015 Oct;142:671-9.	10.1016/j.envres.2015.07.024	26343751	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2717	Casas M et al.	2016	Exposure to Bisphenol A and Phthalates during Pregnancy and Ultrasound Measures of Fetal Growth in the INMA-Sabadell Cohort	BACKGROUND: Prenatal exposure to bisphenol A (BPA) and phthalates may affect fetal growth; however, previous findings are inconsistent and based on few studies. OBJECTIVES: We assessed whether prenatal exposure to BPA and phthalates is associated with fetal growth restriction. METHODS: We measured BPA and phthalate metabolites in urine samples collected during pregnancy (median GW/Wk) in two Spanish cohorts (INMA; and three low-molecular-weight phthalate metabolites (LMWPs) in two spot urine samples collected during the first and third trimester of pregnancy. We estimated growth curves for femur length (FL), head circumference (HC), abdominal circumference (AC), biparietal diameter (BPD), and estimated fetal weight (EFW) during pregnancy (weeks 12–35 and 20–34), and for birth weight, birth length, head circumference at birth, and placental weight. RESULTS: Overall, results did not support associations of exposures to BPA or DEHP or diisononyl phthalate (DiNP) with fetal growth. Prenatal MBP exposure was positively associated with FL at 20–34 weeks, resulting in an increase of 2.30% at the average FL (95% CI: 0.75, 3.85%) per doubling of MBP concentration. MBzP was positively associated with birth weight among girls (β = 0.06; 95% CI: 0.01, 0.11) and with birth length among boys (β = 0.05; 95% CI: 0.00, 0.10). CONCLUSIONS: Prenatal exposure to BPA, DEHP, and DiNP was not associated with fetal growth restriction. Prenatal exposure to MBP was positively associated with FL at 20–34 weeks, and exposure to MBzP was associated with birth weight among girls and birth length among boys. Prenatal exposure to BPA or phthalates may affect ultrasound measures of fetal growth in the INMA-Sabadell cohort. Environ Health Perspect 124:521–528; http://dx.doi.org/10.1289/ehp.1409190	Environ Health Perspect. 2016 Apr;124(4):521-8.	10.1289/ehp.1409190	26196298	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2718	Chavarro JE et al.	2016	Soy Intake Modifies the Relation Between Urinary Bisphenol A Concentrations and Pregnancy Outcomes Among Women Undergoing Assisted Reproduction	CONTEXT: Experimental data in rodents suggest that the adverse reproductive health effects of bisphenol A (BPA) can be modified by intake of soy phytoestrogens. Whether the same is true in humans is not known. OBJECTIVE: The purpose of this study was to evaluate whether soy consumption modifies the relation between urinary BPA levels and infertility treatment outcomes among women undergoing assisted reproduction. SETTING: The study was conducted at a fertility center in a teaching hospital. DESIGN: We evaluated 239 women enrolled between 2007 and 2012 in the Environment and Reproductive Health (EARTH) Study, a prospective cohort study. METHODS: We measured urinary BPA concentrations in specimens collected on the day of oocyte retrieval. Soy intake was assessed using a validated food frequency questionnaire. RESULTS: Of 239 women who underwent oocyte retrieval, 141 had a clinical pregnancy, 99 had a live birth, and 42 had a pregnancy loss. Urinary BPA concentrations were not associated with these outcomes overall. However, the relation between urinary BPA concentrations and IVF outcomes was modified by soy intake. With 50 ITT/ITT-SME/SME-I Low birth rates per initiated treatment cycle were measured. RESULTS: Soy food consumption modified the association of urinary BPA concentrations with the birth rate (P for interaction = .01). Among women in the bottom two-thirds of consumption of soy foods, the adjusted live birth rates per initiated cycle in increasing quartiles of cycle-specific urinary BPA concentrations were 54%, 39%, 15%, and 17%. In the top third of soy consumers, the corresponding live birth rates among women reporting contrast consumption of soy foods were 38%, 42%, 47%, and 39% (P for trend = .3). A similar pattern was found for implantation (P for interaction = .02) and clinical pregnancy rates (P for interaction = .03) per initiated cycle, where urinary BPA was inversely related to these outcomes among women not consuming soy foods but unrelated to them among soy consumers. CONCLUSIONS: Soy food intake may protect against the adverse reproductive effects of BPA. As these findings represent the first report suggesting a potential interaction between soy and BPA in humans, they should be further evaluated in other populations.	J Clin Endocrinol Metab. 2016 Mar;101(3):1082-90.	10.1210/jc.2015-3473	26815879	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2719	Chin HB et al.	2019	Association of urinary concentrations of phthalate metabolites and bisphenol A with early pregnancy endpoints	BACKGROUND: Phthalates and bisphenol A (BPA) are environmental contaminants that may affect early embryonic development. OBJECTIVE: To assess the association between phthalate metabolites and BPA with early pregnancy endpoints in a cohort of women followed from before conception. METHODS: We quantified 11 phthalate metabolites and BPA in 157 conception cycles from naturally conceived, clinical pregnancies. Phthalate metabolites were combined to molecular weight sum (ΣDEHP, ΣDBP, ΣBBzP, ΣDiBP, ΣDnBP, ΣDMP) and molar sum (Σall) concentrations. We used Cox proportional hazards models to estimate fecundability ratios (FR) and 95% confidence intervals (CI) for time-to-pregnancy (TTP) and pregnancy loss. We assessed associations between conception cycle exposures (phthalate/bisphenol and BPA) and 12-item fecundity perception (FP) scores using linear mixed-effects models with a random intercept. We assessed associations between conception cycle exposures (phthalate/bisphenol and BPA) and 12-item fecundity perception (FP) scores using linear mixed-effects models with a random intercept. RESULTS: Among 157 women, 111 (71%) had a pregnancy and 39 (25%) had a pregnancy loss. Higher ΣDEHP, ΣDBP, ΣBBzP, ΣDiBP, ΣDnBP, ΣDMP, and Σall concentrations were associated with lower FR for TTP (e.g., FR = 0.68; 95% CI: 0.49, 0.94 for ΣDEHP). Higher ΣDEHP, ΣDBP, ΣBBzP, ΣDiBP, ΣDnBP, ΣDMP, and Σall concentrations were associated with lower FP scores (e.g., β = −0.08; 95% CI: −0.15, −0.01

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2720	Chiu YH et al.	2017	Trimester-Specific Urinary Bisphenol A Concentrations and Blood Glucose Levels Among Pregnant Women From a Fertility Clinic	CONTEXT: Women with a history of infertility are at increased risk of impaired glucose tolerance during pregnancy. Studies suggest higher urinary bisphenol A (BPA) concentrations are associated with diabetes in nonpregnant populations, but the association between BPA and glucose levels among pregnant women is unclear. OBJECTIVE: To assess trimester-specific urinary BPA concentrations in relation to blood glucose level during pregnancy among women undergoing fertility treatment. DESIGN, SETTING, AND PARTICIPANTS: Prospective cohort study of 501 women undergoing fertility treatment at a Boston, Massachusetts, academic medical center and urine samples during third and to second trimesters, delivered a singleton or twin pregnancy, and had available blood glucose data (2005 to 2011). MAIN OUTCOME MEASURE: Blood glucose levels after a nonfasting 50-g glucose challenge test at 10 to 28 weeks of gestation. RESULTS: The specific gravity–adjusted geometric mean urinary BPA concentrations during first- and second-trimesters were 2.39 and 1.27 μg/L, respectively. Adjusted mean glucose levels were 5.2 mg/dL (95% confidence interval [CI], 3.2 to 7.3 mg/dL; P < .001) and 3.4 mg/dL (95% CI, 1.3 to 5.5 mg/dL; P = .002) higher, respectively, for women in the highest quartile of second-trimester BPA concentrations than for those in the lowest quartile. In secondary analyses, second-trimester BPA concentrations and glucose levels (1.04 [95% CI, 1.00 to 1.07] mg/dL increase) were associated with GDM. CONCLUSIONS: Higher exposure during the second trimester may have adverse effects on blood glucose levels among subfertile women. As the findings represent the first report suggesting a potential etiologically relevant window for BPA and glucose in humans, further studies are needed.	J Clin Endocrinol Metab. 2017 Apr 1;102(4):1350-1357.	10.1210/jc.2017-00022	28323984	ヒト	生殖発生(妊娠糖尿病)	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-
統合_2721	Choi YJ et al.	2017	Exposure to bisphenol A is directly associated with inflammation in healthy Korean adults	It was recently discovered that bisphenol A (BPA) and phthalates are cardiovascular disruptors. Inflammation is central to the initiation and progression of cardiovascular disease (CVD). This study evaluated whether BPA and phthalate exposure is associated with inflammation in healthy Korean adults. We analyzed data from 1,000 participants (≥ 19 years old) who were enrolled in the Korean Genome and Epidemiology Study (KoGES) 2012 Korean adults (50–59 years of age) conducted at the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC). The study enrolled 200 healthy volunteers (100 men, 100 women). Plasma hs-CRP was measured as an inflammation factor. BPA and five phthalate metabolites in urine were analyzed by using liquid chromatography/tandem mass spectrometry. BPA and monobenzyl phthalate (MBzP) differed significantly between the low- (< 1 mg/L) and high- (≥ 1 mg/L) hs-CRP (≥ 3 mg/L) groups. BPA and MBzP were associated with hs-CRP in a U-shaped manner. High BPA levels (> 75th percentile) had significant odd ratios (ORs) for high-CRP even after adjusting for confounding factors related to obesity and insulin resistance, such as visceral fat volume, body mass index (BMI), adiponectin, high-density lipoprotein (HDL) cholesterol, hemoglobin A1c (HbA1c), and homeostasis model assessment-insulin resistance (HOMA-IR). Low BPA levels (< 25th percentile) also had significant ORs for high-CRP. Participants with relatively moderate to high hs-CRP, even after adjusting for factors related to obesity and insulin resistance. Therefore, BPA could have a direct relationship with systemic inflammation regardless of obesity or insulin resistance.	Environmental Science and Pollution Research.2017;24(1):284-290	10.1007/s11356-016-7806-7	27714659	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2722	Dambkowski CL et al.	2018	Does Urinary Bisphenol-A Change after Bariatric Surgery?	BACKGROUND: One of the world's highest volume interfaces is bisphenol-A (BPA), an organic compound with a high solubility in fat. An emerging body of literature has suggested a link between BPA, obesity, and insulin resistance. The purpose of this study was to determine if urinary BPA changes after bariatric surgery. METHODS: This was a prospective cohort study of patients undergoing bariatric surgery. Urine was prospectively collected on 22 bariatric surgery patients at a single academic institution. Laboratory values, hemoglobin A1C, fasting insulin, and fasting glucose. Demographic, preoperative and postoperative data, and urinary BPA levels were compared using Student's t-tests and simple regression analyses using GraphPad Prism® software. RESULTS: Patients were predominantly privately insured (86%), female (95%), and Caucasian (91%). Mean age was 46 years (range 23-65) and mean BMI was 48 kg/m2 (range 35-70). Urinary BPA was detectable in 100% of patients at 6 months and 91% of patients at 12 months. Mean urinary BPA creatinine was 2.6 ng/mL (SD = 1.9 ng/mL) in patients higher than average weight and 2.3 ng/mL (SD = 1.7 ng/mL) in patients heavier than average weight (p = 0.656). Average BPA level was 2.2 creatinine at 12 months was 3.5 ng/mL (SD = 2.2 ng/mL) among lighter patients and 0.58 ng/mL (SD = 0.3 ng/mL) among heavier patients (p = 0.06). Follow-up included 18 patients at 3 months, 22 patients at 6 months, and 16 patients at 12 months. Higher urinary excretion of BPA preoperatively associated with lower 6-month patient weight (r = -0.67, p = 0.025). Higher preoperative fasting insulin concentrations significantly with reduced BPA excretion at 6 months postoperatively (r = -0.868, p = 0.023). CONCLUSIONS: Excretion of BPA increases as bariatric surgery patients lose weight. Heavier patients with insulin resistance may store more BPA in adipose tissue and therefore excrete less BPA.	J Am Coll Surg. 2018 Aug;227(2):232-237.	10.1016/j.jamcollsurg.2018.04.033	29753982	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2723	Ding GD et al.	2017	Prenatal low-level phenol exposures and birth outcomes in China	Phenolic compounds are among the endocrine disruptors which are widely used in daily life products. Studies in laboratory animals showed reproductive and developmental effects. In spite of widespread exposure to phenols, only few studies examined their effects on human development. This study was designed to investigate the relationship between antenatal phenol exposure and birth outcomes in a Chinese obstetric population. Phenol concentrations were measured in urine samples collected from 1,239 pregnant women in Wuhan, China. Birth outcomes were abstracted from medical records. Multivariate regression models were used to examine associations between phenol concentrations and birth outcomes, adjusting for potential confounders. Urinary phenol concentrations were associated with adverse birth outcomes including birth weight, crown-heel length, head circumference, gestational age, and preterm birth. Each doubling of BPA2 and triclosan (TCS) in urine were 1.27 and 0.55 μg/g creatinine, respectively. After adjusting for confounders, a 10-fold increase in BPA levels was associated with a 0.28-kg (95% confidence interval (CI): 0.26 to 1.62) increase in birth weight among boys, but not among girls. No associations were found between TCS levels and any birth outcomes. The positive association of prenatal low-level BPA exposure with enhancement in measures observed among boys, suggests gender differences in the response to antenatal phenol exposure. Given the variability in urinary phenol levels reported during pregnancy, our findings based on levels of the target biomarkers in a single urine sample need to be confirmed in additional studies.	Sci Total Environ. 2017 Dec 31;607-608:1400-1407.	10.1016/j.scitotenv.2017.07.084	28738530	ヒト	生殖発生	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2724	Dodge LE et al.	2015	Paternal Urinary Concentrations of Parabens and Other Phenols in Relation to Reproductive Outcomes among Couples from a Fertility Clinic	BACKGROUND: Human exposure to phenols, including bisphenol A and parabens, is widespread. Evidence suggests that paternal exposure to environmental chemicals may adversely affect reproductive outcomes. OBJECTIVES: We evaluated associations of paternal phenol urinary concentrations with fertilization rate, embryo quality, implantation, and live birth. METHODS: Male fertile couples, who underwent in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) at a fertility clinic, provided a urine sample on the day of oocyte retrieval. We measured 13 phenol urinary concentrations, assessed before/after female cycle was quantified. Associations between male urinary phenol concentrations and fertilization rate, embryo quality, implantation, and live birth were investigated using generalized linear mixed models to account for multiple cycles per couple. RESULTS: Couples (n = 256) underwent 395 IVF and 212 ICSI* cycles. Paternal phenol concentrations were not associated with fertilization or live birth following IVF. In adjusted models, we observed 12% fewer oocytes fertilized [95% confidence interval (CI): 0.78, 0.99] and 13% lower fertilization (CI: 0.74, 1.02) for each doubling of paternal urinary triclosan (TCS) concentrations. Male TCS concentrations were also associated with 14% lower odds of high-quality embryos (OR = 0.86; 95% CI: 0.74, 1.00) and 13% lower odds of implantation (OR = 0.87; 95% CI: 0.76, 1.00) following ICSI. Paternal BPA concentrations were associated with 13% lower odds of live birth following ICSI (adjusted odds ratio = 0.74; 95% CI: 0.55, 0.98). CONCLUSIONS: To our knowledge, these are some of the first data on the association of paternal urinary phenol concentrations with reproduction and pregnancy outcomes. Although these results do not provide possible adverse effects of paternal parabens exposures on such outcomes, given the modest sample size, further understanding could result from confirmation using a larger and more diverse population.	Environ Health Perspect. 2015 Jul;123(7):665-71.	10.1289/ehp.1408605	25767892	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2725	Evans SF et al.	2014	Prenatal bisphenol A exposure and maternally reported behavior in boys and girls	Prenatal exposure to gonadal hormones plays a major role in the normal development of the male and female brain and sexually dimorphic behaviors. Hormone-dependent differences in brain structure and function suggest that developmental exposure to bisphenol A (BPA), a known endocrine disruptor, may alter behavioral outcomes. Animal studies have shown that BPA exposure can affect behavior, and thyroid hormone signaling pathways. Epidemiological and experimental studies suggest associations between prenatal exposure to BPA and child behavior, however data are inconsistent, and few studies have examined school age children. We examined BPA concentration in spot urine samples from women at mean 27 weeks of pregnancy in relation to child behavior assessed at age 8.10 years using the parent-completed Child Behavior Checklist (CBCL). We report associations between maternal BPA urinary concentrations, and several CBCL scores in 515 children (177 boys and 76 girls). We observed a significant interaction between maternal urinary BPA and sex for several behaviors (externalizing, aggression, Anxiety/Disorder, Oppositional/Defiant Disorder and Conduct Disorder traits), but no significant associations between BPA and scores on any CBCL scales among girls. Among boys, higher prenatal BPA concentrations were associated with higher scores on the externalizing scale, aggressive behavior scale, rule-breaking behavior scale, somatic problems, and Oppositional/Defiant Disorder traits. In addition we observed a significant interaction between BPA and sex for several behaviors (externalizing, withdrawn/depressed, rule-breaking, Oppositional/Defiant Disorder traits, and Conduct Disorder traits). These results suggest that prenatal exposure to BPA may be related to increased behavior problems in school-age boys, but not girls.	Sci Total Environ. 2017 Dec 31;607-608:1400-1407.	10.1016/j.neuro.2014.10.003	25307304	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2726	Ferguson KK et al.	2015	Phthalate metabolites and bisphenol-A in association with circulating angiogenic biomarkers across pregnancy	INTRODUCTION: Phthalates and bisphenol-a (BPA) are endocrine-disrupting compounds with widespread exposure that have been linked to adverse birth outcomes and developmental effects. We hypothesized that these associations may be mediated in part through altered placental development and function consequent to exposure. To investigate this question, we examined associations between plasma biomarkers of angiogenesis and urinary biomarkers of exposure to phthalates and bisphenol-a (BPA) measured at repeated time points across pregnancy. METHODS: We utilized a nested case-control population of 130 mothers who delivered preterm (<37 weeks gestation) and 130 matched controls who delivered at term (≥37 weeks gestation). Maternal urine samples were collected at three time points during pregnancy (median 16, 18, 26, and 30 weeks). Phthalate metabolites and BPA were measured in urine samples collected at the same visits as indices of exposure. PlGF, sFlt-1, Endoglin, and sEndoglin, indicators of urine dilution and gestational age at sample collection, collected at 3 ethylhexyl phthalate (DEHP) metabolites were associated with decreases in PlGF as well as increases in the sFlt-1 to PlGF ratio. These results were slightly attenuated in fully adjusted models. Other phthalate metabolites did not show consistent relationships with either sFlt-1 or PlGF. BPA, however, was associated with increased sFlt-1 as well as the sFlt-1 to PlGF ratio in both crude and adjusted models. DISCUSSION: We observed associations between urinary DEHP metabolites and BPA and biomarkers of angiogenesis during pregnancy that may be indicative of disrupted placental development and/or function during gestation.	Placenta. 2015 Jun;36(6):699-703.	10.1016/j.placenta.2015.04.002	25913709	ヒト	その他	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2727	Ferguson KK et al.	2014	Prenatal and peripubertal phthalates and bisphenol A in relation to sex hormones and puberty in boys	Phthalates and BPA are known endocrine disruptors, and exposure in pregnant mothers and children is ubiquitous. We explored the relationship of prenatal and childhood exposures with potential onset and sex hormones in boys (ages 8–16). Phthalate metabolites and BPA were measured in maternal 3rd trimester or childhood urine. Sex hormones (SHBG, estradiol, testosterone, DHEA, androstenedione, LH, FSH) and testicular volume were assessed by pediatrician. Prenatal exposure to some phthalates was associated with decreased DHEAS and inhibin B levels, and with increased SHBG. Prenatal exposure to most phthalates and BPA was associated with greater testicular volume. Many phthalate metabolites did not show consistent relationships with either sFlt-1 or PlGF. BPA, however, was associated with increased sFlt-1 as well as the sFlt-1 to PlGF ratio in both crude and adjusted models. DISCUSSION: We observed associations between urinary DEHP metabolites and BPA and biomarkers of angiogenesis during pregnancy that may be indicative of disrupted placental development and/or function during gestation.	Reprod Toxicol. 2014 Aug;47:70-6.	10.1016/j.reprotox.2014.06.002	24945889	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2728	Fisher BG et al.	2018	Serum Phthalate and Triclosan Levels Have Opposing Associations With Risk Factors for Gestational Diabetes Mellitus	Certain phthalates and bisphenol A (BPA) have been associated with insulin resistance and type 2 diabetes. In non-pregnant adults, but studies of gestational diabetes mellitus (GDM) have reported conflicting results for phthalates and no associations with BPA. Our aim was to investigate the relationship between maternal serum levels of phthalate metabolites and phenols at 10-17 weeks of gestation and glucose homeostasis at 28 weeks of gestation. 220 women aged >/=18 years without type 1 or 2 diabetes with singleton male pregnancies were recruited from a single UK maternity service between 2009 to 2011 as part of a prospective observational study (Cambridge Baby Growth Study). Serum levels of 16 phthalate metabolites and 4 phenols (including BPA) were measured using liquid chromatography/tandem mass spectrometry. Oral glucose tolerance tests were performed at 28 weeks. GDM was diagnosed according to World Health Organization criteria. Multivariable logistic regression models were used to examine associations between GDM and phthalates and phenols. Women with GDM (n = 16) had higher serum levels of monoethyl phthalate (MEP) (adjusted odds ratio (aOR) 2.0 (95% confidence interval (CI) 0.98, 4.1; p = 0.058). Strongest women without GDM. Non-trimester mean (T) ethylhexyl phthalate and mono(carboxyoctyl) phthalate levels were also associated with GDM risk (mono-(carboxyoctyl)phthalate) 0.268 and 0.181, p = 0.002 and 0.018, respectively) in mid-pregnancy. No other monotonic associations were detected between phthalate or phenol levels and fasting or stimulated glucose concentrations, beta cell function, insulin resistance, or 60 min disposition index. Our results support a glycaemic-raising effect of phthalates during pregnancy, consistent with findings in non-pregnant populations and suggest a possible protective effect of exposure to TCS against GDM.	Front Endocrinol (Lausanne). 2018 Mar 13;9:99.	10.3389/fendo.2018.00099	29593656	ヒト	生殖(妊娠糖尿病)	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2729	Geens T et al.	2015	Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals	Bisphenol A (BPA) and triclosan (TCS) were determined in urine of Belgian overweight and obese (n=252) and lean (n=30) individuals. After the first urine collection (BL), obese patients started a diet program or bariatric surgery. Hereafter, three additional urine samples from obese patients were collected after 1 (M1), 6 (M6) and 12 (M12) months. Both compounds were detected in >99% of the samples. BPA had median concentrations of 1.7 and 2.0ng/mL in obese and lean groups, respectively, while TCS had median concentrations of 1.5 and 0.9ng/mL in the obese and lean groups, respectively. The obese group had higher concentrations than the lean group (p<0.05). Urinary concentrations were not significantly correlated with body mass index, waist circumference, body fat percentage or body fat mass. BPA concentrations in the obese group were negatively associated with age, while no gender difference or relationship with body mass index was documented. For TCS, no relationships with gender, BMI, or age were found. The temporal variability of BPA and TCS was assessed with calculation of the intraclass correlation coefficient. Spearman rank correlation coefficients, and surrogate category analysis. We observed evidence that single spot urine samples might be predictive of exposure over a longer period of time. Dietary intakes of BPA and TCS did not differ significantly among the urine points considered after obese individuals started losing weight (0 and 3 months). Multiple linear regression analyses after adjusting for age and weight loss revealed negative associations between urinary TCS and serum FT4 in the BL and M3 female obese individuals and positive associations between urinary BPA and serum TSH in the lean group.	Environ Int. 2015 Mar;76:98-105.	10.1016/j.envint.2014.12.003	25575039	ヒト	代謝	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2730	Ghassabian A et al.	2018	Concentrations of perfluoroalkyl substances and bisphenol A in newborn dried blood spots and the association with child behavior	Experimental studies suggest that prenatal exposure to endocrine-disrupting chemicals interferes with developmental processes in the fetal brain. Yet, epidemiological evidence is inconclusive. In a birth cohort (2008-2010) in the Generation R Study, we measured concentrations of perfluoroalkyl substances (PFAS) and bisphenol A (BPA) in newborn dried blood spots collected 2-4 days after birth using liquid chromatography/tandem mass spectrometry. Mothers reported on children's behavior using the Strengths and Difficulties Questionnaire at age 7. DNA singletons and 338 twins (total 1,038 children, mixed behavior (i.e., emotional, conduct, hyperactivity, and peer problems) and prosocial behavior score classified using validated cut-offs. We used logistic regression to estimate the odds of having difficulties on separate scales. In total, 111 children (12.2%) had total behavioral difficulties and 90 (10.0%) had difficulties in prosocial behavior. The median (interquartile range) of PFOA was 1.3 (1.1-1.5) ng/mL, of PFOS was 1.3 (ng/mL (1.05, 1.12 ng/mL) and 7.83 (ng/ml (5.9-10.9), respectively. Higher PFOS levels were associated with increased odds of having behavioral difficulties (OR per SD of log PFOS = 1.18; 95%CI: 1.03-1.40). No associations were observed for PFOA, PFHxS, PFNA, and BPA. Compared to children in the lowest quartile of PFOS (<1.1 ng/mL), children in the highest quartile (>1.5 ng/mL) had increased odds of total difficulties (OR=1.52; 95%CI: 1.01-2.29), emotional problems (OR=1.67; 95%CI: 1.07-2.62; 95%CI: 1.04-2.72) compared to 1.1-1.3 ng/mL). The associations between higher concentrations of PFOS and behavioral difficulties at age 7 were more driven by emotional and emotional symptoms. Higher PFOA levels were associated with difficulties in prosocial behavior (OR= 1.36; 95%CI: 1.03-1.79). There was an inverse association between BPA concentrations and difficulties in prosocial behavior but only in the 2nd and 4th quartiles. We found no interactions between sex and chemical concentrations. Increasing prenatal exposure to PFOS and PFOA, as reflected in neonatal concentrations, may pose risk for child behavioral difficulties.	Environ Pollut. 2018 Dec;243(Pt B):1629-1636.	10.1016/j.envpol.2018.09.107	30296759	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2731	Giesbrecht GF et al.	2017	Prenatal bisphenol a exposure and dysregulation of infant hypothalamic-pituitary-adrenal axis function: findings from the APrON cohort study	BACKGROUND: Animal models show that prenatal bisphenol A (BPA) exposure leads to sexually dimorphic disruption of the neuroendocrine system in offspring, including the hypothalamic-pituitary-adrenal (HPA) neuroendocrine system, but human data are lacking. In humans, prenatal BPA exposure is associated with sex-specific behavioural problems in children, and HPA axis dysregulation may be a biological mechanism. The current study tested whether prenatal BPA exposure is associated with dysregulation of infant HPA axis function in the Applied Research on Prenatal Outcomes of Neurodevelopment (APrON) cohort. APrON is a sub-cohort of the Alberta Pregnancy Outcomes and Nutrition cohort, a longitudinal birth cohort recruited (2009-2012) during pregnancy. Maternal urine samples collected during the 3rd trimester were analyzed for total BPA and creatinine. Infant saliva samples collected prior to and after a blood draw were analyzed for cortisol. Linear growth curve models were used to characterize changes in infant cortisol as a function of prenatal BPA exposure. RESULTS: Higher concentrations of total BPA were associated with increased reactivity in females (beta = .32 ng/mL; 95%CI: 0.02, 0.62) but decreased reactivity in females (beta = -0.23 ng/mL; 95% CI: -0.36, -0.09). In contrast, higher BPA was associated with increased reactivity in males (beta = .30 ng/mL; 95%CI: 0.02, 0.58) but decreased reactivity in females (beta = -0.23 ng/mL; 95% CI: -0.36, -0.09). Models adjusting for creatinine yielded similar results. CONCLUSIONS: Prenatal BPA exposure is associated with sex-specific changes in infant HPA axis function. The biological plausibility of these findings is supported by their consistency with evidence in rodent models. Furthermore, these data support the hypothesis that sexually dimorphic changes in children's behaviour following prenatal BPA exposure are mediated by sexually dimorphic changes in HPA axis function.	Environ Health. 2017 May 19;16(1):47.	10.1186/s12940-017-0259-8	28526030	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	●	-	-	-	-	-	-	-	-	-	-
統合_2732	Giesbrecht GF et al.	2016	Urinary bisphenol A is associated with dysregulation of HPA-axis function in pregnant women: Findings from the APrON cohort study	BACKGROUND: Bisphenol A (BPA) is associated with dysregulation of hypothalamic-pituitary-adrenal (HPA) axis activity in rodents, but evidence in humans is lacking. OBJECTIVE: To determine whether BPA exposure during pregnancy is associated with dysregulation of the HPA-axis, we examined this association between urinary BPA concentrations and diurnal salivary cortisol in pregnant women. Secondary analyses investigated whether the association between BPA and cortisol was dependent on fetal sex. METHODS: Diurnal salivary cortisol and urinary BPA were collected during pregnancy from 173 women in a longitudinal cohort study, the Applied Research on Prenatal Outcomes of Neurodevelopment (APrON) study. Linear mixed models were used to examine associations between BPA and cortisol. RESULTS: Higher concentrations of total BPA were associated with increased cortisol at waking, ($b = .065$, 95% CI = .001, .130) and a flatter daytime pattern, ($b = .011$, 95% CI: .006, .017) and ($b = .0007$ 95% CI = .000, .0002) for the linear and quadratic slopes, respectively. Effects were in creatinine corrected BPA models were slightly smaller. Tests of the interactions between fetal sex and BPA were significant (all 95% CI's include zero). CONCLUSIONS: These findings provide the first human evidence suggesting that BPA exposure is associated with dysregulation of HPA axis function during pregnancy.	Environ Res. 2016 Nov;151:689-697.	10.1016/j.envres.2016.09.007	27640068	ヒト	腎	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-

適格性評価（動物）1：該当、0：該当しない

適格性評価（疫学）1：該当、0：該当しない

適格性評価（in vitro）1：該当、0：該当しない

適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2733	Goldstone AE et al.	2015	Urinary bisphenol A and semen quality, the LIFE Study	Bisphenol A (BPA), a high-production volume industrial chemical found in several consumer products, has been negatively associated with sperm quality. This study aimed to estimate the association between BPA and its measures of semen quality among reproductive-aged men recruited from 10 counties in Michigan and Texas, 2005-2009. Of 501 enrolled males, 228 (45.5%) provided at least one sample and at least one semen quality. Linear and logistic regression models assessed the association between urinary BPA levels and individual semen quality endpoints. Generalized estimating equations were used to account for repeated measures of semen quality and adjusted models accounted for: (1) actors' covariates, (2) semen's mean-total urinary BPA concentration among participants was 3.0 (log-10) ng/mL (95% CI 0.89-5.60). A negative relation between BPA and DNA fragmentation was the sole significant finding in adjusted linear regression (beta= -0.0045; p=0.005) and suggestive of less sperm DNA damage.	Reproductive Toxicology.2015;51:43659	10.1016/j.reprotox.2014.11.003	25462789	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2734	Gonzalez-Casanova I et al.	2018	Prenatal exposure to environmental pollutants and child development trajectories through 7 years	BACKGROUND: Prenatal exposure to environmental pollutants such as mold, lead, pesticides, tobacco, and air pollutants has been suggested to impact cognitive development. Evidence is needed from longitudinal studies to understand their joint impact on child development across time. OBJECTIVE: To study associations between exposure to indoor environmental pollutants, or outdoor air pollution during pregnancy and offspring cognitive development trajectories through 7 years. METHODS: 1,196 children from the Spanish INMA birth cohort study were followed-up to age 7 years. Prenatal exposure to indoor pollutants (environmental tobacco smoke (ETS), mold, and NO2/CO) in room subbacoms. Participants (n = 1,027) from the Early-Life Exposures in Mexico to Environmental Toxicants (ELEMENT) birth cohorts were followed-up to assess between the ages of 9 and 14 years, and concurrent exposures were measured in biospecimens collected at that time (blood Pb, urinary BPA, and phthalate metabolites). Prenatal and childhood exposures to Pb were previously approximated using maternal and child samples. BPA and phthalate metabolites were measured in third trimester maternal urine samples. Significant associations (Pr < 0.05) in models with a p120 log-scale risk of incident central obesity (95% confidence interval [CI]: 1.29-3.79; P = 0.005) after adjustment for confounders. Compared with the lowest tertile of urinary BPA concentration, Tertiles 2 and 3 were associated with a higher risk of incident central obesity (odds ratios, 1.72 [95% CI: 1.00-2.98] and 1.81 [95% CI: 1.08-3.06], respectively). Stratified analysis showed significant associations of BPA with incident central obesity in women and individuals <30 years of age, with normal weight, non-smokers, non-hypertensives, CONCLUSIONS: The results indicate that higher urinary BPA concentrations may be associated with a greater risk of incident central obesity in Chinese adults. The study emphasizes the effects of BPA exposure on metabolic risk from a public health perspective.	Int J Hyg Environ Health. 2018 May;221(4):616-622.	10.1016/j.ijheh.2018.04.004	29699913	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2735	Goodrich JM et al.	2016	Adolescent epigenetic profiles and environmental exposures from early life through peri-adolescence	Epigenetic perturbations induced by environmental exposures at susceptible lifestages contribute to disease development. Even so, the influence of early life and ongoing exposures on the adolescent epigenome is rarely studied. We leveraged the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) longitudinal birth cohort to examine associations between exposures (ETS, PAH, and PHDE/DDE) in peri-adolescents. Participants (n = 247) from the Early-Life Exposures in Mexico to Environmental Toxicants (ELEMENT) birth cohorts were followed-up to assess between the ages of 9 and 14 years, and concurrent exposures were measured in biospecimens collected at that time (blood Pb, urinary BPA, and phthalate metabolites). Prenatal and childhood exposures to Pb were previously approximated using maternal and child samples. BPA and phthalate metabolites were measured in third trimester maternal urine samples. Significant associations (Pr < 0.05) in models with a p120 log-scale risk of incident central obesity (95% confidence interval [CI]: 1.29-3.79; P = 0.005) after adjustment for confounders. Compared with the lowest tertile of urinary BPA concentration, Tertiles 2 and 3 were associated with a higher risk of incident central obesity (odds ratios, 1.72 [95% CI: 1.00-2.98] and 1.81 [95% CI: 1.08-3.06], respectively). Stratified analysis showed significant associations of BPA with incident central obesity in women and individuals <30 years of age, with normal weight, non-smokers, non-hypertensives, CONCLUSIONS: The results indicate that higher urinary BPA concentrations may be associated with a greater risk of incident central obesity in Chinese adults. The study emphasizes the effects of BPA exposure on metabolic risk from a public health perspective.	Environ Epigenet. 2016 Aug 14;2(3):dvw018.	10.1093/eep/dvw018	29492298	ヒト	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-
統合_2736	Hao M et al.	2018	Urinary bisphenol A concentration and the risk of central obesity in Chinese adults: A prospective study	BACKGROUND: Bisphenol A (BPA) exposure has been associated with diabetes and related metabolic disorders, such as obesity, but studies of the association of urinary BPA concentrations with central obesity risk are limited. The aim of this study was to prospectively investigate the association between urinary BPA and incident central obesity in a Chinese population aged ≥ ≥18 years. METHODS: The study followed 888 participants aged ≥18 years at baseline (2009) in Tianjin, China, for 4 years. Urinary BPA concentrations were measured at baseline. Central obesity was defined as waist circumference (WC) ≥ ≥90 cm in men and ≥ ≥80 cm in women. RESULTS: During a mean follow-up of 4 years, 133 (14.9%) incident cases of central obesity were identified. Participants in the highest tertile of urinary BPA concentration had a 2.03-fold risk of incident central obesity (95% confidence interval [CI] 1.39-2.78; P < 0.001) after adjustment for confounders. Compared with the lowest tertile of urinary BPA concentration, Tertiles 2 and 3 were associated with a higher risk of incident central obesity (odds ratios, 1.72 [95% CI 1.00-2.98] and 1.81 [95% CI 1.08-3.06], respectively). Stratified analysis showed significant associations of BPA with incident central obesity in women and individuals <30 years of age, with normal weight, non-smokers, non-hypertensives, CONCLUSIONS: The results indicate that higher urinary BPA concentrations may be associated with a greater risk of incident central obesity in Chinese adults. The study emphasizes the effects of BPA exposure on metabolic risk from a public health perspective.	J Diabetes. 2018 Jun;10(6):442-448.	10.1111/1753-0407.12531	28097815	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-
統合_2737	Hart RJ et al.	2018	The impact of antenatal Bisphenol A exposure on male reproductive function at 20-22 years of age	Bisphenol A (BPA) is a ubiquitous chemical suspected to possess oestrogenic hormonal activities. Male population studies suggest a negative impact on testicular function. As Sertoli cell proliferation occurs during fetal life, we hypothesised that antenatal BPA exposure would be associated with reduced testicular function in young adulthood. Pregnant women were recruited to the Barwon Infant Study birth cohort and levels of bio-active and total BPA (conjugated and unconjugated) in urine were measured at 28 weeks gestation (n=2154) from archived maternal urine samples. Of these, 1556 had maternal serum available for BPA analysis. Maternal serum collected at 18 and 30 weeks' gestation was pooled and assayed for concentrations of total BPA (free plus conjugated) as an estimate of antenatal exposure. Testicular volume was calculated by ultrasonography, and semen analysis performed. Serum LH, FSH and inhibin B were measured by immunoassay; testosterone, oestradiol, sex hormone binding globulin were measured by liquid chromatography-mass spectrometry. BPA levels were detectable in most (89%) maternal serum samples. After adjustment for maternal smoking, alcoholence and sex work, sperm concentration and motility were significantly correlated with maternal serum BPA (-0.16 (B.-F -0.04 to both). No other associations of maternal serum BPA with testicular function were observed.	Reprod Biomed Online. 2018 Mar;36(3):340-347.	10.1016/j.rbmo.2017.11.009	29291929	ヒト	精巣	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2738	Hoepner LA et al.	2016	Bisphenol A and Adiposity in an Inner-City Birth Cohort	BACKGROUND: Early-life exposure to the endocrine disruptor bisphenol A (BPA) may contribute to the development of obesity. Prospective evidence in humans on this topic is limited. OBJECTIVES: We examined prenatal and early-childhood BPA exposure in relation to childhood measures of adiposity in the Columbia Center for Children's Environmental Health (CCCEH) New York City birth cohort. METHODS: BPA concentrations were measured in prenatal (n = 373) and child ages 3 (n = 338), 5 (n = 348), and 7 years (n = 328) spot urine samples. Childhood anthropometric and bioelectrical impedance measures included body mass index z-score (BMIZ) at 5 and 7 years, and fat mass index (FMI, percent body fat [%BF], and total circumference [WC] at 7 years. Associations were evaluated using multiple linear regression with continuous and tertile BPA concentrations. RESULTS: Geometric mean (GM) prenatal BPA concentration was 1.1 ng/mL (95% CI: 1.0, 1.2). GM BPA was 1.2 ng/mL (95% CI: 1.1, 1.3) at age 3, 1.1 ng/mL (95% CI: 1.0, 1.2) at age 5, and 1.0 ng/mL (95% CI: 0.9, 1.1) at age 7. Prenatal BPA was not associated with childhood BMIZ, %BF, or WC. Age 3 BPA was associated with FMI at age 7 (β = 0.02; 95% CI: 0.00, 0.04; p = 0.02), but most BMIZ or change in BMIZ between ages 5 and 7 years (all p values ≥ 0.2). FMI results were non-specific. Child urinary BPA concentrations were not associated with child anthropometric outcomes (all p values > 0.05). CONCLUSIONS: Analyses of the CCCEH longitudinal birth cohort found associations between prenatal urinary BPA concentrations and FMI, %BF, and WC. Our results suggest that postnatal BPA exposure may contribute to developmental origins of adiposity. These findings are consistent with several prior studies, starting concern about the persistence of BPA. CITATIONS: Hoepner LA, Whyatt RM, Widen EM, Hassoun A, Oberfield SE, Mueller NT, Diaz D, Calafat AM, Perera FP, Rundle AG. 2016. Bisphenol A and adiposity in an inner-city birth cohort. Environ Health Perspect 124:1644–1650; http://dx.doi.org/10.1289/EHP205.	Environ Health Perspect. 2016 Oct;124(10):1644-1650.	10.1289/EHP205	27187982	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-
統合_2739	Hu J et al.	2019	Serum Bisphenol A is an independent risk factor of hyperuricemia: A 6-year prospective study	OBJECTIVE: This study aims to evaluate whether serum Bisphenol A (BPA) is a risk factor for hyperuricemia. METHODS: In this prospective study, a total of 682 participants without hyperuricemia were enrolled at baseline and followed up for 6 years. Clinical characteristics were recorded, and serum levels of uric acid and BPA were measured. Participants were stratified into tertiles according to low, median, and high baseline BPA concentrations. Multivariable logistic regression models were used to analyze the associations of serum BPA with the change in eGFR and the risk of CKD development. RESULTS: Baseline serum BPA concentrations (0.01 < 0.24, 0.24-0.32 ng/mL, and 0.32 < 5.47ng/mL for low, median, and high tertiles, respectively, P < 0.001). When adjusted for potential confounders, such as age, renal function, and history of diabetes and hypertension, multivariable logistic analysis showed that subjects in the median or high baseline BPA tertiles exhibited a tenfold higher risk of 6-year hyperuricemia incidence compared to subjects in the low baseline BPA tertile (odds ratio (OR) = 2.38 (95% CI: 1.09-5.95) for the median tertile, 2.42 (1.07-5.48) for the high tertile, P for Trend = 0.003). CONCLUSIONS: In conclusion, serum BPA is an independent risk factor for hyperuricemia.	Semin Arthritis Rheum. 2019 Feb;48(4):644-648.	10.1016/j.semarthrit.2018.03.009	29650240	ヒト	高尿酸血症	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	●	-	●	-	-	-	-	-
統合_2740	Hu JB et al.	2015	Serum bisphenol A and progression of type 2 diabetic nephropathy: a 6-year prospective study	AIMS: Bisphenol A (BPA) is associated with diabetes and cardiovascular diseases. The aim of our study was to evaluate whether serum BPA could predict the progression of chronic kidney disease (CKD) in patients with type 2 diabetes. (T2D). METHODS: In this prospective study, a total of 121 patients with T2D and estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73 m(2) were followed up for 6 years. The baseline values of serum BPA were measured. Renal function was measured as eGFR calculated by the Chronic Kidney Disease Epidemiology Collaboration creatinine equation. Annual change in eGFR was defined as eGFR slope. RESULTS: Baseline serum BPA concentrations (0.01 < 0.24, 0.24-0.32 ng/mL, and 0.32 < 5.47ng/mL for low, median, and high tertiles, respectively, P < 0.001). When adjusted for potential confounders, such as age, renal function, and history of diabetes and hypertension, multivariable logistic analysis showed that subjects in the median or high baseline BPA tertiles exhibited a tenfold higher risk of 6-year hyperuricemia incidence compared to subjects in the low baseline BPA tertile (odds ratio (OR) = 2.38 (95% CI: 1.09-5.95) for the median tertile, 2.42 (1.07-5.48) for the high tertile, P for Trend = 0.003). CONCLUSIONS: In conclusion, serum BPA is an independent risk factor for hyperuricemia.	Acta Diabetol. 2015 Dec;52(6):1135-41.	10.1007/s00592-015-0801-5	26321107	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-
統合_2741	Huang YF et al.	2017	Concurrent exposures to nonylphenol, bisphenol A, phthalates, and organophosphate pesticides on birth outcomes: A cohort study in Taipei, Taiwan	Prenatal exposure to phenols, phthalates (PAEs), and organophosphate (OP) pesticides may increase the risk of abnormal birth outcomes. However, many previous studies have examined exposure to a limited number of chemical classes or exposure profiles. Fetal life is a specific stage of pregnancy. This study aims to characterize the concurrent exposure scenario throughout pregnancy and to examine the relationship between concurrent exposure to several endocrine-disrupting compounds (EDCs), including 3 phenols (nonylphenol (NP) and bisphenol A (BPA)), 9 PAEs, and 6 OP pesticide metabolites, and to assess the relationships between concurrent exposure to EDCs, and infant birth weight, length, and head and chest circumference. One hundred and sixty-two women provided three spot urine samples at approximately 12, 24, and 36 gestational weeks and at delivery. We applied multivariable linear regression and ridge regression models to estimate the effects of urinary EDC concentrations on birth outcomes. Multivariable linear regression models revealed that women with short birth length infants had significantly higher urinary concentrations of NP, BPA, MBP, 3-PAEs, DEP, and ΣDAPs simultaneously. Ridge

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2746	Kasper N et al.	2016	Association of Bisphenol A Exposure with Breastfeeding and Perceived Insufficient Milk Supply in Mexican Women	Introduction Estrogen inhibits lactation and bisphenol A (BPA) is a high-production environmental estrogen. We hypothesize an inhibitory effect of BPA on lactation and aim to analyze the association between third trimester urinary BPA concentrations and breastfeeding duration. Methods We used data from 1,151 women in the Programming Research in Obesity, Growth Environment and Social Stressors (PROGRESS) cohort. Maternal urine samples were analyzed for BPA using liquid chromatography with tandem mass spectrometry. We calculated Kaplan-Meier survival curves and used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between third trimester BPA and breastfeeding at 1 month and exclusive breastfeeding at 3 months and 6 months. Results Of 1,151 women, 76.1% (n = 876) breastfed for any duration at 1 month, 52.3% (n = 602) at 3 months, and 29.1% (n = 335) at 6 months. Median third trimester BPA was 1.8 ng/mL (interquartile range [IQR]: 0.8, 4.1). Adjusted Cox PH: N 0.72 to 1.00 breastfeeding at 1 month were 0.9 (0.8, 1.0) and 0.8 (0.8, 0.9) for women in the second and third BPA tertiles, respectively, compared to the lowest (p = 0.08; trend). 0.2% reported PMA in the lowest BPA tertile, compared to 0.7% in the highest (p = 0.01). Adjusted ORs (95 % CI) for PMA were 1.8 (0.6, 5.7) and 2.9 (1.0, 9.1), for the second and third BPA tertiles, respectively, compared to the lowest (p = 0.05; trend). Discussion These results suggest an association between maternal BPA exposure and decreased breastfeeding.	Matern Child Health J. 2016 Aug;20(8):1713-9.	10.1007/s10995-016-1974-4	27150949	ヒト	その他	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2747	Kasper-Sonnenberg M et al.	2017	Pre-pubertal exposure with phthalates and bisphenol A and pubertal development	OBJECTIVE: Epidemiological studies indicate associations between childhood exposure with phthalates and bisphenol A (BPA) and the pubertal development. We examined associations between the pre-pubertal phthalate and BPA body burden and the longitudinally assessed sexual maturation of eight- to thirteen- year old children. METHODS: We started with eight- to ten-year-old children in the baseline study and quantified urinary concentrations of BPA, 5 phthalate metabolites and 2 DEHP metabolites. Sexual maturation was assessed by trained physicians according to Tanner and by questionnaires (PDS scales), and the chemical exposure from the baseline visit were longitudinally associated with pubertarian maturation. RESULTS: The number of children with both chemical measures and PDS scores. Calculated from the PDS scales' mean. 68. In the first follow- up, 69% of the girls and 28% of the boys had reached mid-puberty. For girls, we observed a delayed pubertal development with the of benzyl ethyl phthalate (BEHP) metabolites (beta: -0.24; 95% CI: -0.39; -0.09; p <= 0.01 and p <= 0.1), more in-boys phthalate (beta: -0.11; 95% CI: -0.21; -0.02), and mono-ethyl phthalate (MEP) (beta: -0.21; 95% CI: -0.39; -0.03). In addition, significant non- these associations of the DEHP metabolites and BPA with the PDS scores were found, when their quadratic effects were included in the GEE models = 0.01). CONCLUSIONS: We found indications that pre-pubertal exposures with phthalates and BPA were associated with pubertal timing in children, particularly in girls. For boys, associations were inconsistent, and not necessarily in line with the known anti- androgenicity of some phthalates during prenatal exposure.	PLoS One. 2017 Nov 20;12(11):e0187922.	10.1371/journal.pone.0187922	29155850	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	-	●	-	-	-	-	-	-	-	-
統合_2748	Khan A et al.	2017	Elevated Metabolites of Steroidogenesis and Amino Acid Metabolism in Preadolescent Female Children With High Urinary Bisphenol A Levels: A High-Resolution Metabolomics Study	Health risks associated with bisphenol A (BPA) exposure are controversially highlighted by numerous studies. High-resolution metabolomics (HRM) can confirm these proposed associations and may provide a mechanistic insight into the connections between BPA exposure and metabolic perturbations. This study was aimed to identify the changes in metabolomics profile due to BPA exposure in urine and serum samples collected from female and male children (n = 130 aged 7-9). Urine was measured for BPA concentrations, and the children were subsequently classified into high and low BPA groups. HRM, coupled with Liquid Chromatography-Mass Spectrometry (LC-MS), was employed to measure metabolomics profiles in urine and serum samples. Multivariate statistical analysis, such as orthogonal partial least-squares-discriminant analysis (OPLS-DA), as well as t-tests and Kruskal-Wallis tests, followed by further validation of such findings in serum samples, observed from urine specimens. Metabolic pathway analysis revealed that bisphenol A exposure may affect steroid hormone and Tryptophan metabolism, arginine and proline metabolism, glycine, serine and alanine metabolism, cysteine and methionine metabolism, tryptophan metabolism, tyrosine metabolism, lysine degradation, pyruvate metabolism, and arginine biosynthesis. were affected in high BPA children. Elevated levels of metabolites associated with these pathways in urine and serum were mainly observed in female children, while these changes were negligible in male children. Our results suggest that the steroidogenesis, pathway and amino acid metabolism are the main targets of perturbation by BPA in preadolescent girls.	Toxicological Sciences.2017;160(2):371-385	10.1093/toxsci/kfx189	28973422	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2749	Kim JH et al.	2017	Increase of urinary malondialdehyde level by bisphenol A exposure: a longitudinal panel study	BACKGROUND: To verify oxidative stress as a possible mechanism that establishes a relationship between exposure to bisphenol A (BPA) and adverse health outcomes. In the elderly Korean population, we evaluated the relation between short- to mid- variations in urinary BPA and oxidative stress biomarker. METHODS: To assess the relation between BPA and urinary malondialdehyde (MDA) as an oxidative stress biomarker, we used a mixed effect model after controlling for age, sex, BMI, drinking status, exercise, urinary cotinine level, and urinary creatinine level. Participants were recruited from the Korean Elderly Environmental Panel (KEEP) study. We repeatedly measured urine samples from 70 participants and polymorphisms of oxidative stress-related genes (CCS2, EPHX1, HSPD1 from, PON1, ARE2, CAT, GRB10, SOD2, and NPY2) was also evaluated. RESULTS: A significant association was found between urinary BPA and MDA concentrations (β = 0.0004, 95% confidence interval [CI] = 0.0001, 0.0007, p = 0.0109). The association between urinary BPA and MDA was found regardless of any genotype of the nine oxidative stress-related genes. CONCLUSIONS: The results of our study suggest a strong association of BPA with oxidative stress, not related with sex and oxidative stress- related gene polymorphisms.	Environmental Health.2017;16:9	10.1186/s12940-017-0221-9	28202054	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2750	Kim KN et al.	2014	Bisphenol A Exposure and Asthma Development in School-Age Children: A Longitudinal Study	BACKGROUND: Although the effect of bisphenol A on various health outcomes has been extensively examined, few studies have investigated its effect on asthma. OBJECTIVE: We hypothesized that exposure to bisphenol A in school-age children was associated with wheezing and asthma. METHODS: Participants included 127 children aged 7–8 years without a previous asthma diagnosis in an elementary school in Seoul, Korea. Three survey were conducted in each 2 years apart. Bisphenol A concentrations were measured at the baseline survey. Wheeze and FCZA, which is defined as wheeze, were assessed in the three surveys. Of the 127 children at baseline, one measured at many survey. Associations between bisphenol A concentration at 7–8 years of age and wheezing, asthma, and FCZA at ages up to 11–12 years were examined using generalized estimating equations. RESULTS: Bisphenol A concentrations at 7–8 years of age were significantly associated with wheezing at 9–10 years of age (adjusted odds ratio [aOR] = 1.68; 95% confidence interval [CI]: 1.08, 2.60) and with FCZA at 11–12 years of age (aOR = 1.66; 95% CI: 1.04, 2.65). Bisphenol A was also significantly associated with FCZA

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2759	Lee MR et al.	2015	Association of bisphenol A exposure with overweight in the elderly: a panel study	Bisphenol A (BPA) is an ubiquitous chemical, which is an endocrine disruptor. Recent epidemiological studies have suggested a relationship between BPA exposure and body weight. However, most of these studies were cross-sectional and not on elderly people. We conducted a panel study with repeated measurements to evaluate the relationship between BPA and overweight in elderly people. A total of 982 elderly participants aged >65 years were recruited in Taichung City, Taiwan, from 2011 to 2012. Urinary BPA concentrations were measured in 1,905 urine samples at 0, 3 and 15 years. Overweight was defined as BMI ≥ 24 kg/m2. Repeated measures analysis was performed after adjusting for age, sex, low-density lipoprotein cholesterol levels, alcohol consumption, exercise, total calorie intake, fatty acid intake, urinary cotinine levels, and the status of diabetes mellitus. The geometric mean of BPA was 0.87 μg/g creatinine. The odds ratio (OR) of overweight was 1.17 (95 % confidence interval [CI]: 1.02–1.32) per interquartile range increase of log-transformed BPA. When stratified based on sex, we observed a significant association in women (OR: 1.26, 95 % CI: 1.05–1.49) but not in men (OR 0.97, 95 % CI: 0.75–1.27). The 15th of overweight increased with quartiles of BPA in women (quartile 2 vs. 1: OR 1.56, 95 % CI: 1.07–2.32; 3 vs. 1: OR 1.76, 95 % CI: 1.18–2.62; and 4 vs. 1: OR 1.81, 95 % CI: 1.13–2.92). Our results suggest that urinary BPA levels are significantly associated with overweight in elderly women but not elderly men.	Environ Sci Pollut Res Int. 2015 Jun;22(12):9370-7.	10.1007/s11356-015-4087-5	25874422	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2760	Lee S et al.	2018	A prospective cohort study of the association between bisphenol A exposure and the serum levels of liver enzymes in children	BACKGROUND: Bisphenol A (BPA) is an endocrine disruptor that acts in an estrogen like manner. Few studies have investigated the association between urinary BPA concentrations, and adverse liver function. Additionally, most studies were cross-sectional in nature and included only adults. OBJECTIVES: We evaluated BPA exposure levels and prospectively explored the association between BPA exposure and liver function in children. METHODS: Data were retrieved from the ongoing prospective Korea Mothers and Children's Environmental Health (MOCEH) Cohort Study. Urinary BPA concentrations were measured in 1,001 children at 3 and 7.5 years of age. At each visit, fasting blood and urine samples were collected, and questionnaires were completed. The associations between the BPA concentrations at these ages and the serum levels of liver enzymes measured at 10 (13 years of age was also evaluated. RESULTS: The geometric mean urinary BPA concentrations were 1.29 μg/g creatinine at 3 years of age and 1.26 μg/g creatinine at 7.5 years of age. The 50th percentile of the BPA concentrations in the two ages were correlated (Spearman's r = 0.31, p < 0.01). The median urinary BPA concentrations were 0.76 μg/g creatinine at 3.5 years and 0.61 μg/g creatinine at 7.4 years of age. The urinary BPA concentrations at the two ages were correlated (Spearman's r = 0.31, p < 0.01). The urinary BPA concentrations at 7-9 years, but not that at 3-5 years, was associated significantly with the serum levels of liver enzymes at 10-13 years of age (p < 0.05). These trends for log-tertile of urinary BPA concentration had higher levels of liver enzymes than did others. After adjustment for covariates, dose-response relationships of the BPA level with liver enzyme levels were evident at 7-9 years, but not at 3-5 years. Notably, the effect size was large and the dose-response relationships were more evident in boys than in girls. CONCLUSIONS: Exposure of children to even low doses of BPA may adversely affect later liver function.	Environ Res. 2018 Feb;161:195-201.	10.1016/j.envres.2017.11.007	29156342	ヒト	肝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2761	Lee YM et al.	2018	Prenatal Bisphenol-A exposure affects fetal length growth by maternal glutathione transferase polymorphisms, and neonatal exposure affects child volume growth by sex: From multiregional prospective birth cohort MOCEH study	We aimed to evaluate the effects of Bisphenol A (BPA) exposure on fetal/child growth from the fetal period to 12months after birth. The MOCEH study is a prospective birth cohort study in Korea. A total of 786 mother-child pairs were recruited from 2006 to 2009. Maternal urinary BPA levels were measured at 3 trimesters and at birth. Fetal growth was evaluated by ultrasound, and estimated fetal weight was calculated. Child growth outcomes including three z-scores for age-specific length, weight for length (WFL) and weight were calculated. Analysis was performed according to infant sex and maternal glutathione transferases (GSTs) polymorphisms. When maternal urinary BPA levels and birth outcomes were used(1st), controlled. When the perinatal BPA concentration is increased by 1 log-transformed unit of BPA, 1st, there was a 0.0% (95% CI: -0.1, 0.1) increase in fetal length and 0.0% (95% CI: -0.1, 0.1) increase in maternal urinary BPA levels, and birth outcomes were used(1st), controlled. When the perinatal BPA concentration is increased by 1 log-transformed unit of BPA, 1st, there was a 0.0% (95% CI: -0.1, 0.1) increase in fetal length and 0.0% (95% CI: -0.1, 0.1) increase in fetal weight

毒性性評価（動物）1：該当、0：該当しない

毒性性評価（疫学）1：該当、0：該当しない

毒性性評価（in vitro）1：該当、0：該当しない

毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは除き経験性評価へ進め、当該性評価段階で除害に基づき除害。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2772	Minatoya M et al.	2018	Association between prenatal bisphenol A and phthalate exposures and fetal metabolic related biomarkers: The Hokkaido study on Environment and Children's Health	Bisphenol A and phthalates are widely detected in human urine, blood, breast milk, and amniotic fluid. Both bisphenol A and phthalates have been suggested as playing a role in obesity epidemics. Exposure to these chemicals during fetal development, and its consequences, should be concerning because they can cross the placenta. Thus, this study aimed to assess the association between prenatal exposure to bisphenol A and phthalates and fetal metabolic biomarkers. Participants were pregnant women in the Hokkaido Study on Environment and Children's Health, a prospective birth cohort. A multivariate multiple regression model controlled some also determined. Linear regression models were applied to the 361 participants with both, exposure and biomarker assessments, adjusted for maternal age, pre-pregnancy body mass index, parity, education, and sex of the child. The level of bisphenol A was negatively associated with the leptin level (beta = -0.06; 95% confidence interval (CI): -0.11, -0.01), but was positively associated with the high-molecular-weight adiponectin level, with marginal significance (beta = 0.03; 95%CI: 0.00, 0.06). The mono-isobutyl phthalate (MiBP), mono-(2-ethylhexyl) phthalate (MEHP), and summation of MiBP and MEHP (Σ₂DEHP) in maternal DEHP exposure (summation operation)MiBP level were inversely associated with the leptin levels (beta=-0.12, 95%CI: -0.21, -0.01; beta = -0.12, 95%CI: -0.24, 0.00 with marginal significance; beta=-0.08, 95%CI: -0.15, -0.01; and beta = -0.09, 95%CI: -0.16, -0.02, respectively). The present study provided some evidence that prenatal exposure to bisphenol A and certain phthalates may modify fetal adipocentric and leptin levels.	Environ Res. 2018 Feb;161:505-511.	10.1016/j.envres.2017.11.052	29223775	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2773	Minatoya M et al.	2017	Cord blood BPA level and child neurodevelopment and behavioral problems: The Hokkaido Study on Environment and Children's Health	Introduction Child mental and behavioral disorders are growing concern in public health as the prevalence is increasing and its impact on child, family and community and even economy is enormous (Perou et al. 2015). The prevalence of childhood and adolescent mental disorders including behavioral problems has been reported around 20% (WHO 2005). There are multiple factors, including socioeconomic and environmental factors that play a role in etiology of mental disorders. Bisphenol A (BPA) is a ubiquitous environmental chemical used in manufacture polycarbonate plastics, epoxy resins, dental sealants, and thermal paper (Vandenberg et al. 2007). A recent biomonitoring study reported that BPA was detectable in dust, air particles, and water (Vandenbroucke A et al. 2011). Even though BPA use in infant feeding bottles has been banned in Canada and Europe, it is still used in many of manufactured products. A study suggested that canned food was responsible for 10–50% of the daily BPA intake (van Osten et al. 2010). In the late 1980s, Japanese use manufacturers had developed "BPA free" products (Kawamoto T et al. 2011). Considering the widespread use of BPA, it is important to assess the effects of BPA exposure on child neurodevelopment and behavioral problems. Objectives To examine the association between BPA exposure and child behavioral problems (Shibuya et al. 2003). It is difficult to determine a level of BPA that has no risk to children, pregnant women and other populations based on current scientific knowledge. BPA is widely detected from different populations including children and pregnant women (Casas l et al. 2015; Yamamoto et al. 2011).BPA has endocrine disrupting property and been recognized as a suspected agent causing developmental neurotoxicity (Wolstenholme et al. 2011; Rochester 2013; Vandenberg et al. 2012). Animal studies have suggested that BPA exposure may affect brain development and behavior (Kobayashi et al. 2010; Kubo et al. 2011). Some evidences of changes in gene expression and DNA methylation in estrogen signaling pathways and estrogen receptors support these effects of BPA exposure on neurodevelopment (Kundakovic et al. 2013; Vandenberg et al. 2009; Wetherill et al. 2007).Epidemiological studies reported that prenatal BPA exposures were associated with various health outcomes including behavioral problems in children (Braun et al. 2009; Braun et al. 2011; Casas et al. 2015; Harley et al. 2013; Miodovnik et al. 2011; Perera et al. 2012; Ryan et al. 2010). Yet findings from these studies were inconsistent. Exposure assessments, the time window of exposure, the sex specific directions of the associations, the specific behavioral domain and sociodemographic of the populations varied from study to study (Miodovnik et al. 2011). Previously, we reported that BPA level detected in maternal urine samples was associated with behavioral problems at 3 years of age (Shibuya et al. 2013). However, the association between BPA exposure and behavioral problems at later ages is unclear. BPA exposure at a very sensitive time in development can lead long-lasting developmental adverse effects (Sun et al. 2002), and thus investigating association between early life exposure to BPA and child neurobehavioral development is warranted. In this study, we conducted various neuropsychological tests covering wide range of mental, psychomotor, intelligence and behavioral domains at different ages to verify the. The aim of this study was to evaluate whether cord blood BPA level was associated with neural and behavioral development of children at 6, 18 and 42 months of age in a longitudinal birth cohort study.	Sci Total Environ. 2017 Dec 31:607-608:351-356.	10.1016/j.scitotenv.2017.06.060	28697388	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2774	Minatoya M et al.	2018	Prenatal exposure to bisphenol A and phthalates and behavioral problems in children at preschool age: the Hokkaido Study on Environment and Children's Health	BACKGROUND: Studies reported adverse behavioral development including internalizing and externalizing problems in association with prenatal exposure to bisphenol A (BPA) and phthalates; however, findings were not sufficient due to using different assessment tools and child ages among studies. This study aimed to examine associations between maternal urinary levels of BPA and phthalate metabolites and behavioral problems at preschool age.METHODS: The Strengths and Difficulties Questionnaire (SDQ) was used to assess behavioral problems at 5 years of age. BPA and phthalate metabolite levels in the first trimester maternal urine samples were measured by liquid chromatography-tandem mass spectrometry. Multivariate logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between tertile levels of urinary BPA and phthalate metabolites and SDQ total difficulties problems (TDP), internalizing problems (IP), externalizing problems (EP), and prosocial behavior (PB). Models were adjusted for maternal age, parity, maternal education, household income, and child sex. Stratified analyses by child sex were conducted. Sensitivity analyses were performed using the Strengths and Difficulties Questionnaire-Hyperactivity/Inattention (SDQ-HI) and Conduct problem (SDQ-CP) scores.RESULTS: Of 1289 mother-child pairs, 1,289 (100%) and 1,284 (99.6%) had complete data for BPA and phthalate metabolites, respectively. BPA was not associated with SDQ-TDP, SDQ-IP, SDQ-EP, or SDQ-PB. Mono-n-butyl phthalate (MnBP) and mono-(2-ethylhexyl) phthalate (MEHP) were associated with increased odds of SDQ-TDP (MnBP: OR = 1.33, 95% CI: 1.01, 1.76; MEHP: OR = 1.34, 95% CI: 1.02, 1.77), SDQ-IP (MnBP: OR = 1.39, 95% CI: 1.04, 1.86; MEHP: OR = 1.41, 95% CI: 1.05, 1.89), and SDQ-EP (MnBP: OR = 1.33, 95% CI: 1.01, 1.76; MEHP: OR = 1.34, 95% CI: 1.02, 1.77) for boys, respectively. BPA, summation operation(BPA)=(BPA-SMAP) + (BPA-SMAP), and summation operation(DEHP)=(DEHP-MEHP) levels were not associated with any of the child behavioral problems. CONCLUSIONS: Our analyses found no significant association between BPA or summation of phthalate metabolite levels and any of the behavioral problems at 5 years of age but suggested possible associations between MEHP levels and increased risks of conduct problems.	Environ Health Prev Med. 2018 Sep 7;23(1):43.	10.1186/s12199-018-0732-1	30193567	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2775	Mínguez-Alarcón L et al.	2015	Urinary bisphenol A concentrations and association with in vitro fertilization outcomes among women from a fertility clinic	STUDY QUESTION: Are urinary BPA concentrations associated with in vitro fertilization (IVF) outcomes among women attending an academic fertility center? SUMMARY ANSWER: Urinary BPA concentrations were not associated with adverse reproductive and pregnancy outcomes among women from a fertility clinic. WHAT IS KNOWN ALREADY: Bisphenol A (BPA), an endocrine disruptor, is detected in the urine of most Americans. Although animal studies have demonstrated that BPA induces female fertility through effects on the ovarian follicle and uterus, data from human populations are scarce and equivocal. STUDY DESIGN, SIZE AND DURATION: We analyzed data from 256 women undergoing IVF at a fertility clinic between 2005 and 2009. PARTICIPANTS/MATERIALS, SETTING, METHODS: Study participants were women enrolled in the Environment and Reproductive Health (EARTH) Study. Intermediate and clinical end points of IVF treatments were abstracted from electronic medical records. We used generalized linear mixed models with random intercepts to evaluate the association between urinary BPA concentrations and IVF outcomes adjusted for age, race, body mass index, smoking status and infertility diagnosis. MAIN RESULTS AND THE ROLE OF CHANCE: The specific gravity-adjusted geometric mean of BPA was 1.80 ng/mL, which is comparable to that for female participants in the National Health and Nutrition Examination Survey, 2011-2012. Urinary BPA concentrations were not associated with endometrial wall thickness, peak estradiol levels, number of oocytes retrieved, mature oocytes, fertilization rate, number of embryos transferred, embryo quality, implantation, clinical pregnancy, miscarriage or live birth in our study. Although we did not find any associations between urinary BPA concentrations and IVF outcomes, the relation between BPA and endometrial wall thickness was modified by age. Younger women (<37 years old) had thicker endometrial thickness across increasing quartiles of urinary BPA concentrations, while older women (>=37 years old) had thinner endometrial thickness across increasing quartiles of urinary BPA concentrations. LIMITATIONS, REASONS FOR CAUTION: Limitations to this study include a possible misclassification of BPA exposure and difficulties in extrapolating the findings to the general population. WIDER IMPLICATIONS OF THE FINDINGS: Data on the relation between urinary BPA concentrations and reproductive outcomes remain scarce and additional research is needed to clarify its role in human reproduction. STUDY FUNDING/COMPETING INTEREST(S): This study was supported by the National Institute of Environmental Health Sciences (NIEHS) (R01ES009718, R01ES022955, R01ES020392, P30ES023515) and the U.S. Environmental Protection Agency (RD834798). CDC/NIOSH/DRDS/EPHTB/ECSB/ESTES and the National Institute of Child Health and Human Development (NICHD). None of the authors has any conflicts of interest to declare. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.	Hum Reprod. 2015 Sep;30(9):2120-8.	10.1093/humrep/dev183	26209788	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	●	-	-	-	-	-	-	-	-
統合_2776	Montrose L et al.	2018	Maternal levels of endocrine disrupting chemicals in the first trimester of pregnancy are associated with infant cord blood DNA methylation	Endocrine disrupting chemicals (EDCs) pose a public health risk through disruption of normal biological processes. Identifying toxicologically-mechanisms of developmental exposure induced effects by EDCs, such as epigenetic changes, is critical for understanding the developmental origins of health and disease hypothesis. We measured 95 EDCs in first trimester maternal urine samples collected from the Mothers and Newborns cohort. DNA was extracted from cord blood leukocytes for methylation analysis by pyrosequencing for LINE-1 and methylation changes related to first trimester levels of 9 phthalate metabolites and BPA. Growth and metabolism related genes selected for methylation analysis included imprinted IGF2/H19 and non-imprinted PPARA. EDEC genes along with LINE-1 repetitive elements. Findings revealed decreases in methylation of LINE-1, IGF2, and PPARA with increasing phthalate concentrations. For example, a log unit increase in Σ[penDEHP corresponded to a 0.28(95% confidence interval (CI): -0.48, -0.07) percentage point decrease in PPARA methylation. Changes in DNA methylation were also inversely correlated with PPARA gene expression determined by RT-qPCR (r = -0.34, P = 0.02), thereby providing evidence in support of functional relevance. A one log unit increase in Σ[penDEHP corresponded to a 0.28 percentage point decrease in IGF2 methylation (95% CI: -0.48, -0.07). Σ[penDEHP was also associated with a 0.27 decrease in IGF2 methylation and a 1.27 (95%CI: -2.37, -0.16) percentage point decrease in PPARA methylation in females only. These findings add to a body of evidence suggesting epigenetically labile regions may provide a conduit linking early exposures with disease risk later in life and that toxicosusgeneric susceptibility may be sex specific.	Epigenetics. 2018;13(3):301-309.	10.1080/15592294.2018.1448680	29513082	ヒト	その他(DNAメチル化)	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2777	Mustieles V et al.	2018	Bisphenol A and reproductive hormones and cortisol in peripubertal boys: The INMA-Granada cohort	INTRODUCTION: Bisphenol A (BPA) is a well known endocrine disrupting compound. Although animal studies have investigated the effect of BPA exposure and reproductive hormones in humans, results have been inconsistent. OBJECTIVE: To assess the association between urinary BPA concentrations and reproductive hormones in boys. METHODS: In 2014-2015, 111 boys from the INMA-Granada cohort were assessed in 2 follow-up visits. Urinary BPA concentrations were quantified by liquid chromatography-tandem mass spectrometry, and levels of serum total testosterone (TT), luteinizing hormone (LH), follicle-stimulating hormone (FSH) and cortisol were measured by electrochemiluminescence immunoassay. RESULTS: After adjustment for confounders, linear regression models showed that each natural log unit increase in urinary BPA concentrations was associated with a 19% increase in geometric mean serum FT levels, and a 16% decrease in SHBG serum cortisol levels. When urinary BPA concentrations were categorized in tertiles, boys in the 3rd tertile showed 29% higher TT levels and 23% lower cortisol concentrations compared to boys in the 1st tertile. Urinary BPA concentrations were not associated with LH or FSH levels. CONCLUSIONS: Our findings suggest that BPA exposure may alter the hypothalamic-pituitary-testicular axis and endocrine disrupting potential of BPA during this important period of development. Although activities of the testis or pituitary cannot be ruled out, our findings are compatible with a possible hindrance of BPA at the adrenal gland, resulting in a differential production of androgens/cortisol. However, given the cross- sectional design of our study, the heterogeneous results reported in the literature, and the scant experimental research on BPA effects at the adrenal gland, the present findings should be interpreted with caution.	Sci Total Environ. 2018 Mar 15:618:1046-1053.	10.1016/j.scitotenv.2017.09.093	29100688	ヒト	生殖発生	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2778	Mustieles V et al.	2018	Maternal and paternal preconception exposure to bisphenols and size at birth	STUDY QUESTION: Are maternal and paternal preconception urinary bisphenol A (BPA) or bisphenol S (BPS) concentrations associated with offspring birth size? SUMMARY ANSWER: Maternal but not paternal preconception urinary BPA concentrations were associated with lower birth size among couples seeking fertility evaluation. WHAT IS KNOWN ALREADY: Prenatal BPA exposure has been previously associated with reduced birth size in some but not all epidemiologic studies. However, the potential effect of BPA exposure before conception in either parent is unknown. Data on BPS is practically absent. STUDY DESIGN, SIZE, AND DURATION: We conducted a preconception cohort study of 501 couples undergoing fertility evaluation between 2007 and 2015 in Granada, Spain. PARTICIPANTS/MATERIALS, SETTING, METHODS: We examined the association between maternal and paternal pre-conception, and first trimester urinary BPA and BPS concentrations, and size at birth among 501 singletons from couples recruited in the Environment and Reproductive Health (EARTH) Study using multivariable linear regression. Infant birth weight and head circumference were abstracted from delivery records. Three preconception and prenatal exposure scores were estimated by averaging urinary (n=501) and (n=387) concentrations to include maternal and paternal urine samples at one and two visits, and maternal urine samples collected in each trimester. MAIN RESULTS AND THE ROLE OF CHANCE: Maternal preconception urinary BPA concentrations were inversely associated with birth weight and head circumference in adjusted models. For example, a 10-fold increase in maternal BPA was associated with a 0.19 SD (95% CI: -0.34, -0.04) decrease in birth weight z-score. Similar associations were observed for prenatal BPA exposure models. Women with higher prenatal BPA concentrations had infants with lower mean birth weight (-75 g, 95% CI: -151, 2) although this did not achieve statistical significance. Paternal preconception urinary BPA concentrations were not associated with either birth weight or head circumference. No consistent patterns emerged for BPS concentrations measured in either parent. LIMITATIONS, REASONS FOR CAUTION: We observed a strong negative association between maternal but not paternal preconception BPA concentrations and offspring birth size among a subfertile population. Although these results are overall consistent with prior studies on prenatal BPA exposure, these findings may not be generalizable to women without fertility concerns. WIDER IMPLICATIONS OF THE FINDINGS: This study suggests that the developmental toxicity of BPA may extend to periods before conception. STUDY FUNDING/COMPETING INTEREST(S): This study was funded by FIS PI13/01284, PI16/01797, and CB06/02/0069 from the National Institute of Environmental Health Sciences (NIEHS) -CIB- was supported by a post-doctoral fellowship award from the Canadian Institutes of Health Research. There are no competing interests to declare.	Hum Reprod. 2018 Aug 1;33(8):1528-1537.	10.1093/humrep/dey234	29982563	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	●	-	-	-	-	-	-	-	-
統合_2779	Nakiwala D et al.	2018	In-utero exposure to phenols and phthalates and the intelligence quotient of boys at 5 years	BACKGROUND: There are concerns that developmental exposure to endocrine disrupting chemicals such as phenolic compounds and phthalates could affect child cognitive function. Epidemiological studies tackling this question have mainly focused on phthalate metabolites and bisphenol A, but not on the other phenolic compounds. Our study aimed to assess the relationship between in-utero exposure to phthalates, bisphenol A and other phenolic compounds (parabens, triclosan, dichlorophenols) and the intelligence quotient (IQ) of boys at 5 years.METHODS: In the Health Outcome and Exposure Study from the Female EDB Cohort, we measured 12 phthalate metabolites and 9 phenolic compounds (3 parabens, benzophenone-3, bisphenol A, 2',4-dichlorophenol, and triclosan) in spot urine samples collected between 20 and 28 gestational weeks. Verbal and performance IQ were assessed in 5-year-old boys (n = 200) using the Wechsler Preschool and Primary Scale of Intelligence, third edition (WPPSI-III). We used multivariable linear regression and Benjamini and Hochberg false discovery rate correction to assess the associations between maternal urine phenol and phthalate metabolite concentrations, considered as a mixture, and boys' IQ.RESULTS: No phenol or phthalate metabolite concentration was negatively associated with the boys' verbal or performance IQ (uncorrected p- values >/=0.05). Mono(3-carboxypropyl) phthalate tended to be associated with increased verbal IQ (beta = 0.06, 95% confidence interval, 0.01; 0.11). This association disappeared after correction for multiple comparison (corrected p-value, 0.71). CONCLUSION: Our results did not provide evidence of an inverse association between in-utero exposure to phenols or phthalates and verbal and performance IQ among boys. Since phenols and phthalates may have non-specific effects, these null findings cannot be generalized to girls. Limitations included use of a single spot urine sample to assess exposures and lack of consideration of postnatal exposures.	Environ Health. 2018 Feb 20;17(1):17.	10.1186/s12940-018-0359-0	29458359	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2780	Ohlstein JF et al.	2014	Bisphenol A enhances adipogenic differentiation of human adipose stromal/stem cells	Exposure of humans to the endocrine disruptor bisphenol A (BPA) has been associated with increased weight and obesity. However, the mechanism(s) by which BPA increases adipose tissue in humans remains to be determined. The goal of this study was to determine the effects of BPA on adipogenesis of cultured human adipose stromal/stem cells (ASCs), a precursor to mature adipocytes. ASCs from three donors were cultured for either 12 days in adipogenic differentiation media containing increasing concentrations of BPA (100 pM–10 mM). The extent of adipogenic differentiation in the ASCs was assessed by staining with Oil Red O to visualize adipogenic differentiation and then quantified by extraction and optical density measurement of the retained dye. BPA significantly enhanced adipogenesis at a concentration of 1 nM after 12 days of culture. Additionally, we found that BPA increased transcription of the estrogen receptor (ER β)(ESR2) and that treatment with the ER β antagonist ICI 182,780, blocked the effects of BPA, indicating that BPA may act via an ER β-mediated pathway. Finally, we found that BPA treatment increased the phosphorylation of the mitogen-activated protein kinase (MAPK) p44/42. Pre-treatment with the MAPK/ERK kinase (MEK) inhibitor, U0126, blocked the BPA-induced phosphorylation of p44/42 MAPK. Taken together, these data suggest that BPA significantly enhances adipogenesis in ASCs through an ER-mediated pathway at physiologically relevant concentrations.	Journal of Molecular Endocrinology.2014;53(3):345-353	10.1530/JME-14-0052	25143472	ex vivo	-	-	-	-	1	0	100 pM-10 muM	-	-	-	-	-	●	-	-	-	-	-	-	-
統合_2781	Perera F et al.	2016	Bisphenol A exposure and symptoms of anxiety and depression among inner city children at 10-12 years of age	BACKGROUND: Experimental and epidemiological studies suggest that gestational exposure to Bisphenol A (BPA), an ubiquitous endocrine disrupting chemical, may lead to neurobehavioral problems in childhood. However, not all results have been consistent. We previously reported a positive association between prenatal BPA exposure and symptoms of anxiety/depression reported by the mother at child age 7-9 years in boys, but not girls. OBJECTIVE: To evaluate if this association persisted in the cohort at child age 10-12 years.METHODS: We measured BPA in maternal urine collected during pregnancy and in child urine collected at ages 3 and 5 years. Children were evaluated using the Revised Children's Anxiety and Depression Scale (RCADS) parent version, which yields a total score and six subscales: separation anxiety, social phobia, obsessive compulsive disorder, major depression, generalized anxiety, and panic disorder. We used multivariate linear regression models, stratified by sex, to examine associations between prenatal BPA and symptoms of depression and anxiety. Models adjusted for maternal education, child age, race/ethnicity, caregiver strain, caregiver depression, and secondhand smoke exposure. RESULTS: Significant associations were observed between prenatal BPA and symptoms of depression and anxiety were observed among boys. Prenatal BPA exposure was not significantly associated with outcomes. There was substantial co-occurrence of anxiety and depressive symptoms in this sample. CONCLUSION: These results provide evidence that prenatal BPA exposure is associated with more symptoms of anxiety and depression in boys but not in girls at age 10-12 years.	Environ Res. 2016 Nov:151:195-202.	10.1016/j.envres.2016.07.028	27497082	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2782	Perez-Lobato R et al.	2016	Exposure to bisphenol A and behavior in school-age children	INTRODUCTION: Bisphenol A (BPA) exposure has been shown to affect human brain neurodevelopment and behavior. OBJECTIVE: We aimed to investigate whether environmental exposure to BPA in children was associated with their childhood behavior. METHODS: Urinary BPA concentrations, and behavioral characteristics were assessed in 500 children belonging to the INMA "Environment and Childhood" Granada birth cohort to their follow- up at 9-11 years of age. BPA concentrations were quantified in urine using liquid chromatography-tandem mass spectrometry (LC-MS/MS), and behavior reported by parents using the Child Behavior Checklist (CBCL/6-18) under supervision of a psychologist. The association between BPA concentrations and CBCL -standardized scores was analyzed using linear regression models, adjusted for important covariates. RESULTS: Geometric mean urinary BPA concentration was 1.67 ng/mL (95% CI: 1.52, 1.84). Urinary BPA concentrations were positively associated with CBCL Externalizing problems, Rule-breaking behavior and Aggressive behavior scales, adjusted for maternal IQ, social class, environmental tobacco smoke exposure, and child's sex, age, and BMI. Boys showed statistically significant associations, whereas girls showed inverse associations without statistical significance. Urinary BPA concentrations were also associated to poorer child executive function and poorer working memory. Boys with BPA concentrations in the 3rd quartile had more somatic complaints (beta= 2.56; 95% CI: 0.35, 4.81) and social items (1.71; 95% CI: 0.09, 3.32) and thought problems (beta=2.58; 95% CI: 0.48, 4.67) in comparison to those in the 1st quartile. Children with values in the 3rd quartile of BPA concentrations also showed greater social problems (beta= 2.46; 95% CI: 0.43, 5.48). CONCLUSIONS: Our results suggest that exposure to BPA in childhood may affect children's behavior. Although further investigations are required, prevention measures should be undertaken to reduce inadvertent exposure to BPA.	Neurotoxicology. 2016 Mar:53:12-19.	10.1016/j.neuro.2015.12.001	26654821	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2783	Peng W et al.	2017	Exposure to phthalates is associated with lipid profile in peripubertal Mexican youth	Animal models indicate that endocrine disrupting chemicals (EDCs) affect circulating lipid concentrations by interfering with hepatic fatty acid oxidation. Little is known of this relationship between EDC exposure and lipid profile in humans. We measured bisphenol A (BPA) and 9 phthalate metabolites in maternal urine collected at up to three time points during pregnancy as a measure of in utero exposure, and in the adolescents at 8-14 years as a measure of concurrent, peripubertal exposure among 258 participants of a Mexico City pre-birth cohort. We used linear regressions to examine relations of BPA and phthalate exposure with peripubertal serum lipids, while also adjusting for child age, sex, and specific gravity. While in utero EDC exposure was not associated with lipid profile, higher concurrent levels of mono (3-carboxypropyl) phthalate (MCPP), monoethyl phthalate (MEP), and dibutyl phthalate metabolites (MBP) corresponded with lower total cholesterol and low- density lipoprotein (LDL-C) in boys, e.g., an interquartile range increment in MCPP corresponded with 7.4% (95% CI:3%) lower total cholesterol and 10.7% (95% CI:4%) lower LDL-C in girls. Higher urinary di-2-ethylhexyl phthalate metabolites (Σ[penDEHP) correlated with lower LDL-C (-7.9%) (-16.0%, +0.2%). Additional longitudinal research is needed to determine whether these associations persist beyond adolescence.	Environ Res. 2017 Apr:154:311-317.	10.1016/j.envres.2017.01.033	28152472	ヒト	代謝	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2784	Philippat C et al.	2014	Prenatal Exposure to Phenols and Growth in Boys	BACKGROUND: Phenols interact with nuclear receptors implicated in growth and adiposogenic regulation. Only a few studies have explored their effects on growth in humans. OBJECTIVES: We studied the associations of maternal exposure to phenols during pregnancy with prenatal and postnatal growth of male newborns. METHODS: Within a cohort of women recruited during pregnancy, we selected 420 mother–son pairs and quantified 11 phenols in maternal urine collected during pregnancy among EDEN mother–newborn pairs who delivered a boy. Mothers completed the Strength and Difficulties Questionnaire (SDQ) when their children were 3.1 to 5.0 years and 5.6 to 7.5 years. RESULTS: Triclosan concentrations were negatively associated with prenatal growth parameters measured at the third trimester ultrasound examination but not with growth in pregnancy. At birth, this phenol tended to be negatively associated with head circumference (-1.2 mm for an interquartile range [IQR] increase in triclosinemia) in triclosinemia (triclosan concentration) (95% confidence interval [−3.9 to 0.5]) but not with length or height. Parabens were positively associated with weight at birth. This association remained for 5 years. For methylparaben (beta = 196 g; 1 to 1,890) for an IQR increase in co-transformed concentrations. CONCLUSIONS: We relied on only 1 spot urine sample to assess exposure, because of the high variability in phenol urinary concentrations reported during pregnancy, using only 1 sample may result in exposure misclassification, in particular for bisphenol A. Our study suggested associations between prenatal exposure to parabens and triclosan and prenatal or early postnatal growth.	Epidemiology. 2014 Sep;25(5):625-35.	10.1097/EDE.0000000000000132	25061923	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2785	Philippat C et al.	2017	Prenatal Exposure to Nonpersistent Endocrine Disruptors and Behavior in Boys at 3 and 5 Years	BACKGROUND: Sex-specific associations have been reported between phthalates, bisphenol A (BPA), and child behavior. No data on large study populations are available for other phenols with possible endocrine disrupting properties. OBJECTIVES: We aimed to study associations between prenatal exposure to phthalates and several phenols on behavior among male infants. METHODS: We quantified 11 phthalate metabolites and nine phenols (four parabens, benzophenone-3, BPA, two dichlorophenols, triclosan) in spot urine samples collected during pregnancy among EDEN mother–newborn cohort who delivered a boy. Mothers completed the Strength and Difficulties Questionnaire (SDQ) when their children were 3.1 to 5.0 years and 5.6 to 7.5 years. RESULTS: BPA was positively associated with the relationship problems subscale at 3 y [boys/girls beta = 1.0; 95% confidence interval (CI): 0.2, 1.8; boys beta = 1.1; 95% CI: 0.2, 2.0 for an interquartile range increase in urinary BPA concentrations]. Triclosan was positively associated with the hyperactivity/inattention problems and emotional symptoms scores at 3 y. Benzophenone-3 was positively associated with the relationship problems and emotional symptoms scores at 3 y. Most of the relationships were stronger in boys. Exposure to phthalates was not consistently associated with behavior. Associations between BPA, MnBP, and behavior in boys are consistent with previous findings. Further health impact assessment studies based on dose–response functions corrected for exposure misclassification are required to quantify the public health burden possibly entailed by such associations. https://doi.org/10.1289/EHP1314.	Environ Health Perspect. 2017 Sep 15;125(9):097014.	10.1289/EHP1314	28937960	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2786	Philips EM et al.	2018	First Trimester Urinary Bisphenol and Phthalate Concentrations and Time to Pregnancy: A Population-Based Cohort Analysis	BACKGROUND: Increasing evidence suggests that exposure to synthetic chemicals such as bisphenols and phthalates can influence fecundability. The current study describes associations of first trimester urinary concentrations of bisphenol A (BPA) and phthalate metabolites with fecundability. METHODS: We used data from 1,221 pregnancies in the Generation R Study, a population-based cohort. First trimester urinary concentrations of bisphenols and phthalate metabolites (median gestational age: 12.9 weeks; Semiparametric range: 10.1, 16.0). We used time-to-event analysis with Cox proportional hazard models to examine associations of bisphenol and phthalate concentrations with TTP. Participants who conceived using infertility treatment were censored at 12 months. Biologically plausible effect measure modification by folic acid supplement use was tested. RESULTS: In the main models, bisphenol and phthalate compounds were not associated with fecundability. In stratified models, total bisphenol concentrations were associated with longer TTP among women who did not use folic acid supplements; pronounced/significant/ for fecundability ratios per each natural log increase were 0.90 (95% CI: 0.81 to 1.00) and 0.88 (95% CI: 0.79 to 0.98). Using an interaction term for the exposure and folic acid supplement use showed additional effect measure modification by folic acid supplement use for high molecular weight phthalate metabolites. CONCLUSIONS: We found no associations of bisphenols and phthalates with fecundability. Preconception folic acid supplementation seems to modify effects of bisphenols and phthalates on fecundability. Folic acid supplements may protect against reduced fecundability among women exposed to these chemicals. Further studies are needed to replicate these findings and investigate potential mechanisms.	J Clin Endocrinol Metab. 2018 Sep 1;103(9):3540-3547.	10.1210/jc.2018-00855	30016447	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2787	Piccoy SE et al.	2017	Second trimester amniotic fluid bisphenol A concentration is associated with decreased birth weight in term infants	Bisphenol A (BPA) is an endocrine disrupting chemical with ubiquitous environmental exposure. Animal studies have demonstrated that in utero BPA exposure leads to increased adult body weight. Our aim was to characterize human fetal BPA exposure by measuring BPA concentrations in second trimester amniotic fluid (AF) samples and to study its relationship with fetal growth and birth weight in humans. To achieve these goals, we developed a novel BPA assay utilizing derivatization with pentafluorobenzoyl followed by analysis with LC-ECAPCI-MS/MS with a limit of detection of 0.08ng/mL and limit of quantification 0.26 g/mL or 0.26ng/mL. The mean BPA concentration in AF was 0.4ng/mL (SD=0.6ng/mL). Multivariate linear regression models were used to estimate the change in birth weight (BW) associated with a 1 unit increase in ln(BPA) after controlling for covariates. (p=0.049). No effect was seen outside this range indicating a non-monotonic effect. Our data suggest that low level BPA exposure in utero decreases BW and needs further study.	Reprod Toxicol. 2017 Jan;67:1-9.	10.1016/j.reprotox.2016.11.007	27829162	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2788	Pollack AZ et al.	2018	Exposure to bisphenol A, chlorophenols, benzophenones, and parabens in relation to reproductive hormones in healthy women: A chemical mixture approach	BACKGROUND: Little is known about the associations of bisphenol A, chlorophenols, benzophenones, and parabens with reproductive hormone levels in women. Our goal was to evaluate the associations between repeated measures of these chemicals and hormone measures with reproductive hormones in women. METHODS: Longitudinal urine samples from healthy, premenopausal women (n = 118) with 5 urine samples each were measured for bisphenol A, five chlorophenols (2,4-dichlorophenol (2,4-DCP), 2,5-dichlorophenol, 2,4,5-trichlorophenol, 2,4,6-trichlorophenol, triclosan), two oxybenzone (OXY) filters (benzophenone-1, benzophenone-3), and four parabens (methyl, ethyl, propyl, butyl). Hormone measures included estradiol (E2), progesterone (P4), luteinizing hormone (LH), follicle stimulating hormone (FSH), and sex hormone binding globulin (SHBG). Linear mixed models were used to estimate percent change and 95% confidence intervals for hormone levels in relation to chemical analytes. Four factors were identified including: paraben; paraben metabolites; and BPA, phenols, and OXY filters. Models were adjusted for creatinine, age, race, and body mass index and weighted with inverse probability of exposure weights to account for time-varying confounding. RESULTS: In single-chemical models, 3,4 DHB was associated with increased E2 (0.046; 95% confidence interval (CI): 0.001, 0.101). 2,4-DCP with increased progesterone (0.118; 0.012 and decreased FSH -0.08 (-0.11, -0.02), and 2-HB was associated with increased FSH (0.07 (0.02, 0.13). In multi-chemical models, all factors were associated with increased progesterone (0.118; 0.012, 0.224), and decreased FSH (-0.08 (-0.11, -0.02), and LH (-0.08; -0.15, -0.01). Paraben was associated with increased E2 (0.046; 0.001, 0.101). BPA, phenols, and OXY filters were associated with increased FSH (0.07; 0.02, 0.13). Paraben was associated with decreased FSH, and LH. The LH filter was associated with increased E2. The E2 filter increased the strongest hence association with estradiol. 0.18 (0.03 , 0.33) FSH -0.12 (-0.21 , -0.03), and LH 0.17 (-0.25, -0.09). CONCLUSION: Mixtures of phenols were associated with changes in reproductive hormones. Each changes could contribute to adverse health in women but additional research is necessary.	Environ Int. 2018 Nov;120:137-144.	10.1016/j.envint.2018.07.028	30092451	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2789	Rian EL et al.	2015	Bisphenol A exposure and behavioral problems among inner city children at 7-9 years of age	BACKGROUND: Bisphenol A (BPA) is a ubiquitous endocrine disrupting compound. Several experimental and epidemiological studies suggest that gestational BPA exposure can lead to neurodevelopmental and behavioral problems in early life, but results have been inconsistent. We previously reported that prenatal BPA exposure may affect child behavior and differently among boys and girls at ages 3-5 years. OBJECTIVES: We investigated the association of prenatal and early childhood BPA exposure with behavioral outcomes in 7-9 year old minority children and hypothesized that as a result observe the same sex-specific pattern observed at earlier ages. METHODS: We measured BPA concentrations in maternal urine samples collected during pregnancy and in child urine samples collected at ages 3, 5, 7 and 9 years. We assessed the association between BPA concentrations of pregnancy and child at ages 3 and 5 years using repeated urine samples. BPA exposure was categorized by tertiles of BPA urinary concentrations. The Child Behavior Checklist (CBCL) was administered at ages 7 and 9 to assess multiple child behavior domains. Associations between behavior and prenatal (maternal) BPA concentrations and behavior and postnatal (child) BPA concentration were assessed via Poisson regression in models stratified by sex. These models accounted for potential confounders including prenatal or postnatal urinary BPA concentrations, child age at CBCL assessment, ethnicity, gestational age, maternal intelligence, maternal education and domestication, quality of child's home environment, prenatal/environmental tobacco smoke exposure, and prenatal/maternal depressive symptoms. RESULTS: The direction of associations between prenatal BPA exposure and CBCL scores differed significantly between boys and girls for the internalizing composite score (p=0.04), externalizing composite score (p=0.04), and total problems score (p=0.03). Among boys, the internalizing composite score (beta= -0.17, p=0.06) and total problems score (beta= -0.17, p=0.06) were inversely associated with prenatal BPA exposure. Among girls, the internalizing composite score (beta= -0.17, p=0.06) and total problems score (beta= -0.17, p=0.06) were inversely associated with prenatal BPA exposure. Among girls, the internalizing composite score (beta= 0.21, p=0.003) and externalizing composite scores (beta=0.15, p=0.005) and individual subscores in girls but boys symptoms. These results remained significant in girls after accounting for exclusion bias. CONCLUSION: These results suggest BPA exposure may affect childhood behavioral outcomes in a sex-specific manner and differently depending on timing of exposure.	Environ Res. 2015 Oct;142:739-45.	10.1016/j.envres.2015.01.014	25724466	ヒト	発達神経	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2790	Romano ME et al.	2015	Gestational urinary bisphenol A and maternal and newborn thyroid hormone concentrations: The HOME Study	Bisphenol A (BPA), an endocrine disrupter used in consumer products, may perturb thyroid function. Prenatal BPA exposure may have sex-specific effects on thyroid hormones (THs). Our objectives were to investigate whether maternal urinary BPA concentrations during pregnancy were associated with THs in maternal second serum, and whether these associations differed by newborn sex or maternal iodine status. We measured BPA concentrations in urine collected at 16 and 26 weeks gestation and TSH, free thyroxine (FT4), and total T4 (TT4) in second trimester maternal serum in 389 mother-child pairs. Maternal urinary BPA concentrations were averaged to estimate second trimester exposure. Maternal iodine status was classified by urinary iodine concentration (UIC) from mean maternal second trimester UIC (<150 μg/L was considered mild-moderate deficiency). We used multivariate linear models to estimate associations between BPA concentrations and maternal or cord serum TH levels; sex-stratified models were estimated by multivariable linear regression. Mean maternal urinary BPA was not associated with cord TTs in cell newborns, but a 10 fold increase in mean BPA was associated with lower cord TSH in girls (percent change= -36.0%; 95% confidence interval (CI): -56.1, -7.7%), but not boys (-2%; 95% CI: -29.5, 32.7%; p for effect modification=0.09). We observed a significant associations between 16 week BPA and TH in maternal serum but 26 week maternal BPA was inversely associated with TSH (girls (-42.9%; 95% CI: -70.9, -16.5%), but not boys (3.4%; 95% CI: -17.3, 42.0%; p for effect modification=0.008) at birth. The inverse BPA–TSH relationship among girls was strongest, but less precise, among iodine-deficient versus sufficient mothers. Prenatal BPA exposure may reduce TSH among newborn girls, particularly when exposure occurs later in gestation.	Environ Res. 2015 Apr;138:453-60.	10.1016/j.envres.2015.03.003	25794847	ヒト	甲状腺	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2791	Rone M et al.	2014	Bisphenol A is related to circulating levels of adiponectin, leptin and ghrelin, but not to fat mass or fat distribution in humans	OBJECTIVE: Since bisphenol A (BPA) has been shown to induce obesity in experimental studies, we explored the associations between BPA and fat mass, fat distribution and circulating levels of adipocytokine, leptin and ghrelin in humans. METHODS: In the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS), fat mass and fat distribution were determined in 70 -year-old men and women (n=890) by dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI). Serum levels of BPA were analyzed using a novel ultra-sensitive liquid chromatography/tandem mass spectrometry (LC-MS/MS). Hormone levels were analyzed with radioimmunoassays (RIA) or enzyme linked immunosorbent assay (ELISA). Imaging was performed approximately two years following collection of other data. RESULTS: Serum concentrations of BPA were detectable in 89% of the participants. Men had higher BPA levels than women (median 0.4 vs. 0.3 ng/ml, p<0.001). In univariate analyses, BPA was related to body mass index, fat mass, waist circumference, physical activity, energy intake, and cardiovascular traits (p=0.001, p=0.008, p=0.006, respectively). The relationship between BPA and ghrelin was stronger in women than in men. CONCLUSIONS: Although the relationships between BPA levels and measures of fat mass were rare, BPA associated strongly with the adipokines adiponectin and leptin and with the gut hormone ghrelin suggesting that BPA may interfere with hormonal control of hunger and satiety.	Chemosphere.2014;112:42-48	10.1016/j.chemosphere.2014.03.042	25048886	ヒト	横断研究	1	1	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2792	Shapiro GD et al.	2015	Exposure to phthalates, bisphenol A and metals in pregnancy and the association with impaired glucose tolerance and gestational diabetes mellitus: The MIREC study	BACKGROUND: Studies from several countries report increases in rates of gestational diabetes mellitus (GDM) over recent decades. Exposure to environmental chemicals could contribute to this trend. OBJECTIVES: To evaluate associations between exposure to phthalates, bisphenol A (BPA) and metals and impaired glucose tolerance (IGT) and GDM. METHODS: We used data from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study were included if they had a singleton delivery and did not have pre-existing diabetes. Eleven phthalate metabolites and bisphenol A (BPA) were measured in first trimester urine samples, and four metals (lead, cadmium, mercury and arsenic) were measured in first trimester blood samples. IGT and GDM were assessed in accordance with standard guidelines by chart review. Chemical concentrations were grouped by quartiles, and associations with outcomes were examined using logistic regression with adjustment for maternal age, race, pre-pregnancy BMI, and education. Restricted cubic spline analysis was performed to help assess (linearity) and nature of any dose–response relationships. RESULTS: Of 2,350 women recruited into the MIREC cohort, 1,251 met the inclusion criteria and had outcome ascertainment. Of these, 132 (10.5%) had IGT and 36 (2.9%) had GDM. Adjusted odds ratios (aOR) for IGT were 1.72 (95% CI: 1.01, 2.93) for the highest vs. lowest quartile of BPA analysis. A significant dose–response relationship was observed in a cubic spline model between arsenic and odds of GDM (p = 0.01). No statistically significant associations were observed between phthalates or BPA or other metals with IGT or GDM. CONCLUSIONS: Our findings add to the growing body of evidence supporting the role of maternal arsenic exposure as a risk factor for gestational diabetes.	Environ Int. 2015 Oct;83:63-71.	10.1016/j.envint.2015.05.016	26101084	ヒト	生殖発生 (妊娠糖尿病)	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2793	Shiue I et al.	2014	Higher urinary heavy metal, arsenic, and phthalate concentrations in people with high blood pressure: US NHANES, 2009-2010	BACKGROUND: A link between environmental chemicals and human health has emerged but not complete in risk factors. This work aimed to study the relationships of different sets of urinary environmental chemical concentrations with high blood pressure (HBP) and hypertension (HTN). METHODS: Data from the US National Health and Nutrition Examination Survey (NHANES) 2009-2010 were analyzed. Urinary demographics, BP readings, and urinary environmental chemical concentrations. Analyses included t-test and survey-weighted logistic regression models. RESULTS: Urinary mercury concentrations were not associated with high BP (OR = 1.06, 95% CI: 0.87-1.30, p = 0.586). Urinary cobalt (OR = 1.36, 95% CI: 1.01-1.81, p = 0.043), lead (OR = 1.37, 95% CI: 1.11-1.68, p = 0.003), antimony (OR = 1.07, 95% CI: 1.01-1.13, p = 0.018) and tungsten (OR = 1.12, 95% CI: 1.07-1.18, p < 0.001) concentrations were observed to increase the risk of high BP. There are no clear associations between environmental chemicals and high BP. The effect of environmental exposure to DEP, 1.14, 95% CI: 0.89-1.39, p = 0.092) disappeared after additionally adjusting for subsample weighting (OR = 1.12, 95% CI: 0.93-1.35, p = 0.231). People with higher urinary mono-2-ethyl-5-carboxypentyl phthalate and mono-n-octyl phthalate concentrations had higher odds of HBP (OR = 1.19, 95% CI: 1.04-1.37, p = 0.015 and OR = 1.18, 95% CI: 1.03-1.35, p = 0.021, respectively). However, urinary cobalt concentrations (OR = 1.19, 95% CI: 0.94-1.51, p = 0.151) and dimethylarsinic acid concentrations (OR = 1.36, 95% CI: 0.90-2.05, p = 0.151) were not associated with high BP. CONCLUSIONS: Urinary environmental chemical concentrations were associated with risk of high BP, although the causal effect cannot be established. Elimination of environmental chemicals to humans could need to be continued.	Blood Pressure.2014;23(6):363-369	10.3109/08037051.2014.925228	24945898	ヒト	横断研究	1	1	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2794	Smarr MM et al.	2015	Parental urinary biomarkers of preconception exposure to bisphenol A and phthalates in relation to birth outcomes	BACKGROUND: Bisphenol A (BPA) and phthalates are ubiquitous non-persistent endocrine-disrupting chemicals whose relation with infant birth size is not clearly understood. METHODS: We examined associations between maternal and paternal preconception urinary concentrations of total BPA and 10 phthalate metabolites, and birth size for 230 infants. Multiple linear regression models were used to estimate parental quartile or log2-unit differences in birth weight, length, head circumference, and ponderal index (PI). Models were adjusted for maternal age, race, education, pre-pregnancy BMI, and infant sex. Bayesian kernel machine regression (BKMR) models were conducted to include the other parent's chemical concentrations. RESULTS: In maternal models adjusted for paternal exposures and covariates, reductions in birth weight (range: 278-310 g; p < 0.05) were observed for the 2nd quartile of maternal monoethyl phthalate, mono-(2-carboxyethyl) hexyl phthalate and mono-n-octyl phthalate concentrations, and the 3rd quartile of maternal BPA concentrations. Reductions in birth length (range: 0.5-0.7 cm; p < 0.05) were observed for the 2nd quartile of maternal BPA and mono-(2-carboxyethyl) hexyl phthalate concentrations. Reductions in birth length and head circumference (range: 0.4-0.6 cm; p < 0.05) were observed for the 2nd quartile of paternal mono-n-octyl phthalate concentrations. Reductions in birth length and gestational age (range: 0.4-0.5 cm; p < 0.05) were observed for the 3rd quartile of paternal BPA. Maternal urinary phthalate concentrations were associated with birth length and gestational age. CONCLUSIONS: We observed some suggestion that preconception maternal and paternal urinary concentration of BPA and specific phthalate metabolites may be associated with smaller birth size and increased gestational age, though the findings appeared to be parent and chemical-specific.	Environ Health. 2015 Sep 11:14:73.	10.1186/s12940-015-0060-5	26362861	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-
統合_2795	Souter I et al.	2013	The association of bisphenol-A urinary concentrations with antral follicle counts and other measures of ovarian reserve in women undergoing infertility treatments	In this prospective cohort of women undergoing infertility treatments, we measured specific gravity adjusted urinary BPA (SG-BPA) concentrations and used regression models to evaluate the association of BPA with antral follicle count (AFC), day 3 serum follicle stimulating hormone levels (FSH), and ovarian volume (OV). BPA, detected in >80% of women, had a geometric mean (+/- SD) of 1.4+/-2.6, 1.7+/-2.1, and 1.5+/-1.8ng/mL in the first, second, and third trimesters, respectively. Adjusted mean (95% CI) AFC was 15.1 (13.8, 16.4), 15.0 (13.7, 16.3), and 14.8 (13.5, 16.1) follicles for the 1st, 2nd, and 3rd BPA tertiles (p = 0.79, 0.91, 0.76, respectively). Adjusted mean (95% CI) FSH was 7.5 (6.9, 8.1), 7.5 (6.9, 8.1), and 7.6 (7.0, 8.2) IU/L for the 1st, 2nd, and 3rd SG-BPA tertiles (p = 0.79, 0.91, 0.76, respectively). Adjusted mean (95% CI) OV was 9.2 (8.4, 10.0), 9.2 (8.4, 10.0), and 9.1 (8.3, 9.9) cm3 for the 1st, 2nd, and 3rd SG-BPA tertiles (p = 0.79, 0.91, 0.76, respectively). Adjusted mean (95% CI) AFC was 15.1 (13.8, 16.4), 15.0 (13.7, 16.3), and 14.8 (13.5, 16.1) follicles for the 1st, 2nd, and 3rd SG-

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統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 複数掲不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2810	Wang U et al.	2016	Bisphenol A exposure may increase the risk of development of atopic disorders in children	BACKGROUND: Little is known about the effect of Bisphenol A (BPA) on atopic disorders. OBJECTIVE: To investigated the associations 1) between postnatal BPA exposure and allergic diseases in children 2) between BPA and IgE levels for the possible disease pathogenesis, and 3) gender based differences. METHODS: A total of 653 children from Childhood Environment and Allergic Diseases Study cohort with urine and blood samples at 1 and 3 years of age were included in the analysis. Urinary BPA was measured by high performance liquid chromatography. Physician diagnosed allergic disease at 3 years of age. Development of allergic diseases were evaluated by multivariate linear regression and logistic regression. A mediation analysis was also conducted to evaluate how much risk of allergic diseases in relation to BPA exposure is explained by IgE changes. RESULTS: The BPA levels at age 3 were positively associated with IgE levels at age 3 (beta=0.0181(1 95% CI: 0.1138-0.0224)) for unit increase BPA(0 next 95% CI: 1439-0.0224)). Stratified by gender, BPA(1 levels at age 3 were positively associated with IgE levels at age 3, particularly in girls (beta=0.0261(1 95% CI: 0.1738-0.0784)). Similar results were also found at age 6. Urinary BPA(1 levels at age 3 were significantly associated with asthma at ages 3 and 6, with OR (95%CI) at 1.29(1.08-1.56) and 1.27(1.08-1.50). We estimated that 35% of the total effect of BPA exposure on asthma is mediated by IgE levels. CONCLUSIONS: BPA exposures were associated with IgE levels and may increase the risk of development of allergic diseases in children particularly in girls.	Int J Hyg Environ Health. 2016 May;219(3):311-6.	10.1016/j.ijheh.2015.12.001	26765087	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	1	-	-	●	-	-	-	-	-	-	-	-
統合_2811	Wang Z et al.	2019	Bisphenol A and pubertal height growth in school-aged children	BACKGROUND: Bisphenol A (BPA) is an environmental endocrine disruptor and is found in many consumer products. Studies suggest that BPA may perturb pubertal development, although evidence on BPA-influenced pubertal height growth is scarce. METHODS: A total of 754 children aged 9-10 years from three schools (one elementary, one middle, and one high school) in Shanghai were included in this longitudinal study. Height was measured annually for 3 years to determine age at first breast or pubic hair development. Urinary BPA was measured at baseline and annually using high performance liquid chromatography-tandem mass spectrometry. Inflammation among participants in the Puerto Rico Trends in Exploring Contraceptive Threats (PROTECT) project. Serum markers of inflammation (c-reactive protein (CRP), IL-1beta, IL-4, IL-6, and tumor necrosis factor alpha (TNF-alpha)) were measured twice during pregnancy (n=105 subjects, 387 measurements) and urinary markers of oxidative stress (8-hydroxydeoxyguanosine (8-OHdG) and isoprostanes) were measured three times during pregnancy (n=54 subjects, 158 measurements). We used linear mixed-models to assess relationships between natural log-transformed exposure and oxidative stress markers, accounting for within-individual correlation across study visits. After adjustment for urinary specific gravity, study visit, maternal pre-pregnancy BMI, and maternal education, an interquartile range (IQR) increase in urinary BPA was associated with 4.1% (95% CI: 0.1, 8.2) and 3.8% (95% CI: 0.1, 7.6) increases in urinary 8-OHdG and 8-isoprostane concentrations, respectively. Urinary BPA was also associated with 4.2% (95% CI: 0.1, 8.4), 4.2% (95% CI: 0.1, 8.4), and 3.9% (95% CI: 0.1, 7.8) increases in serum CRP, IL-6, and TNF-alpha, respectively. Associations were stronger among participants with higher GA. Among participants in the highest tertile of urinary BPA, we observed 5.7% (95% CI: 1.1, 10.5), 5.7% (95% CI: 1.1, 10.5), and 5.4% (95% CI: 1.0, 10.0) increases in serum CRP, IL-6, and TNF-alpha, respectively. Urinary BPA was not associated with height growth in girls. CONCLUSIONS: Our findings indicate an inverse association between urine BPA level and height growth in boys. These findings need to be confirmed in further studies.	J Expo Sci Environ Epidemiol. 2019 Jan;29(1):109-117.	10.1038/s41370-018-0063-8	30185943	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2812	Watkins DJ et al.	2015	Associations between urinary phenol and paraben concentrations and markers of oxidative stress and inflammation among pregnant women in Puerto Rico	Phenols and parabens are used in a multitude of consumer products resulting in ubiquitous human exposure. Animal and in vitro studies suggest that exposure to these compounds may be related to a number of adverse health outcomes, as well as potential mediators such as oxidative stress and inflammation. We examined urinary phenol (bisphenol A (BPA), triclosan (TCS), benzophenone-3 (BP-3)) and paraben (ethyl (EPB), methyl (MPB), propyl (PPB), and butyl (BPB)) concentrations in relation to biomarkers of oxidative stress and inflammation among participants in the Puerto Rico Trends in Exploring Contraceptive Threats (PROTECT) project. Serum markers of inflammation (c-reactive protein (CRP), IL-1beta, IL-4, IL-6, and tumor necrosis factor alpha (TNF-alpha)) were measured twice during pregnancy (n=105 subjects, 387 measurements) and urinary markers of oxidative stress (8-hydroxydeoxyguanosine (8-OHdG) and isoprostanes) were measured three times during pregnancy (n=54 subjects, 158 measurements). We used linear mixed-models to assess relationships between natural log-transformed exposure and oxidative stress markers, accounting for within-individual correlation across study visits. After adjustment for urinary specific gravity, study visit, maternal pre-pregnancy BMI, and maternal education, an interquartile range (IQR) increase in urinary BPA was associated with 4.1% (95% CI: 0.1, 8.2) and 3.8% (95% CI: 0.1, 7.6) increases in urinary 8-OHdG and 8-isoprostane concentrations, respectively. Urinary BPA was also associated with 4.2% (95% CI: 0.1, 8.4), 4.2% (95% CI: 0.1, 8.4), and 3.9% (95% CI: 0.1, 7.8) increases in serum CRP, IL-6, and TNF-alpha, respectively. Associations were stronger among participants with higher GA. Among participants in the highest tertile of urinary BPA, we observed 5.7% (95% CI: 1.1, 10.5), 5.7% (95% CI: 1.1, 10.5), and 5.4% (95% CI: 1.0, 10.0) increases in serum CRP, IL-6, and TNF-alpha, respectively. Urinary BPA was not associated with height growth in girls. CONCLUSIONS: Our findings indicate an inverse association between urine BPA level and height growth in boys. These findings need to be confirmed in further studies.	Int J Hyg Environ Health. 2015 Mar;218(2):212-9.	10.1016/j.ijheh.2014.11.001	25435060	ヒト	その他(酸化ストレス)	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-
統合_2813	Watkins DJ et al.	2016	Maternal phthalate exposure during early pregnancy and at delivery in relation to gestational age and size at birth: A preliminary analysis	Epidemiologic studies of in utero phthalate exposure and birth outcomes have had conflicting findings. The objective of this study was to characterize maternal phthalate exposure across pregnancy, examine associations between maternal phthalate levels and infant size and gestational age at birth, and investigate relationships between concurrent treatment (TRT) and phthalate exposure. Women in the Michigan Mother Infant Pairs cohort provided urine and blood samples during their first trimester and at delivery. Urinary phthalate metabolites and serum MPA were measured at both time points, and birth weight, length, head circumference, and gestational age were collected from medical records. Associations between phthalate exposure and birth outcomes were examined using linear regression. Women had increased DEHP exposure late in pregnancy. A number of phthalate metabolites were associated with birth size and gestational age in patterns that varied by sex and timing of exposure, independent of BPA exposure.	Reprod Toxicol. 2016 Oct;65:59-66.	10.1016/j.reprotox.2016.06.021	27352641	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2814	Watkins DJ et al.	2016	Relating Phthalate and BPA Exposure to Metabolism in Peripubescence: The Role of Exposure Timing, Sex, and Puberty	CONTEXT: Exposure to endocrine disrupting chemicals during development may play a role in the increasing prevalence of metabolic syndrome and type 2 diabetes among children and adolescents by interfering with metabolic homeostasis. OBJECTIVE: To explore associations between in utero and peripubertal urinary phthalate metabolite and bisphenol A (BPA) concentrations and markers of peripubertal metabolic homeostasis. DESIGN: Early Life Exposure to Mexico to Environmental Toxicants (ELEMENT) is a longitudinal cohort study of pregnant women in Mexico City and their offspring. SETTING: Public maternity hospitals in Mexico City. PATIENTS OR OTHER PARTICIPANTS: Women recruited during pregnancy offspring recruited for follow-up at age 9-14 years (n = 250). INTERVENTIONS: None. MAIN OUTCOME MEASURES: Fasting serum c-peptide, IGF-1, leptin, and glucose concentrations, among children at follow-up; calculated measures of insulin secretion and insulin resistance. RESULTS: Phthalate metabolites and BPA were associated with metabolism biomarkers in girls, but not boys. Girls in the highest tertile of urinary monoethyl phthalate (MEP) concentrations had 0.5 ng/mL higher leptin (95% CI: 0.1, 0.9) and 0.3 higher leptin among girls (P = .02). In utero di-2-ethylhexyl phthalate was associated with higher IGF-1 among pubertal girls, peripubertal di-2-ethylhexyl phthalate was associated with higher IGF-1, insulin secretion, and insulinogenic among prepubertal girls. In contrast, peripubertal dibutyl phthalate, monobenzyl phthalate, and mono-3-carboxypropyl phthalate were associated with lower IGF-1 among pubertal boys. Peripubertal BPA was associated with higher leptin in boys (P = .01). CONCLUSIONS: Considering the long-term health effects related to metabolic syndrome, additional research on exposure and metabolic outcomes across developmental periods and early adulthood is needed.	J Clin Endocrinol Metab. 2016 Jan;101(1):79-88.	10.1210/jc.2015-2706	26529628	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2815	Watkins DJ et al.	2017	Phthalate and bisphenol A exposure during in utero windows of susceptibility in relation to reproductive hormones and pubertal development in girls	BACKGROUND: Over the past several decades, the age of pubertal onset in girls has shifted downward worldwide. An early pubertal onset is associated with increased risky behavior and psychological issues during adolescence and cardiometabolic disease and cancer in adulthood; this is an important public health concern. Exposure to endocrine disrupting chemicals during critical windows of in utero development may play a role in this trend. Our objective was to investigate trimester-specific phthalate and BPA exposure in relation to pubertal development among girls in the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) birth cohort. METHODS: We measured maternal urinary phthalate metabolites and BPA in samples collected during the first, second, and third trimesters of pregnancy. To assess reproductive development among third-female offspring, we measured serum levels of reproductive hormones (estradiol, dehydroepiandrosterone sulfate (DHEA-S), inhibin B, and sex hormone binding globulin (SHBG)), and assessed sexual maturation. Tanner staging and testicular volume) among male children at age 9–14 years (n = 139). Linear and logistic regression were used to investigate trimester-specific in utero exposure as predictors of peripubertal hormone levels and sexual maturation, respectively. In sensitivity analyses, we controlled for maternal urinary concentrations of the same phthalate metabolite or BPA measured in the other two trimesters. RESULTS: Several phthalate metabolites were associated with higher odds of having a Tanner stage >1 for pubic hair development (e.g. MBzP OR = 2.18 per interquartile range (IQR) increase; 95% CI: 0.820, 5.817) and higher peripubertal DHEA levels (e.g. MBzP: 8.1% (IQR: 95% CI:2.2, 14.5%), MEP: 6.1% (IQR: 95% CI:2.2, 10.1%), while third-trimester DEHP exposure was not. Sensitivity analyses yielded similar findings. CONCLUSIONS: Associations between in utero phthalate and BPA exposure and peripubertal measures of male reproductive development are dependent on the timing of that exposure during gestation. These findings suggest that future epidemiological studies relating in utero EDC exposure to pubertal outcomes should consider windows of susceptibility.	Environ Res. 2017 Nov;159:143-151.	10.1016/j.envres.2017.07.051	28800472	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2816	Watkins DJ et al.	2017	Impact of phthalate and BPA exposure during in utero windows of susceptibility on reproductive hormones and sexual maturation in peripubertal males	BACKGROUND: Phthalates and BPA are endocrine disrupting chemicals (EDCs) widely used in consumer products. Evidence suggests that phthalate and BPA exposure alters steroid hormone levels in adults, while in utero exposure to phthalates is associated with reduced anogenital distance in baby boys. However, the impact of in utero exposure to these EDCs on male reproductive development and maturation during the pubertal transition has not been examined. The objective of this study was to assess trimester-specific in utero phthalate and BPA exposure in relation to measures of reproductive development among peripubertal boys in a Mexico City birth cohort. METHODS: We measured maternal urinary phthalate metabolites and BPA during the first, second, and third trimesters of pregnancy. We measured serum levels of reproductive hormones, estradiol, dehydroepiandrosterone sulfate (DHEA-S), inhibin B, and sex hormone binding globulin (SHBG), and assessed sexual maturation (Tanner staging and testicular volume) among male children at age 9–14 years (n = 139). Linear and logistic regression were used to investigate trimester-specific in utero exposure as predictors of peripubertal hormone levels and sexual maturation, respectively. In sensitivity analyses, we controlled for maternal urinary concentrations of the same phthalate metabolite or BPA measured in the other two trimesters. RESULTS: Several phthalate metabolites were associated with higher odds of having a Tanner stage >1 for pubic hair development (e.g. MBzP OR = 2.18 per interquartile range (IQR) increase; 95% CI:0.820, 5.817) and higher peripubertal DHEA levels (e.g. MBzP: 8.1% (IQR: 95% CI:2.2, 14%), while first and second trimester phthalates were not. In contrast, exposure to DEHP during the first trimester was associated with higher estradiol (11%; IQR: 95% CI:2.9, 21%), while second or third trimester DEHP exposure was not. Sensitivity analyses yielded similar findings. CONCLUSIONS: Associations between in utero phthalate and BPA exposure and peripubertal measures of male reproductive development are dependent on the timing of that exposure during gestation. These findings suggest that future epidemiological studies relating in utero EDC exposure to pubertal outcomes should consider windows of susceptibility.	Environ Res. 2014 Oct;134:233-41.	10.1016/j.envres.2014.08.010	25173057	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2817	Watkins DJ et al.	2014	In utero and peripubertal exposure to phthalates and BPA in relation to female sexual maturation	The age of pubertal onset for girls has declined over past decades. Research suggests that endocrine disrupting chemicals (EDCs) may play a role but exposure at multiple stages of development has not been considered. We examined in utero and peripubertal exposure to bisphenol A (BPA) and phthalates in relation to serum hormones and sexual maturation among females in a Mexico City birth cohort. We measured phthalate metabolite and BPA concentrations in urine collected from mothers during their third trimester (n = 219) and from their female children at ages 8–13 years (n = 239). Among girls, we measured concurrent serum hormone concentrations and Tanner breast and pubic hair stages. Associations between exposure biomarkers and hormones were examined using linear regression. Associations between exposure biomarkers and sexual maturation, controlling for covariates, were examined using logistic regression. In utero urinary mono-2-ethylhexyl phthalate (MEHP) was positively associated with 29% (95% CI: 5.7–57.6%) higher diethylhexyladipate/cosmetic sulfate (DHEA-S), an early indicator of adrenarche, and 5.3 (95% CI: 1.13–10.3) times higher odds of a Tanner stage >1 for pubic hair development. Similar relationships were observed with other in utero but not peripubertal di-2-ethylhexyl phthalate (DEHP) metabolites. Sensitivity analyses yielded similar findings. Peripubertal phthalate and BPA exposure was not associated with 29% and 25% higher serum testosterone concentrations (95% CI: 2.78–9.2; 1.4–42.1, respectively). In addition, we observed suggestive associations between in utero and peripubertal DEHP concentrations and higher estradiol concentrations among girls at early stages of breast development. Maternal DEHP concentrations and the estradiol:testosterone ratio at Tanner stage 2–3 for both breast and pubic hair development. BPA was not associated with in utero or peripubertal serum hormones or sexual maturation. Our findings suggest in utero phthalate exposure may impact hormone concentrations during peripubescence and timing of sexual maturation. Efforts to control phthalate exposure during pregnancy should be of high priority.	Environ Res. 2014 Oct;134:233-41.	10.1016/j.envres.2014.08.010	25173057	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2818	Wolff MS et al.	2017	Associations of urinary phthalate and phenol biomarkers with menarche in a multiethnic cohort of young girls	To study potential environmental influences on puberty in girls, we investigated urinary biomarkers in relation to age at menarche. Phenols and phthalates were measured at baseline (6–8 years of age). Menarche was ascertained over 11 years for 1001 girls with menarche and biomarkers. Parametric models were estimated from Cox models adjusted for race/ethnicity and caregiver education (anR, 95% confidence intervals (CI) for 5th vs. 95th percentile biomarker concentrations). Higher urinary concentrations of bisphenol A (BPA) (HR = 0.82; 95% CI: 0.68, 0.98), triclosan (HR = 0.81; 95% CI: 0.67, 0.98), and the sum of four orthophosphate metabolites (MCPP) (anR 0.7 (0.509-0.952)) like those in meals were 61–81 (Mexico differed by 6–7 months across this range). Dichlorobenzene and MCPP were associated with higher urinary concentrations in girls with later menarche. These analyses were also associated with age at breast development in this cohort. Findings, from this prospective study suggest that some childhood exposures are associated with pubertal timing.	Reprod Toxicol. 2017 Jan;67:56-64.	10.1016/j.reprotox.2016.11.009	27851993	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2819	Wolff MS et al.	2015	Environmental phenols and pubertal development in girls	Environmental exposures to many phenols are documented worldwide and exposures can be quite high (>1 mcM of urine metabolites). Phenols have a range of hormonal activity, but knowledge of effects on child reproductive development is limited, coming mostly from cross-sectional studies. We examined a prospective study of pubertal development among 1,239 girls recruited at 6–8 years old, and some followed annually for 7 years to determine age at first breast or pubic hair development. Ten phenols were measured in urine collected at enrollment (bisphenol A, triclosan, benzophenone-3, three parabens, and four chlorophenols). Adjusted hazard ratios (aHR) and 95% confidence intervals (CI) were estimated using Cox models with interval-censored data, accounting for correlation among urine samples from the Health Outcomes and Measures of the Environment (HOME) Study, race/ethnicity and SES-appropriate models were stratified between 1005-1060. HOME concentrations were quantified in 95% and 100% of samples collected at 6-9 and 10 years, respectively. We used Bayesian Hierarchical Linear Models (BHLM) to examine the associations between newborn birth weight and 63 EDCs, 2 organochlorine pesticides, DPPE and 7 heavy metals. RESULTS: For a 10-fold increase in chemical concentration, the mean difference in birth weight (-95% credible intervals (CI)) were 1 g (-29, 33) for phthalates, -11 g (-52, 32) for PFAS, 0.2 g (-9, 10) for PCBs, -2 g (-52, 21) for PBDEs, and 7 g (-35, 48) for OCPs. CONCLUSION: Gestational exposure to phthalates, PFAS, PCBs, PBDEs, OCPs or DPPs had null or small associations with birth weight. Gestational DPP, Pb, and PFAS exposures were most strongly associated with lower birth weight.	Environ Int. 2015 Nov;84:174-80.	10.1016/j.envint.2015.08.008	26335517	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2820	Woods MM et al.	2017	Gestational exposure to endocrine disrupting chemicals in relation to infant birth weight: a Bayesian analysis of the HOME Study	BACKGROUND: Pregnant women are exposed to a mixture of endocrine disrupting chemicals (EDCs). Gestational EDC exposures may be associated with changes in fetal growth that elevates the risk for poor health later in life, but few studies have examined the health effects of simultaneous exposure to multiple chemicals. This study aimed to examine the association of gestational exposure to five chemical classes of potential EDCs-organochlorine pesticides, DPPE, perfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs)-and infant birth weight. METHODS: Data were drawn from the Health Outcomes and Measures of the Environment (HOME) Study, a prospective pregnancy cohort enrolled between 2003-2006. EDC concentrations were quantified in 249 and 244 maternal serum samples collected at 16 and 26 weeks gestation. We used Bayesian Hierarchical Linear Models (BHLM) to examine the associations between newborn birth weight and 63 EDCs, 2 organochlorine pesticides, DPPE, and 7 heavy metals. RESULTS: For a 10-fold increase in chemical concentration, the mean difference in birth weight (-95% credible intervals (CI)) were 1 g (-29, 33) for phthalates, -11 g (-52, 32) for PFAS, 0.2 g (-9, 10) for PCBs, -2 g (-52, 21) for PBDEs, and 7 g (-35, 48) for OCPs. CONCLUSION: Gestational exposure to phthalates, PFAS, PCBs, PBDEs, OCPs or DPPs had null or small associations with birth weight. Gestational DPP, Pb, and PFAS exposures were most strongly associated with lower birth weight.	Environ Health. 2017 Oct 27;16(1):115.	10.1186/s12940-017-0332-3	29078782	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-
統合_2821	Xu XJ et al.	2015	Associations of cadmium, bisphenol A and polychlorinated biphenyl co-exposure in utero with placental gene expression and neonatal outcomes	In utero co-exposure to endocrine disrupting compounds can perturb fetal development. However, the effect of co-exposure on pivotal regulatory genes has seldom been investigated. We explored the effects of in utero co-exposure to cadmium (Cd), bisphenol A (BPA) and polychlorinated biphenyls (PCBs) on master regulator genes. We recruited 286 healthy pregnant women, of whom 262 provided both cord blood and placenta samples at delivery. Concentrations of Cd, BPA and PCBs in maternal urine, cord blood and placenta were measured. Gene expression profiles in placenta from reference group (n=10), exposure to Cd alone (n=10), co-exposure to Cd and BPA (n=10), co-exposure to Cd and PCBs (n=10) were determined by microarray. Candidate genes were selected and validated by quantitative real-time PCR (qPCR). Associations between exposure biomarkers and neonatal outcomes were also investigated. Cadmium and BPA co-exposure altered the expression of 1,413 genes in placenta from the reference, and was positively associated with all neonates. Cadmium and leptin receptor expressions were also significantly higher, but were only associated with BPA. From our findings, we conclude that lower birth weight is correlated with Cd and PCBs, and may result from the increased ADD1 mRNA expression.	Reproductive Toxicology.2015;52:62-70	10.1016/j.reprotox.2015.02.004	25687722	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2822	Yang TC et al.	2018	Exposure to Bisphenol A and phthalates metabolites in the third trimester of pregnancy and BMI trajectories	BACKGROUND: Bisphenol A (BPA) and phthalates metabolites can linked to a variety of adverse health consequences but studies have not explored their association with growth trajectories. OBJECTIVE: Explore body mass index (BMI) trajectories for tertile exposures to BPA and phthalates metabolites in the third trimester of pregnancy. METHODS: We conducted BMI (kg/m2) trajectories from birth to 10 years in a birth cohort of 724 children from Mexico City using tertiles of third trimester maternal urinary concentrations of BPA and phthalates metabolites. Fractional age polynomials and mixed effects models were fit separately by sex. Predictive BMI trajectories were compared between tertiles of exposure. RESULTS: Boys in the highest tertile of mono-(3-carboxypropyl) phthalate (MCPP) had higher BMI trajectories than those in the lowest tertile. Girls in the highest tertile of BPA, mono-(2-ethyl-5-hydroxyhexyl) phthalate and mono(2-ethyl-5-hydroxyhexyl) phthalate predicted the highest BMI trajectory by adolescence. There was no relationship between BPA and child growth trajectory. CONCLUSIONS: These results suggest sex-specific differences in BMI trajectories by levels of metabolite exposure. Additional studies are needed to consider growth through adolescence in assessing the association of pregnancy exposures on children's BMI.	Pediatr Obes. 2018 Sep;13(9):550-557.	10.1111/ijpo.12279	29700996	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-

通毒性評価（動物）1：該当、0：該当しない

通毒性評価（疫学）1：該当、0：該当しない

通毒性評価（in vitro）1：該当、0：該当しない

通毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通毒性基準不適合と判断されるもの以外を後続性評価へ進め、当該性評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通毒性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2823	Yang TC et al.	2017	Bisphenol A and phthalates in utero and in childhood: association with child BMI z-score and adiposity	OBJECTIVE: To assess the relationship between in utero and concurrent child urinary exposures to bisphenol A (BPA) and phthalates with BMI z-score, waist circumference, and sum of triceps and subscapular skinfold thickness in children at 8 years of age. METHODS: In this prospective birth cohort study, we measured maternal urinary BPA and phthalate metabolite concentrations during pregnancy and concurrent urinary BPA and individual and summed phthalate metabolites (Σ-unoxidative-opened DEHP-ethylhexyl phthalate), summation-personal-life-weight, summation-summation-molecular-weight, summation-summation-molecular-weight) with measures of weight status and adiposity in children aged 8-10 years. Linear regressions with specific gravity-corrected and natural log-transformed urinary concentrations were estimated, adjusting for covariates. Effect modification by child sex was examined. RESULTS: Median urinary concentrations were 2.1 μg/L for BPA, 19.5 μg/L for MEP, 3.4 μg/L for MBP, 12.2 μg/L for MBzP, 3.2 μg/L for MEHP, 11.2 μg/L for MEHHP, 8.1 μg/L for MEOHP, and 5.6 μg/L for MECPP. Urinary BPA was inversely associated with waist circumference (Beta = -1.86, 95%CI: -3.66, -0.07) after adjusting for covariates. In the childhood exposure period, we modified the relationships with BPA, MEHP, MBzP, monoethyl phthalate (MEP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono(2-ethyl-5-carboxypentyl) phthalate (MECPP). In girls, increased BPA exposure was positively associated with sum of skinfold thickness (Beta: 2.27, 95%CI: 0.45, 4.10) while increased MEHP was inversely associated with sum of skinfold thicknesses in boys (beta= -3.96, 95%CI: -5.65, -2.27). These results remained in sensitivity analyses after excluding children who had inferred paternal development ("tanner stage >1 for pubic hair"). We did not observe relationships between summed phthalates, metabolites or any exposure period with outcome measures. CONCLUSION: Our results identified associations between urinary BPA and phthalates metabolites with measures of weight status and adiposity that differed by timing of exposure, sex, and paternal status. Additional studies are needed to explore how associations may differ between those who are pre- and post-pubertal.	Environ Res. 2017 Jul;156:326-333.	10.1016/j.envres.2017.03.038	28390300	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2824	Zbucka-Kretowska M et al.	2018	Evaluation of Bisphenol A influence on endocannabinoid system in pregnant women	Bisphenol A (BPA) is a synthetic chemical widely used in the industry, which may potentially evoke negative effects on human health, especially on reproductive processes and fetal development. BPA has been reported to act on estrogen, estrogen-related, androgen, thyroid hormone, progrone-X, peroxisome proliferation activated, and aryl hydrocarbon receptors. However, other potential mechanisms of BPA action on pregnancy cannot be excluded. Comprehensive evaluation of BPA effect on pregnant women can be performed by the use of metabolomic approach. The aim of the present study is (1) blood plasma metabolomic profile in pregnant women with known concentrations of free, conjugated and total BPA. Significant positive correlations were observed between several endocannabinoids (fatty acid amides) and free (r = 0.307, 0.307, p-value = 0.00 0.00002) and total BPA (r = 0.307, 0.307, p-value = 0.00 0.00002) concentrations in maternal blood plasma. Significant negative correlations were observed between free BPA and 2-AG (r = -0.307, p-value = 0.00 0.00002) and AEA (r = -0.00000) BPA concentrations. The docking calculations of BPA and fatty acid amide hydrolases (enzyme degrading endocannabinoids, FAAH) indicated that it can act as a competitive inhibitor by blocking FAAH catalytic residues. In vitro study showed that BPA moderately inhibits FAAH activity (20% decrease for 280 ng/mL C and almost 50% for 280 μg/mL C of BPA). In the present study for the first time inhibitory potential of BPA on FAAH hydrolase is reported. Inhibition of FAAH may lead to a rise of plasma endocannabinoids level. BPA exposure and increased level of endocannabinoids are miscarriage risk factors. Based on obtained results it can be hypothesized that BPA may induce adverse pregnancy outcomes by acting on endocannabinoid system.	Chemosphere.2018;203:387-392	10.1016/j.chemosphere.2018.03.195	29627605	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2825	Zheng HJ et al.	2017	Genome-wide alteration in DNA hydroxymethylation in the sperm from bisphenol A-exposed men	Environmental BPA exposure has been shown to impact human sperm concentration and motility, as well as rodent sperm epigenomics. However, it is unclear whether BPA exposure is associated with alteration in DNA hydroxymethylation, a marker for epigenetic modification, in human sperm. A genome-wide DNA hydroxymethylation study was performed using sperm samples of men who were occupationally exposed to BPA. Compared with the control group (median urinary BPA level = 1.2 ng/mL), the exposed group (median urinary BPA level = 3.5 ng/mL) had significantly lower sperm concentration (median = 52.4 vs. 84.0 million/mL; P = 0.03) and a lower percentage of motile sperm (median = 50.0% vs. 60.0%; P = 0.04). Genome-wide DNA hydroxymethylation profiling revealed a total of 4,633 differential three-regions (DHRRs) were revealed in BPA-exposed men relative to controls, which were mainly located in intergenic and intron regions. These DHRRs were annotated to 3,633 hyper-MHRs and 965 hypo-MHRs, affecting 2,588 genes and the repetitive elements. The hyper-MHRs affected genes were enriched in pathways associated with nervous system, development, cardiovascular diseases and signal transduction. Additionally, enrichment of three was observed in the promoters of eight maternally expressed imprinted genes in BPA-exposed sperm. Some of the BPA-associated DHRRs, such as DHRR_5910 and DHRR_5970 and DHRR_7529 might participate in the response to DNA damage in germ cells caused by BPA. Our analysis showed that enrichment of three- both in promoters and gene bodies is higher in the genes whose expression has been reported to be significantly altered in response to BPA exposure. Finally, we also observed that BPA exposure tends to change the three-enrichment in the genes whose expression was previously reported to be associated with the reproduction (P-score = 0.06057) and 1,000 basal or cell-based) in sperm. Thus, these results suggest that BPA exposure likely interferes with gene expression via affecting DNA hydroxymethylation in a way partially dependent on it methylation of BPA in human spermatogenesis. Our current study reveals a new mechanism by which BPA exposure reduces human sperm quality.	PLoS One. 2017 Jun 5;12(6):e0178535.	10.1371/journal.pone.0178535	28582417	ヒト	精巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2826	Zhou AF et al.	2017	Prenatal exposure to bisphenol A and risk of allergic diseases in early life	BACKGROUND: Prenatal exposure to bisphenol A (BPA) affects immune system and promotes allergy and asthma in mice, but findings in human studies are limited. We investigated whether prenatal exposure to BPA is associated with increased risk of allergic diseases in infants. METHODS: We measured BPA concentrations in maternal urine samples collected at delivery from 612 women in Wuhan, China. The occurrence of allergic diseases including eczema and asthma were assessed at age 2 via through questionnaires. We used logistic regression to evaluate the association between maternal BPA and the risk of allergic diseases. RESULTS: Mothers of infants with allergic diseases had significantly higher urinary BPA levels than those of infants without allergic diseases (median: 2.34 vs. 1.59 ng/mL; P = 0.01). Increased risk of infant allergic diseases was associated with maternal BPA exposure (adjusted odds ratio [aOR] = 1.50; 95% confidence interval [CI]: 1.02, 2.20) after adjusting for confounders. The aOR for the highest BPA quartile was 2.03 (95% CI: 1.16, 3.56) compared with the lowest quartile. The association was stronger in the stratification by maternal age; the association was only significant in infants of mothers who were younger than 25 y (aOR = 1.96; 95% CI: 1.09-3.29). CONCLUSIONS: Prenatal exposure to BPA may potentially increase the risk of allergic diseases at an early life in female infants.	Pediatr Res. 2017 Jun;81(6):851-856.	10.1038/pr.2017.20	28141789	ヒト	免疫	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	●	-	-	-	-	-	-	-	-	-
統合_2827	Zhou W et al.	2017	Bisphenol A and Ovarian Reserve among Infertile Women with Polycystic Ovarian Syndrome	To better understand possible effects of bisphenol A (BPA) exposure on ovarian reserve in women with polycystic ovary syndrome (PCOS), we measured creatinine-adjusted urinary BPA (BPA, C-r) concentrations and used regression models to evaluate the association between urinary BPA level and antral follicle count (AFC). Antimullerian hormone (AMH) day 3 follicle stimulating hormone (FSH) and inhibin B (INHB) in 348 infertile women diagnosed with PCOS. BPA was detected in all women with a median concentration of 2.36 ng/mL (the 25th and 75th percentiles of 1.47 ng/mL and 3.95 ng/mL). A unit increase in BPA, Cre was associated with a significant decrease of 0.30 in AFC (beta = -0.30, 95% CI: -0.60, -0.00; p = 0.01). Likewise, BPA was negatively associated with AMH and day 3 FSH levels, but neither of them reached statistical significance. No association was observed between BPA and INHB. Our results suggest that in women with PCOS, BPA may affect ovarian follicles and, therefore, reduce ovarian reserve.	International Journal of Environmental Research and Public Health.2017;14(1):7	10.3390/ijerph14010018	28036005	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2828	Zhuang WL et al.	2015	Association of Serum Bisphenol-A Concentration and Male Reproductive Function Among Exposed Workers	Bisphenol-A (BPA) can alter endocrine function in animals, yet the relationship between human exposure to BPA and male reproductive function is not well understood. We collected serum samples from 261 male workers exposed to BPA and 79 controls. Serum BPA concentrations were analyzed by gas chromatography-mass spectrometry after derivatization. The serum levels of sex hormone (prolactin (PRL)) and total testosterone (TT) were detected by radioimmunoassay and levels of inhibin B (INB) and anti-mullerian (AD) by enzyme-linked immunosorbent assay. We examined the association of BPA exposure and male sex hormone levels. The geometric mean (GM) of serum BPA concentrations was 1.77 ng/mL among workers and 0.17 ng/mL among controls. The GM of TT was 4.16 ng/mL among workers and 5.08 ng/mL among controls (p = 0.02). Compared with exposure to <2 years, exposure for >5 years was associated with increased serum BPA and INB(B) levels and decreased AD levels. Compared with undetectable BPA (<0.10 ng/mL), BPA level (>28.79 ng/mL) was associated with the lowest mean serum AD level (0.28 ng/mL). 95% confidence interval (CI: 0.22 to -0.13) and increased mean serum INB(U) level (1.79 mau/L; 95% CI 1.2- 3.66). Serum BPA levels were increased after occupational exposure. BPA exposure was negatively associated with serum AD level but positively associated with serum INB(U) level.	Arch Environ Contam Toxicol. 2015 Jan;68(1):38-45.	10.1007/s00244-014-0078-7	25213476	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2829	Aduamoi E et al.	2018	Urinary bisphenol A concentrations are associated with reproductive parameters in young men	Bisphenol A (BPA) is a parasite environmental toxicant with known reproductive effects on sperm parameters and hormone levels. Several observational studies have investigated the associations between BPA exposure and male reproductive function, but findings are inconsistent. The objective of this study was to assess the associations between urinary BPA concentrations and semen quality and reproductive hormone levels in a cross-sectional study with 216 healthy young university students (18-23 years old). Investigated between 2010 and 2011 in Southern Spain (Murcia Region). All subjects provided urine, blood serum and semen samples on a single day. Urinary BPA concentrations were measured by dispersive liquid-liquid microextraction and ultra-high performance liquid chromatography with tandem mass spectrometry detection. Semen quality was assessed by computer-assisted sperm analysis. Reproductive hormones (FSH, LH, testosterone, estradiol and inhibin B) were measured by immunoassay. Multivariate regression models were used to evaluate associations between BPA concentrations, and sex hormones and semen quality parameters. Relationships between urinary BPA concentrations and semen quality parameters and reproductive hormones levels were examined using linear regression, adjusting for potential confounders and covariates. Ninety-five percent of the men had detectable urinary BPA concentrations, with unadjusted median (95th-90th) of 2.8 (0.14-11.5) ng/mL. After adjustment for important covariates, there was a significant positive association between urinary BPA concentrations and serum LH levels (β = 0.07, 90%CI: 0.020-0.12; p-value = 0.02). Urinary BPA concentrations was also significantly and inversely associated with sperm concentration (β = -0.06, 90%CI: -0.07- -0.02; p-value = 0.02) and TSC (β = -0.05, 90%CI: -0.06- -0.02; p-value = 0.01). No significant associations were found between BPA and other semen parameters or reproductive hormone levels. Our results support the hypothesis that BPA exposure may be associated with a reduction in Leydig cell capacity (increased LH levels) and decreased sperm counts in young men.	Environ Res.2018;161:122-128	10.1016/j.envres.2017.11.002	29156341	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2830	Aekplakorn W et al.	2015	Relationship of serum bisphenol A with diabetes in the Thai population, National Health Examination Survey IV, 2009	BACKGROUND: Epidemiological studies of the association between bisphenol A (BPA) exposure and diabetes have been inconsistent. The present study determined serum BPA concentrations in the Thai population and their association with hyperglycemia and diabetes. METHODS: In all, 2965 serum samples from the Thai National Health Examination Survey (NHES) were used to determine BPA levels. Impaired fasting glucose (IFG) was defined as fasting plasma glucose (FPG) 100-125 mg/dL and diabetes as FPG ≥ 126 mg/dL or self-reported diabetes. Multivariate logistic regression was used to examine the association of serum BPA with IFG and diabetes. RESULTS: Of 2965 samples, detectable BPA was observed in 2228 samples (unadjusted percentage 74.5%), with a geometric mean and median of 0.36 ng/mL. Serum BPA levels were significantly higher among those with diabetes or IFG compared to normoglycemic individuals (0.62 and 0.38 vs 0.33 ng/mL, respectively; P < 0.001). After adjusting for potential confounders, compared to the lowest BPA quartile (<0.17 ng/mL), the second-highest adds ratios (OR) of serum BPA concentration in the third and fourth quartiles (0.19-0.50 ng/mL and >0.50 ng/mL, respectively) were 1.72 (95% confidence interval [CI] 1.19, 2.49) and 2.19 (95% CI 1.48, 3.24), respectively, for diabetes, the adjusted ORs were 1.66 (95% CI 1.16, 2.38) and 2.30 (95% CI 1.52, 3.49), respectively, with a slightly stronger association among men than in women. CONCLUSIONS: Serum BPA concentrations were not associated with IFG, but were positively associated with diabetes in the Thai population. Further prospective studies are needed to confirm the relationship.	Journal of Diabetes.2015;7(2):240-249	10.1111/1753-0407.12159	24720399	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2831	Aekplakorn W et al.	2015	Association of Serum Bisphenol A with Hypertension in Thai Population	Objective. The present study aimed to examine the association between serum BPA and hypertension and evaluated whether it was influenced by estradiol level. Methods. A subsample of 2686 was randomly selected from the Thai National Health Examination Survey IV, 2009, was measured for serum BPA and estradiol. Logistic regression was used to examine the association controlling for age, sex, diabetes, body mass index, and estradiol level. Results. Compared with the lowest quartile, the adjusted odds ratio (AOR) of hypertension for the fourth quartile of serum BPA was 2.16 (95% CI 1.15, 3.56) in women and 1.61 (0.99, 2.59) in men. There was no interaction between serum BPA and estradiol level. For analysis using logBPA as a continuous variable, the BCSD per unit change in logBPA was 1.09 (95% CI 1.03, 1.16). Among postmenopausal women, the AOR for the fourth quartile of BPA was 2.03 (95% CI 1.31, 3.32) and, for premenopausal women, it was 2.12 (95% CI 0.87, 5.19). Conclusion. Serum BPA was independently associated with hypertension in women and was not likely to be affected by estrogen; however, its mechanism related to blood pressure needs further investigations.	International Journal of Hypertension.2015;:8	10.1155/2015/594189	25785193	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2832	Agay-Shay K et al.	2015	Exposure to Endocrine-Disrupting Chemicals during Pregnancy and Weight at 7 Years of Age: A Multi-pollutant Approach	BACKGROUND: Prenatal exposure to endocrine disrupting chemicals (EDCs) may induce weight gain and obesity in children, but the obesogenic effects of mixtures have not been studied. OBJECTIVE: We evaluated the associations between pre- and prenatal biomarker concentrations of 37 EDCs and child weight status at 7 years of age. METHODS: In pregnant women enrolled in a Spanish birth cohort study between 2003 and 2006, we measured the concentrations of 16 phthalate metabolites, bisphenol A, cotinine, arsenic, and lead in urine/maternal pregnancy urine samples. A organochlorine compounds in maternal pregnancy serum; mercury in cord blood; and cotinine in maternal serum collected during pregnancy. We measured child weight and height at 7 years of age and calculated body mass index z-scores (BMI-z). We estimated associations with EDCs in a single pollutant models and applied principal component analysis (PCA) on the 37 pollutant concentrations. RESULTS: In single pollutant models, PCB (hexachlorobenzene), beta-HCH (beta-hexachlorocyclohexane), and polychlorinated biphenyl (PCB) congeners 138 and 180 were associated with increased child BMI-z scores, and HCB, beta-HCH, PCB-138, and DDE (dichlorodiphenyldichloroethylene) with overweight risk. PCA generated four factors that accounted for 43.6% of the total variance. The organochlorine factor was positively associated with BMI-z scores and with overweight (adjusted RR, tertile 3 vs. 1: 3.96; 95% CI: 1.74, 9.02), and three associations were robust to adjustment for other EDCs. Exposure to the second tertile of the phthalate factor was inversely associated with overweight. CONCLUSIONS: Prenatal exposure to organochlorines was positively associated with overweight at age 7 years in our study population. Other EDCs exposures did not confound this association.	Environ Health Perspect. 2015 Oct;123(10):1030-7.	10.1289/ehp.1409049	25956007	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2833	Aker AM et al.	2016	Phenols and parabens in relation to reproductive and thyroid hormones in pregnant women	INTRODUCTION: Phenols and parabens are ubiquitous environmental contaminants. Evidence from animal studies and limited human data suggest they may be endocrine disrupters. In the current study, we examined the associations between urinary concentrations of phenols and parabens and hormone levels in pregnant women. METHODS: Urine and blood samples were collected from 379 pregnant women in Norway in 2007-2009. Urinary exposure biomarkers (bisphenol A, triclosan, benzophenone-3, 2,4-dichlorophenol, 2,5-dichlorophenol, butyl-, methyl and propylparaben) and serum hormone levels (estradiol, progesterone, sex hormone binding globulin (SHBG), free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone) were measured at up to two time points during pregnancy (gw 17 weeks and 25 gw weeks). We used linear mixed models to assess relationships between exposure biomarkers and hormone levels across pregnancy, controlling for urinary-specific gravity, maternal age, BMI and smoking. In cross-sectional analysis, we evaluated cross-sectional relationships between exposure and hormone levels stratified by study visit using linear regression. RESULTS: An IQR increase in methyl paraben was associated with a 7.73% increase (95% CI: 1.39, 14.5) in estradiol concentrations across pregnancy. An IQR increase in BPA was associated with a 3.77% (95% CI: 0.08, 7.60) increase in SHBG concentrations across pregnancy. Conversely, an IQR increase in butyl paraben was associated with a 4.66% increase (95% CI: 1.28, 8.16) in FT4. Propylparaben was consistently negatively associated with all hormones, but were not of statistical significance. When stratified on, methyl and propyl paraben were suggestively negatively associated with estradiol at the first time point (14-20 weeks), and suggestively positively associated with estradiol at the second time point (24-28 weeks). CONCLUSIONS: Within this ongoing birth cohort, certain phenols and parabens were associated with altered reproductive and thyroid hormone levels during pregnancy. These changes may contribute to adverse health effects in mothers or their offspring, but additional research is required.	Environmental Research.2016;151:30-37	10.1016/j.envres.2016.07.002	27448730	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2834	Akin L et al.	2015	The endocrine disruptor bisphenol A may play a role in the aetiopathogenesis of polycystic ovary syndrome in adolescent girls	AIM: Experimental in vitro studies have shown that bisphenol A affects steroidogenesis, folliculogenesis and ovarian morphology. The aim of this study was to investigate the role of the endocrine disruptor bisphenol A in the aetiopathogenesis of polycystic ovary syndrome (PCOS) in adolescent girls. METHODS: This case-control study was conducted with 60 adolescent girls with PCOS and 61 controls between 15 and 18 years of age were enrolled in the study. Serum bisphenol A levels were measured by high-pressure liquid chromatography. Its association with PCOS was evaluated. RESULTS: Adolescents with PCOS had markedly increased serum bisphenol A levels (mean ± 2 ng/mL 999; CI: 1.0-1.22) than controls (mean 0.8 ng/mL 95%CI: 0.6-0.9; p < 0.001). When we compared the subgroups according to obesity, the results also determined the significantly increased bisphenol A levels in the presence of PCOS, but not entirely (p = 0.029). Bisphenol A was significantly correlated with luteal testosterone (r = 0.42), dehydroepiandrosterone sulphate (r = 0.37) and Ferriman-Gallwey score (r = 0.43) (p < 0.05). CONCLUSION: Adolescents with PCOS had higher serum bisphenol A levels than controls, independent of obesity. Bisphenol A concentrations were significantly correlated with androgen levels, leading us to consider that bisphenol A might play a role in the aetiopathogenesis of PCOS in adolescents.	Acta Paediatr. 2015 Apr;104(4):e171-7.	10.1111/apa.12885	25469562	ヒト	卵巣	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2835	Akiyama E et al.	2015	Facilitation of adipocyte differentiation of 3T3-L1 cells by debrominated tetrabromobisphenol A compounds detected in Japanese breast milk	Tetrabromobisphenol A (TeBBPA) is widely used type of brominated flame retardant. In this study, we newly synthesized materials for the debrominated congeners, 2,2,6-tribromobisphenol A (TriBBPA), 2,2'-dibromobisphenol A (2,2'-DiBBPA), 2,6-dibromobisphenol A (2,6-DiBBPA), and 2-monobromobisphenol A (MoBBPA) and evaluated the actual extent of contamination with bisphenol A (BPA), TeBBPA and debrominated congeners in Japanese breast milk samples. TeBBPA was detected at higher levels than that of TeBBPA, while DiBBPA and MoBBPA were detected at lower levels than that of TeBBPA. This observation suggested that TeBBPA was debrominated in the human body. Subsequently, we investigated the effects of BPA, TeBBPA and debrominated congeners on adipocyte differentiation of 3T3-L1 cells by in vitro experiment. we assessed the toxic potency of debrominated congeners by studying their effect on adipocyte differentiation in 3T3-L1 cells. We observed 2,6-DiBBPA, TriBBPA and TeBBPA elevated the lipid accumulation and adipocyte-specific protein-2 expression in a manner dependent on the number of substituted bromines. Moreover, PPARγ, transcriptional activities increased in a dose-dependent manner in the presence of 2,6-DiBBPA and TriBBPA as well as TeBBPA. Our study clarified that TeBBPA and its debrominated congeners accumulated in breast milk and the debrominated congeners promoted adipocyte differentiation, should be a comprehensive evaluation of the influences of these compounds including the debrominated congeners of TeBBPA on health in infants is necessary.	Environmental Research.2015;140:157-164	10.1016/j.envres.2015.03.035	25863188	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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別添-2 統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2849	Chakurkli LO et al.	2016	The Association of Serum Bisphenol A with Thyroid Autoimmunity	Introduction: Data on the association of bisphenol A (BPA) exposure and autoimmunity in humans is unclear. Objective: To elucidate the influence of BPA on thyroid autoimmunity, in the present study we assessed the association between BPA and thyroid peroxidase antibodies (TPOAb) and antithyroglobulin antibodies (TgAb) in euthyroid adults. Methods: We measured urinary BPA concentrations and serum antithyroglobulin (TgAb) and thyroperoxidase (TPOAb) and antithyroglobulin enzyme (TPOAb) antibodies. Results: Participants' characteristics according to tertiles of BPA exposure are presented in Table 1. Participants with higher BPA levels were younger, had lower body mass index (BMI), and were more frequently female. Urinary BPA concentrations were significantly higher in participants with TgAb (p = 0.03) and TPOAb (p = 0.001) positivity as BPA quartiles increased, particularly in the highest quartile. In contrast, no relationship between BPA quartiles and TPOAb titre levels was found. Logistic regression analysis showed that age, gender and BPA quartiles were determinants of TPOAb or TgAb positivity, independent of BMI. However, only the association between BPA and TPOAb positivity was consistent in both men and women. Conclusions: BPA was independently associated with TPOAb positivity. However, the mechanism related to TPOAb positivity, subsequently leading to autoimmune thyroid disease, needs further investigation.	International Journal of Environmental Research and Public Health.2016;13(11):7	10.3390/ijerph13111153	27869686	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2850	Chakurkli LO et al.	2017	Is bisphenol A exposure associated with the development of glucose intolerance and increased insulin resistance in Thais?	Bisphenol A (BPA), the monomeric component of polycarbonate plastics, reportedly possesses endocrine-disrupting effects. Exposure to low levels of BPA during more vulnerable periods leads to abnormalities related to sexual development in experimental animals. Moreover, recently a few epidemiological studies in Caucasians have demonstrated the association of BPA exposure with type 2 diabetes. Therefore, in the present study we examined the association of BPA exposure and abnormal glucose tolerance in Thais. This is a cross-sectional study of 200 participants aged over 18 years, randomly selected by computer-generated random numbers within each glucose tolerance status from an oral glucose tolerance study of 601 participants. There were 60 participants in each group of type 2 diabetes, impaired glucose tolerance (IGT) and normal glucose tolerance (NGT). The remaining 20 participants had impaired fasting glucose (IFG). Urinary BPA concentrations were measured by high performance liquid chromatography and isotope mass spectrometry (LC-MS). The participants with type 2 diabetes, IGT, and NGT differ significantly in BMI, waist circumference, and participants with type 2 diabetes were stratified into those with fasting plasma glucose (FPG) under the diabetic threshold (<126 mg/dL) and those over (>126 mg/dL). It was found that those with FPG under the diabetic threshold had measurable rates of BPA comparable to those with IGT, and rates significantly higher than the NGT group (p = 0.05), while those with FPG over the diabetic threshold did not have higher rates of measurable BPA compared with the NGT group. In conclusion, BPA exposure is not uncommon in Thais. There is an association between BPA exposure and IGT, but not type 2 diabetes.	Nutr Health.2017;23(3):185-191	10.1177/0260106017708730	28516806	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2851	Cho S et al.	2018	High resolution metabolomics to determines the risk associated with bisphenol A exposure in humans	Although high BPA exposure has been correlated with several metabolic diseases, the underlying mechanisms are unclear. In the present study, a metabolomics approach was used to explore the metabolic variations caused by low or high BPA exposure in female (n = 66) and male (n = 68) urine. Fatty acid elongation and sphingolipid metabolism were affected by high BPA exposure in males and females. Fatty acid elongation and sphingolipid metabolism were further investigated among age groups consisted of 30-39 yrs old, 40-49 yrs old, and 50-59 yrs old males and females with high or low urinary BPA. High BPA exposed males in 30 s and females in 50 s were found with significant disturbance in fatty acid elongation and sphingolipid metabolism, respectively. Additionally, females in 50 s showed elevated inflammatory metabolites: 6-ketoprostaglandin-E1 and thromboxane. In the present study, we have demonstrated that environmental metabolomics is useful to elucidate the health effects of BPA exposure.	Environ Toxicol Pharmacol.2018;58:434 7-55	10.1016/j.etap.2017.12.008	29276974	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2852	Choi J et al.	2014	Association between some endocrine-disrupting chemicals and childhood obesity in biological samples of young girls: A cross-sectional study	Childhood obesity, a major public health concern, has increased worldwide. Endocrine-disrupting chemicals (EDCs) have recently received attention as a cause of obesity. A cross-sectional study using logistic regression was conducted to investigate the association between some endocrine-disrupting chemicals and obesity in young girls. Endogenous steroids expected to be associated with EDCs were also investigated. The target compounds included 7 phthalates (MEP, DBP, BBP, DEHP, MEHP, MEHHP, and MEOHP), 2 alkylphenols (4-NP and 4-OP), bisphenol A and 9 endogenous steroids (DHT, aet-T, T, DHEA, 4, P, E1, E2, and E3). Fifty-nine and 680 girls were classified into the obese group and the control group, respectively. Urinary MEHP was significantly associated with obesity. In addition, DHEA in serum showed a statistically significant difference between obese and control groups. We concluded that these substances can affect the development of obesity.	Environmental Toxicology and Pharmacology.2014;38(1):51-57	10.1016/j.etap.2014.04.004	24908636	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2853	Corbesson I et al.	2016	Urinary bisphenol-A, phthalate metabolites and body composition in US adults, NHANES 1999-2006	BACKGROUND: Exposure to bisphenol-A (BPA) and phthalates is highly prevalent. Prior studies have not assessed associations between urinary levels of BPA and phthalate metabolites and body composition. METHODS: National Health and Nutrition Examination Survey (NHANES) 1999 to 2006 on adults aged ≥20 years analyzed by linear regression for associations between urinary BPA and phthalates, monoethyl phthalate (MEP), monobenzyl phthalate (MBzP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono(2-ethyl) phthalate (MEHP), and mono(carboxyoctyl) phthalate (MCOP), and monoisobutyl phthalate (MiBP), and monobutyl phthalate (MBP), and mono(carboxynonyl) phthalate (MCNP), and monoethyl phthalate (MEP), and monobenzyl phthalate (MBzP), and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP),

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 複数得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2862	Huang YF et al.	2018	Interactive effects of nonylphenol and bisphenol A exposure with oxidative stress on fetal reproductive indices	Nonylphenol (NP) and/or bisphenol A (BPA) may have reproductive effects. Although the mechanisms of action remain unclear, steroid hormones like synthesis, hypothalamus pituitary adrenal axis activity, oxidative stress, and unusually interaction of NP and BPA mixture and its pathways may play a contributory role. This cross-sectional study examined whether the interactive effects of NP/BPA and oxidative stress biomarkers played a role in reproductive indices in pregnant women. Between 2012 and 2013, 1,032 pregnant women were recruited from the Taiwan Maternal and Infant Cohort Study (TMICS). Urinary NP, BPA, 8-hydroxy-2'-deoxyguanosine (8-OHdG), and 15-F2t-isoprostane (15-F2t-IsoP) levels were measured in the second trimester. Reproductive indices including gestational age, birth weight, and anogenital distance (AGD) were collected. Multiple linear regression models were used to examine the associations between NP and BPA exposure and reproductive indices. Moreover, we used the Sobel test to examine the mediation effects of oxidative stress biomarkers. Maternal exposure to a mixture of NP and BPA may enhance 8-OHdG. Interactive effects were found in the high 8-IsoP/Cr group, and elevated NP exposure was inversely associated with penis length (β = -0.88 mm; p = 0.01). Similar results were noted among boys who were born to mothers in the high 8-IsoP/Cr group, in which BPA was inversely associated with penis length (β = -1.01 mm; p = 0.001). Our findings suggest no proven implications for prenatal exposure to oxidative stress, as evidenced by the 8-IsoP/Cr level. The NP and BPA may interact to shape fetal reproductive tract development, particularly in boys. The interactive effects of NP/BPA, oxidative stress, and reproductive indices should be considered.	Environmental Research.2018;167:567-574	10.1016/j.envres.2018.08.007	30165327	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2863	Joensen UN et al.	2018	Urinary excretion of phenols, parabens and benzophenones in young men: Associations to reproductive hormones and semen quality are modified by mutations in the Filaggrin gene	BACKGROUND: The filaggrin gene (FLG) encodes an epidermal protein, filaggrin, which is important for normal skin barrier functions. We previously showed that FLG loss-of-function mutation carriers have a higher internal exposure to some non-persistent chemicals, such as certain phthalates and parabens, suggesting increased trans- epidermal penetration. Steroid groups of non-persistent chemicals are suspected endocrine disrupting compounds (EDCs) known to disrupt hormonal activities and affect reproductive development in males. However, studies on the health effects of prenatal human exposure are scarce. STUDY DESIGN, SIZE, DURATION: This was a cross-sectional study to investigate the association between maternal phenolic exposure and cord sex steroid hormones and AGD in male newborns. METHODS: We measured urinary concentrations of bisphenol A (BPA) and other cresols, phenols, parabens, and UV-filters, including benzophenone-3 (BP-3). We found a 4-MBP to men participants in FLG R501X, 2282del4, and R2447X loss-of-function mutations, in total 88 mutation carriers and 138 non-carriers (controls) were included. Outcomes were markers of testicular function, assessed by semen reproductive hormones and semen quality. RESULTS: We found that associations between urinary chemical concentrations and outcomes were different in cases and controls. Within the group of FLG mutation carriers, higher urinary concentrations of BPA, BP-1 and BP-3 were associated with higher testosterone and calcitriol serum levels and lower FSH. Similar trends in hormone levels were observed for FLG mutation carriers with measurable 4-MBP levels. Higher urinary concentrations of BP-1 and BP-3 were associated with lower sperm motility and sperm concentration, respectively, in FLG mutation carriers. No such associations were evident in the control group. In the control group, however, lower sperm motility and sperm concentrations were observed in the men with detectable urinary 4-MBP compared to the men non-detectable urinary 4-MBP. We found no association between any parabens and outcomes, nor for the other measured phenols or UV-filters. CONCLUSIONS: Associations between male reproductive health parameters and urinary levels of BPA and benzophenones, such as BP-1, BP-3 and 4-MBP were observed in FLG mutation carriers but not in controls from the same study population. This difference between FLG mutation carriers and non-carriers is not explained solely by differences in exposure levels of the examined compounds as e.g. BPA and 4-MBP urinary levels did not differ between the two groups. We hypothesize that effects of exposure to these compounds may be modulated in FLG mutation carriers by either different levels of cutaneous or by route of uptake, with a higher fraction of the uptake by dermal uptake.	Environ Int.2018;121(Pt 1):365-374	10.1016/j.envint.2018.09.020	30245359	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2864	Ishra LE et al.	2016	Relationships Between Urinary Phthalate Metabolite and Bisphenol A Concentrations and Vitamin D Levels in US Adults: National Health and Nutrition Examination Survey (NHANES), 2005- 2010	Context: Recent research suggests that environmental exposure to endocrine disrupting chemicals may alter circulating 25-hydroxyvitamin D (25(OH)D) levels in humans. To date, no studies have assessed the associations between phthalates and bisphenol A (BPA) and total 25(OH)D in the U.S. general population. Objective: To examine relationships between urinary concentrations of 11 phthalate metabolites and BPA and serum total 25(OH)D in a representative sample of U.S. adults. Design: A cross- sectional study. Setting: U.S. National Health and Nutrition Examination Survey, 2005- 2010. Patients or Other Participants: U.S. general population (aged ≥ 20 years). Interventions: None. Main Outcome Measures: Serum total 25(OH)D measured by liquid chromatography- tandem mass spectrometry. Results: Detection frequencies of all 12 urinary(-) phthalate and BPA(+) were consistently inversely associated with total 25(OH)D in the overall study population and in gender-stratified models. In the overall population, we detected a significant inverse relationship for the molar sum of DEHP metabolites (ΣDEHP) (P = 0.001), with a similar trend for BPA (P = 0.054). Each log-unit increase of ΣDEHP was associated with a 3.5 nmol/L decrease in total 25(OH)D. Each log-unit increase of high molecular- weight (HMW) phthalate metabolites was associated with a 4.5 nmol/L decrease in total 25(OH)D. Subanalyses revealed that the inverse associations between HMW phthalate metabolites and total 25(OH)D were significant (P < 0.05) in Mexican- American and nonwhite participants. Furthermore, we found a statistically significant inverse relationship in women, but not in men, in models that included BPA. Each log-unit increase of BPA, a replacement for BPA, was associated with increased albumin (mg/L) creatinine (g/L) ratio (P = 0.04). Metabolites of HMW phthalates were also associated with decreased bioavailable 25(OH)D, with a 3.5% decrease (95% CI, 0.2- 6.8) in total 25(OH)D. Conclusions: Overall, our results provide suggestive evidence that environmental exposure to phthalates and BPA may alter circulating levels of total 25(OH)D in adults. Future human and animal studies are required to resolve the direction, temporality, and impact of these relationships. J Clin Endocrinol Metab 101: 4062- 4069, 2016)	Journal of Clinical Endocrinology & Metabolism.2016;101(11):4062-4069	10.1210/jc.2016-2134	27648964	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2865	Katarla A et al.	2017	Exposure to bisphenols and phthalates and association with oxidant stress, insulin resistance, and endothelial dysfunction in children	BACKGROUND: The health effects of bisphenol A (BPA) and di (2-ethylhexyl) phthalate (DEHP) have been studied extensively in children. The impact of other chemicals in these two classes has not been investigated as fully. METHODS: We conducted a cross-sectional pilot study of 30, 11(+) old healthy children. We assessed descriptive, univariable, and multivariable associations of urinary metabolites of bisphenols and phthalates with oxidant stress, insulin resistance, and endothelial dysfunction. RESULTS: We enrolled 31 participants (15 (+) F, 16 (+) M) with a median age of 11.5 (+) years. Urinary BPA was detected in 74% of samples. Median urinary concentrations increased in boys across sexual maturity. RESULTS: We enrolled 31 participants (15 (+) F, 16 (+) M) with a median age of 11.5 (+) years. Urinary BPA was detected in 74% of samples. Median urinary concentrations increased in boys across sexual maturity. Increased levels of DEHP metabolites, Each log-unit increase of high molecular- weight (HMW) phthalate metabolites was associated with a 0.082 increase in homeostatic Model Assessment of insulin resistance (HOMA-IR) units (P = 0.018) and attends circulating levels of activated endothelial cell-derived microparticles (P = 0.047). Bisphenol S (BPS), a replacement for BPA, was associated with increased albumin (mg)/creatinine (g) ratio (P = 0.04). Metabolites of HMW phthalates were also associated with decreased bioactive 25(OH)D, with a 3.5% decrease (95% CI, 0.2- 6.8) in total 25(OH)D. Conclusions: Overall, our results provide suggestive evidence that environmental exposure to phthalates and BPA may alter circulating levels of total 25(OH)D in adults. Future human and animal studies are required to resolve the direction, temporality, and impact of these relationships. J Clin Endocrinol Metab 101: 4062- 4069, 2016)	Pediatric Research.2017;81(6):857-864	10.1038/pr.2017.16	28099427	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2866	Khalil N et al.	2014	Bisphenol A and cardiometabolic risk factors in obese children	BACKGROUND AND OBJECTIVE: Bisphenol A (BPA) is an endocrine disruptor (ED) that has been associated with obesity and metabolic changes in liver in humans. Non alcoholic fatty liver disease (NAFLD) affects 40% of all obese children in the United States. Association of BPA with NAFLD in children is poorly understood. We investigated if BPA might play a role. METHODS: In a cross-sectional study of 70 obese and overweight children aged 7-18 years enrolled from the Children Medical Center of Dayton, Ohio, anthropometric, clinical and biochemical assessment of serum samples were conducted. Urinary BPA was measured by liquid chromatography-tandem mass spectrometry. Results are adjusted for urinary creatinine concentrations. RESULTS: Median urinary BPA was 1.2 ng/mL (IQR 0.7-2.1). Biochemical abnormalities commonly associated with increasing free thyroxine, hs-insulin, children BPA is statistical decreased with age, and was associated with elevated systolic blood pressure. The association of BPA (creatinine) persisted even after adjusting for age and ethnicity. Also hs-insulin, BPA concentration unadjusted for creatinine was significantly associated with certain having insulin and homeostasis model assessment for insulin resistance (HOMA-IR) showing non-monotonic exposure-response relationship. CONCLUSION: Urinary BPA in obese children, at least in males is associated with extensive liver and metabolic effects, and high diastolic blood pressure.	Science of the Total Environment.2014;470:726-732	10.1016/j.scitotenv.2013.09.088	24184549	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2867	Kim EJ et al.	2014	Association between urinary levels of bisphenol-A and estrogen metabolism in Korean adults	Bisphenol-A (BPA) possesses estrogenic properties both in vitro and in vivo as an endocrine disrupting chemical. Humans experience a long-term and cumulative exposure to BPA. BPA was detectable in 97.3% of 1904 urine specimens from Koreans adults. We investigated urinary estrogen concentrations in subjects with low and high BPA concentrations and its possible association with estrogen metabolism. Urine samples were collected from a high BPA concentration group (BPA >= 100, 11.20 ± 19.67 μg/g creatinine) and a low BPA concentration group (BPA <= 100, 0.70 ± 0.22 μg/g creatinine) from Korea Biomonitoring Program of Hazardous Materials Survey 2009-2010. Urinary estrogens were enzymatically hydrolyzed, extracted, and then derivatized for quantitative analysis by gas chromatography-mass spectrometry. Estrogen levels were higher in the BPA-H group than in the BPA-L group. Concentrations of estrone, 17β -estradiol, and their hydroxylated metabolites, in both men and women were significantly higher in the BPA-H group than in the BPA-L group. After adjusting for urinary creatinine, age, and body mass index, the BPA-H group showed 1.72-fold (95% confidence interval (CI): 1.38-2.15), 1.58-fold (95% CI: 1.26-1.98), and 1.74-fold (95% CI: 1.39-2.18) higher 2-hydroxylation ratio than the BPA-L group in men and women, respectively. Although each urine sample was collected and re-single-void urine samples, both the measurement of long-term exposure to BPA, we found significant differences of estrogen metabolism in the BPA-H and the BPA-L groups. The increase of hydroxyestrogens, especially 4-hydroxyestrogens, can be important factor resulting negative effects of prolonged exposure to BPA.	Science of the Total Environment.2014;470:1401-1407	10.1016/j.scitotenv.2013.07.040	23954212	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2868	Kim JH et al.	2013	Bisphenol A-associated epigenomic changes in prepubescent girls: a cross-sectional study in Gharbiah, Egypt	BACKGROUND: There is now compelling evidence that epigenetic modifications link adult disease susceptibility to environmental exposures during specific life stages, including pre-pubertal development. Animal studies indicate that bisphenol A (BPA), the monomer used in epoxy resins and polycarbonate plastics, may impact health through epigenetic mechanisms, and epidemiological data associate BPA levels with metabolic disorders, behavior changes, and reproductive effects. Thus, our combined environmental epidemiology study of BPA exposure and CpG methylation in pre-adolescent girls from Sharkieh, Egypt hypothesizing that methylation changes in peripheral blood DNA are associated with BPA exposure. METHODS: We measured urinary BPA concentrations in 249 girls (aged 6-8 years) using high-performance liquid chromatography and tandem mass spectrometry. We used Illumina's Infinium HumanMethylation27 BeadChip to (N = 96) CpG sites from buccal epithelial cell DNA to examine whether promoter methylation was associated with BPA exposure. RESULTS: CpG methylation varied widely among girls, and higher urinary BPA concentrations were generally associated with less genomic methylation. Based on pathway analyses, genes exhibiting reduced methylation with increasing urinary BPA were involved in immune function, transport activity, metabolism, and caspase activity, in particular. Hypermethylation of CpG regions on chromosome 6 was associated with higher urinary BPA. Using the Comparative Toxicogenomics Database, we identified a number of candidate genes in our sample that previously have been associated with BPA-related expression changes. CONCLUSIONS: These data indicate that BPA may affect human health through epigenetic modifications of genes in relevant pathways. Thus, epigenetic epidemiology holds promise for the identification of biomarkers from previous exposures and the development of epigenetic-based diagnostic strategies.	Environmental Health.2013;12:15	10.1186/1476-069X-12-33	23590724	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2869	Liang H et al.	2017	The Association between Exposure to Environmental Bisphenol A and Gonadotropic Hormone Levels among Men	Bisphenol A (BPA) is an extensively used chemical with endocrine-disrupting properties. Although animal and in-vivo studies have suggested possible effects of BPA on levels of gonadotropic hormones, human studies are limited and inconclusive. The study examined whether environmental BPA exposure was associated with gonadotropic hormones levels in men. A total of 568 men aged 18-74 years were recruited from Sanda County, Shanghai, China, in 2012. Urinary BPA concentrations were measured by high-performance liquid chromatography-tandem mass spectrometry. Serum levels of follicle-stimulating hormone (LH), and total testosterone (T). Relative risk (RR) was obtained by log-binomial regression to examine the association between urinary BPA level and hormone levels. BPA was detected in 75.4% of urine samples, with a geometric mean of 0.93 mcg/gCr. Men with detectable levels of BPA had a 1.72-fold increased risk of having a high LH level (>75th percentile) when compared with men with undetectable levels of BPA after adjustment for potential confounders (95% confidence interval (CI): 1.08-2.21). The association persisted and slightly intensified among current smokers (adjusted RR (aRR) = 1.76; 95%CI: 1.08-2.86), while a weakened among non-smokers (aRR= 1.17; 95%CI: 0.68-1.98). Urinary BPA level was associated with an increased FSH level among smokers (aRR = 1.66; 95%CI: 1.02-2.67). Urinary BPA level was inversely associated with T level among non-smokers (aRR = 0.58; 95%CI: 0.34-0.98), but not among smokers (aRR = 0.85; 95%CI: 0.52-1.39). Urinary BPA level was positively associated with increased serum levels of LH and FSH in male smokers, along with decreased serum levels of total T in men with BMI ≥ 25 kg/m2. These findings suggest that the effects of environmental BPA exposure on hormone levels might be modified by smoking and BMI.	Plos One.2017;12(1):12	10.1371/journal.pone.0169217	28085949	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2870	Liu CY et al.	2015	Association between levels of serum bisphenol A, a potentially harmful chemical in plastic containers, and carotid artery intima-media thickness in adolescents and young adults	OBJECTIVE: Bisphenol A (BPA) is a chemical produced at high volumes and used widely in food and drink packaging. In adults, elevated BPA concentrations are associated with cardiovascular disease. BPA exposure is plausibly linked to atherosclerosis in adolescents and young adults, but evidence is lacking to date. METHODS: We recruited 886 subjects, 12-30 years of age(1 from a population-based sample of adolescents and young adults in Taichung City, Taiwan. Serum BPA concentrations were measured using on-line solid phase extraction coupled to high performance liquid chromatography and tandem mass spectrometry. BPA was detected in 51.2% (n = 454) of the subjects, with a median concentration of 0.23 ng/mL. After controlling for confounding factors, linear regression analysis showed a 1-unit increase in natural log-BPA was significantly associated with increased mean CIMT (mm) (β = 0.009; 95% C.I. = 0.000-0.017; p = 0.032) and other measurement of CIMT. Excluding right and left side of common carotid artery, carotid bulb and internal carotid artery). CONCLUSION: Higher serum concentrations of BPA were associated with increased CIMT in this cross- sectional study of adolescents and young adults. Studies to clarify the mechanisms of these associations are needed.	Atherosclerosis.2015;241(2):657-663	10.1016/j.atherosclerosis.2015.06.038	26117403	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2871	Liu B et al.	2017	Bisphenol A substitutes and obesity in US adults: analysis of a population-based, cross-sectional study	BACKGROUND: Bisphenol F (BPF) and bisphenol S (BPS) are increasingly used to substitute bisphenol A (BPA), a widespread environmental endocrine disruptor and putative obesogen. However, studies on effects of BPF and BPS on obesity in humans are lacking. We examined the associations of BPA, BPF, and BPS exposure with obesity in U.S. adults. METHODS: We included 2,631 participants aged 20 years or older from a cross-sectional study, the National Health and Nutrition Examination Survey 2013-2014. Urinary BPA, BPF, and BPS concentrations were measured using on-line solid phase extraction coupled to high performance liquid chromatography and tandem mass spectrometry. We used body mass index and waist circumference to assess general obesity and abdominal obesity, respectively. We used logistic regression with sample weights to estimate the odds ratios (ORs) of obesity and 95% confidence intervals. FINDINGS: Higher BPA, BPF, and BPS concentrations were observed in obese adults than non-obese adults. After adjustment for demographic, behavioral factors, and urinary creatinine, participants in the highest quartile of BPA (OR: 1.52; 95% CI: 1.07 to 2.16), BPF (OR: 1.49; 95% CI: 1.04 to 2.13), and BPS (OR: 1.60; 95% CI: 1.07 to 2.39) had significantly higher odds of obesity than those in the lowest quartile of BPA, 1.52 (0.91-1.67) for BPF, and 1.22 (0.82-1.83) for BPS. The corresponding ORs of abdominal obesity were 1.56 (1.06-2.30) for BPA, 1.36 (0.88-2.10) for BPF, and 1.56 (1.04-2.34) for BPS. INTERPRETATION: Whereas there were significant associations of BPA exposure with general and abdominal obesity, BPF or BPS, at current exposure level, was not significantly associated with obesity in U.S. adults. Continued biomonitoring of these bisphenols in populations and further investigations on their health effects in humans are warranted.	Lancet Planet Health.2017;1(3):e114-e122	10.1016/S2542-5196(17)30049-9	29308453	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	●	-	-	-
統合_2872	Liu CH et al.	2016	Associations between maternal phenolic exposure and cord sex hormones in male newborns	STUDY QUESTION: Are maternal urinary phenol concentrations associated with cord steroid hormone levels and anogenital distance (AGD) in male newborns? SUMMARY ANSWER: High maternal urinary Bisphenol A (BPA) levels are associated with decreases in cord testosterone levels and the ratio of testosterone to estradiol in male newborns, but there was no significant association with AGD. WHAT IS KNOWN ALREADY: Early-life exposure to phenolic endocrine disrupting compounds (EDCs) is known to disrupt hormonal activities and affect reproductive development in males. However, studies on the health effects of prenatal human exposure are scarce. STUDY DESIGN, SIZE, DURATION: This was a cross-sectional study to investigate the association between maternal phenolic exposure and cord sex steroid hormones and AGD in male newborns. We recruited 150 mother-infant pairs from each of two hospitals, one in a polluted town (Guiya) and the other in a cleaner town (Yanjiao), from September 2012 to September 2013. PARTICIPANTS/MATERIALS, SETTING, METHODS: We measured urinary concentrations of bisphenol A (BPA) and other cresols, phenols, parabens, and UV-filters, including benzophenone-3 (BP-3). We found 4-MBP in men participants in FLG R501X, 2282del4, and R2447X loss-of-function mutations, in total 88 mutation carriers and 138 non-carriers (controls) were included. Outcomes were markers of testicular function, assessed by semen reproductive hormones and semen quality. RESULTS: We found that associations between urinary chemical concentrations and outcomes were different in cases and controls. Within the group of FLG mutation carriers, higher urinary concentrations of BPA, BP-1 and BP-3 were associated with higher testosterone and calcitriol serum levels and lower FSH. Similar trends in hormone levels were observed for FLG mutation carriers with measurable 4-MBP levels. Higher urinary concentrations of BP-1 and BP-3 were associated with lower sperm motility and sperm concentration, respectively, in FLG mutation carriers. No such associations were evident in the control group. In the control group, however, lower sperm motility and sperm concentrations were observed in the men with detectable urinary 4-MBP compared to the men non-detectable urinary 4-MBP. We found no association between any parabens and outcomes, nor for the other measured phenols or UV-filters. CONCLUSIONS: Associations between male reproductive health parameters and urinary levels of BPA and benzophenones, such as BP-1, BP-3 and 4-MBP were observed in FLG mutation carriers but not in controls from the same study population. This difference between FLG mutation carriers and non-carriers is not explained solely by differences in exposure levels of the examined compounds as e.g. BPA and 4-MBP urinary levels did not differ between the two groups. We hypothesize that effects of exposure to these compounds may be modulated in FLG mutation carriers by either different levels of cutaneous or by route of uptake, with a higher fraction of the uptake by dermal uptake.	Human Reproduction.2016;31(3):648-656	10.1093/humrep/dev327	26724800	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2873	Liu RQ et al.	2015	Exposure to bisphenol-A and reproductive hormones among male adults	BACKGROUND: Bisphenol A (BPA) is a suspected human endocrine disruptor which is widely used. METHODS: In order to determine whether urine BPA level is associated with serum reproductive hormone levels among male adults, we carried out a cross-sectional study in China. We included 167 male volunteers and collected their urine samples for BPA measurement. We also collected blood samples and examined seven reproductive hormones. We used multiple linear regression and log-binomial model to examine associations between urine BPA level and hormone levels after controlling for age and smoking status. RESULTS: An increased urine BPA level was associated with increased prolactin (p=0.001), estradiol (p=0.001), sex hormone binding globulin level (p=0.001), and a reduced androstenedione (p=0.001) and free androgen index level (p=0.021). Males, whose urine BPA level was in the 2nd, 3rd and highest quartiles, had respectively 1.58, 1.33 and 2.09 fold increased prevalence of having a high prolactin level (>75% level). The highest quartile of BPA level was associated with 1.91 and 1.80 fold increased prevalence of having a high estradiol and sex hormone binding globulin level. Males, with higher quartile of BPA level had a lower relative R level. CONCLUSIONS: High BPA exposure is associated with increased prolactin, estradiol and sex hormone binding globulin level in males, and may contribute to male infertility.	Environmental Toxicology and Pharmacology.2015;39(2):934-941	10.1016/j.etap.2015.03.007	25818109	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_2874	Malits J et al.	2018	Renal Function and exposure to Bisphenol A and phthalates in children with Chronic Kidney Disease	RATIONALE AND OBJECTIVE: Exposure to Bisphenol A (BPA) and phthalates is ubiquitous among adults and children in the United States. Among children and adolescents, those with chronic kidney disease (CKD) are at risk for faster progression to kidney failure. Exposure to BPA and phthalates may be associated with worse kidney function in children with CKD. We examined associations between urinary concentrations of BPA and phthalates and measures of kidney function. STUDY DESIGN: Cross-sectional study. SETTING, PARTICIPANTS, AND MEASUREMENTS: The CKD population was represented by the Chronic Kidney Disease in Children (CKiD) Study, a multicenter, prospective cohort study of children with impaired kidney function in the US. The main outcome was assessment of the relationship between chemical exposures and clinical laboratory findings at enrollment into CKiD. Data collected at baseline from participants 1 to 17 years old (N = 538) were analyzed. Urinary BPA and phthalate levels were evaluated as tibs time point. Data from the National Healthand Nutrition Examination Survey (NHANES), a nationally representative pediatric population, were used for comparison to the CKiD cohort. RESULTS: Urinary BPA and phthalate levels in the CKiD population were consistently lower than those observed in the NHANES population. In the CKiD population, urinary concentrations of BPA, but not phthalates, were associated with lower eGFR. In models that included BPA and phthalates and combined phthalates, there was an inverse relationship between the urinary protein-creatinine ratio & BPA/phthalates. - 9.53% change; 95% CI: -16.1%, -2.4%; p = 0.002), and in most cases, a positive relationship with eGFR (1.34% increase in eGFR; 95% CI: 1.8%, 5.4%; p = 0.002). LIMITATIONS: Lack of longitudinal data, limited assessment of diet and nutritional status. CONCLUSION: In the study cohort, children with CKD did not have increased exposure to BPA and phthalates. Longitudinal studies with repeated measures are likely to be more informative about the possible health effects of prolonged exposure to BPA and phthalates in pediatric patients with CKD.	Environ Res. 2018 Nov;167:575-582.	10.1016/j.envres.2018.08.006	30172191	ヒト	腎	-	-	-	-	-	横断研究	1	1	-	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2875	McGuire LA et al.	2015	Urinary bisphenol A and age at menarche among adolescent girls: Evidence from NHANES 2003-2010	BACKGROUND: Bisphenol A (BPA) is an environmental estrogen used in the manufacture of polycarbonate plastics and epoxy resins used to make food and beverage packaging. Increasing evidence suggests that BPA mimics estrogens in the body and may be associated with a similar markers of breast cancer risk. OBJECTIVES: We analyzed the National Health and Nutrition Examination Survey (NHANES) 2003-2010 data to investigate the association between BPA and age at menarche among adolescent girls. METHODS: We used multivariate linear regression to estimate the adjusted mean age at menarche by urinary BPA concentration. We also used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CI) for the association between urinary BPA and early onset of menarche, with adjustment for sampling weights, clustering, and stratification. We assessed interaction of BPA with BMI. RESULTS: Adolescent girls with moderate BPA levels, exposed to, or less likely to have early onset of menarche than those with the lowest levels (OR=0.61; 95% CI: 0.38, 0.99) after adjusting for age, race/ethnicity, parental education, country of birth, NHANES cycle, BMI and creatinine. BMI appeared to modify the BPA-menarche association (CONCLUSIONS: Although a significant trend suggests that increasing urinary BPA may be associated with delayed menarche in adolescent girls, these results are based on cross-sectional data. Results should be clarified in carefully designed longitudinal cohort studies.	Environmental Research.2015;136:381-386	10.1016/j.envres.2014.10.037	25460659	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2876	Menale C et al.	2017	Bisphenol A is associated with insulin resistance and modulates adiponectin and resistin gene expression in obese children	BACKGROUND: Bisphenol A (BPA) exposure has been associated with increased incidence of diabetes and obesity in adults. OBJECTIVES: To evaluate whether an association between BPA urinary levels and insulin resistance exist, we adjusted in and insulin production and serum concentrations may occur in obese children. METHODS: Clinical and biochemical features of 120 obese children were collected. Serum resistin and adiponectin were evaluated. Insulin resistance and urinary BPA levels were assessed. Moreover, the effect of BPA on adiponectin and resistin gene expression in adipocytes from eight normal-weight prepubertal children undergoing surgery was investigated. RESULTS: BPA urinary levels were significantly higher in obese children with insulin resistance (IR) than in those without IR (p=0.0001). Serum resistin and adiponectin have been found (r = -0.68, p < 0.0001). In adipocytes, resistin expression was determined only after BPA treatment, while adiponectin expression resulted down-regulated after BPA exposure (p < 0.05 at both 10 and 100 nM BPA concentrations). CONCLUSIONS: We suggest the involvement of BPA in the development of insulin resistance in childhood obesity highlighting that urinary BPA levels are directly associated with insulin resistance regardless of BMI. This association may be explained, at least partly, by the findings that BPA affects resistin and adiponectin production in adipose tissue cultures.	Pediatric Obesity.2017;12(5):380-387	10.1111/ijpo.12154	27187765	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2877	Metwally FM et al.	2016	The impact of bisphenol a (BPA) as environmental obesogen on lipids and lipids metabolism	Some obese individuals have normal metabolic profile, and some normal weight persons have impaired metabolic status. Our hypothesis was that one of the potential underlying factors for such differences is environmental obesogens. The aim of the present study was to investigate the role of bisphenol A (BPA) as environmental obesogen and its relation to other risk factors for cardiometabolic disorders in children and adolescents independent of/overweight status. This case control study was conducted on a subsample of 200 participants at national school based surveillance program in Iran. We measured serum BPA and phthalate metabolites by gas chromatography-mass spectrophotometry. We compared them in children and adolescents with and without excess weight and those with and without cardiometabolic risk factors. BPA was detected in 100% of children and adolescents. Children and adolescents with excess weight had significantly higher BPA concentrations than normal weight children and adolescents (p=0.001). BPA concentrations and phthalates score significantly different in the four groups studied. BMISP concentration was associated with higher odds ratio of cardiometabolic risk factors in participants with excess weight (OR: 95% CI: 1.82; 1.001-7.81) and those with excess weight (OR: 95% CI: 1.81; 1.27-7.681). BMIP concentration increased the odds ratio of cardiometabolic risk factors only in normal weight children and adolescents (OR: 95% CI: 6.95; 2.59-18.58; P< 0.001). In participants without cardiometabolic risk factor, MMP and MEHHP were significantly associated with increased risk of excess weight (OR: 95% CI: 1.96; 1.21-18.75 and CI: 1.1- 11.8, respectively). This study showed that the association of BPA and phthalate with cardiometabolic risk factors is independent of the weight status. Our findings suggest that the metabolic impairment in some normal weight children and normal metabolic profile of some obese children can be, in part, related to exposure to these environmental chemicals.	International Journal of Pharmaceutical and Clinical Research.2016;8(9):1323-1330	-	-	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2878	Miao MH et al.	2017	Urinary bisphenol A and pubertal development in Chinese school-aged girls: a cross-sectional study	BACKGROUND: Animal studies suggest that bisphenol A (BPA) may perturb pubertal development in females. However, evidence from human studies is limited. METHODS: This was a cross-sectional study to investigate the association between BPA exposure and pubertal development in school-aged girls. A total of 839 girls aged 8-10 years were selected from three schools in Shanghai, from May to June 2011. We collected one single spot urine sample from each girl. Urine BPA concentrations were measured by modified high-performance liquid chromatography and categorized according to LOD and the median of those above LOD. Pubertal development status was ascertained by using Tanner staging, and age at menarche was collected via a retrospective questionnaire from girls who reported having begun menstruation. Logistic regression models were used to examine the association between urinary BPA and pubertal development, adjusting for potential confounders. RESULTS: After adjustment for potential confounders, girls with detectable BPA were more likely to have developed menarche, a mid-puberty event, compared to girls with undetectable BPA (adjusted odds ratio [aOR] = 1.82, 95% confidence interval [CI]: 1.03, 3.21). Girls with BPA ≥ 1.96 ng/mL were more likely to have developed pubic hair, a mid-puberty event, than girls with BPA < 1.96 ng/mL (aOR = 1.51, 95% CI: 1.01, 2.26). Girls with BPA ≥ 1.96 ng/mL were also more likely to have reached pubic hair stage 3, the late stage of pubic hair development (aOR = 1.60, 95% CI: 1.01, 2.54). CONCLUSIONS: BPA exposure was associated with alterations in the timing of pubertal development. Results in the present study should be interpreted with caution because of its cross-sectional nature and the limited sample size in each age group.	Environmental Health.2017;16:7	10.1186/s12940-017-0290-9	28750633	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2879	Miao MH et al.	2015	Associations between Bisphenol A Exposure and Reproductive Hormones among Female Workers	The associations between Bisphenol A (BPA) exposure and reproductive hormone levels among women are unclear. A cross-sectional study was conducted among female workers from BPA-exposed and unexposed factories in China. Women's blood samples were collected for assay of follicle-stimulating hormone (FSH), luteinizing hormone (LH), China-Estradiol (CE), prolactin (PRL), and progesterone (PROG). Their urine samples were sent to the CDC for BPA measurement. In the exposed group, time-weighted average exposure to BPA is in the range of 0.01-76.7 mg/L, a measure incorporating intensity, frequency and duration of personal air sampling. Multiple linear regression analyses were used to examine linear associations between urine BPA concentration and reproductive hormones after controlling for potential confounders. A total of 104 exposed and 158 unexposed women participated in the study. Urine BPA was detected in 97.1% of exposed women and 31.6% of unexposed women. Urine BPA was significantly associated with FSH, LH, and PROG. After the analysis was carried out separately among the exposed and unexposed workers. In addition, a positive association between urine BPA and PRL was observed among exposed workers, with borderline significance, while a statistically significant inverse association between urine BPA and FSH was observed among unexposed group. The results suggest that BPA exposure may lead to alterations in female reproductive hormone levels.	Int J Environ Res Public Health. 2015 Oct 22;12(10):13240-50.	10.3390/ijerph121013240	26506366	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2880	Milic N et al.	2015	Estimation of in vivo and in vitro exposure to bisphenol A as food contaminant	The goal of this cross-sectional study was to examine the occurrence of bisphenol A (BPA) in the morning spot urine taken from 130 female volunteers of various ages. Total urine BPA concentration was detected in 38.4% samples in the 0.87-7536 mg/g Cr range. The majority of BPA (~ women belonged to the 25 ≤ body mass index (BMI) group (54.9% were overweight and 20.2% were obese women). Its content of BPA in the urine of 18-30 years old was 1.5 times higher than in the 31-45 years old and 2.5 times higher than in the 46-60 years old. Exposure to BPA in the range 0.01-1000 nM for 24 h significantly the growth of all investigated cell lines, i.e. the EC50 values were reached at very low concentrations, in the range from 0.26 to 30.89 mg/mL. The obtained in vivo results suggest that a higher exposure to BPA could contribute to weight problems in women and the absence of the BPA in vitro selective toxicity studies indicates to its general toxic mode of action and raises awareness of the health risks associated with its ubiquitous presence in the environment.	Food and Chemical Toxicology.2015;83:268-274	10.1016/j.fct.2015.07.003	26165726	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2881	Milosevic N et al.	2017	Possible influence of the environmental pollutant bisphenol A on the cardiometabolic risk factors	Bisphenol A (BPA) is a ubiquitous environmental pollutant which is often associated with various health issues. In this study 103 healthy female volunteers, in reproductive age from Serbian multi-province Vojvodina were enrolled and examined for the BPA exposure in the urine samples after 12 hof fasting. BPA was found in 38.81% (33/103) of subjects. Statistically significant increment in waist circumference (p = 0.046) and waist to height ratio (p = 0.007) was observed among the BPA positive women in comparison with the women from the same cohort but the same overweight, balance and habitual lifestyle. Positive correlation was obtained between the BPA concentration in urine samples and body mass index (rS1 = 0.09, p = 0.002) waist circumference (rS1 = 0.21, p = 0.02) and waist to height ratio (rS1 = 0.24, p = 0.02) among the obese. High energetic intake and relevant physical activity additionally pronounced BPA positive association with obesity. So statistically significant difference was observed in triglycerides, HDL and LDL cholesterol levels between the BPA exposed and BPA non-exposed female volunteers.	International Journal of Environmental Health Research.2017;27(1):43795	10.1080/09603123.2016.1246654	27771963	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2882	Minatoya M et al.	2017	Cord Blood Bisphenol A Levels and Reproductive and Thyroid Hormone Levels of Neonates The Hokkaido Study on Environment and Children's Health	BACKGROUND: Bisphenol A (BPA) is widely used and BPA exposure is nearly ubiquitous in developed countries. While animal studies have indicated adverse health effects of prenatal BPA exposure including reproductive dysfunction and thyroid function disruption (possibly in a sex-specific manner), findings from epidemiologic studies have not been enough to prove these adverse effects. Given very limited knowledge on human, the aim of this study was to investigate the association between prenatal BPA exposure and reproductive and thyroid hormone levels of neonates. METHODS: This study was conducted as a birth cohort study. We recruited 563 participants of the Hokkaido study recruited from 2002 to 2005 at one hospital in Sapporo, Japan. The BPA level in cord blood was determined by GC-LC/MS/MS, and the geometric mean of cord blood BPA level was 0.68 ng/mL. We measured nine types of reproductive hormone levels in cord blood, and thyroid hormone levels were obtained from neonatal mass screening test data. There were 283 subjects, who had both BPA and hormone data available. We used multiple regression models to examine the association between BPA and hormone levels. RESULTS: We found a significant positive association between BPA and free testosterone in male neonates (p = 0.04), and a significant negative association was found in female fetus (p = 0.02), whereas a small positive association was found in girls (beta = 0.02). BPA level showed a weak positive association with testosterone, estradiol, and progesterone levels in boys. No association was found between BPA and thyroid hormone levels. CONCLUSIONS: Our findings suggested that fetal BPA levels might be associated with changes in certain reproductive hormone levels of neonates in a sex-specific manner, though further investigations are necessary.	Epidemiology.2017;28:S3-S9	10.1097/EDE.0000000000000716	29028670	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2883	Muhsen MA et al.	2018	May detectable urinary Bisphenol A among children be associated with cardiovascular risk factor?	Bisphenol A (BPA) is suspected to be associated with several chronic metabolic diseases. The aim of the present study was to examine the associations of urinary BPA concentrations, with cardio-metabolic risk factors, including age, gender, lipid profile, High sensitivity C- reactive protein (hs-CRP) levels among children and adolescents. It's a cross-sectional study enrolling 167 children 'Aleppy and Idlib). They aged from 6 to 16 years, randomly selected from primary, and preparatory schools in Deir-Ez-Zour, Al Hasakah governorate in the North-East of Syria. Bisphenol A was determined by high performance liquid chromatography-tandem mass spectrometry (HPLC-T) from total, conjugated, unconjugated, log total, BPA/creatinine and BPA/creatinine were estimated. Serum samples were assayed for total cholesterol, HDL-cholesterol, triglycerides, and hs-CRP. Data were analyzed using SPSS version 20. Mean ± SD of BPA/creatinine was 1.5 ± 1.2 ng/mg, and BPA/total was 1.2 ± 1.1 ng/ml (17.8%, respectively). Serum total cholesterol, HDL- cholesterol, LDL- cholesterol, triglycerides, and hs-CRP showed no statistically significant differences as regard to age and gender (P > 0.05).No significant association between BPA and the age, gender was found(P> 0.05).Total BPA/creatinine ratio was significantly positively correlated with the serum total cholesterol and LDL- cholesterol (P<0.05).We did not find significant associations between BPA and any other cardiovascular risk factors. Our work provides additional evidence of associations between urinary BPA and cardiovascular risk factors among Egyptian children and adolescents.Future policy regulating children's consumer products is mandatory. © 2018 ISDinet- Innovative Scientific Information Services Network. All rights reserved.	Bioscience Research.2018;15(2):1243-1250	-	-	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2884	Mougan M et al.	2017	Environmental estrogen-like endocrine disrupting chemicals and breast cancer	BACKGROUND: Estrogen-mimicking endocrine disruptors (EEDs) such as octylphenol/nonylphenols (PCBs), bisphenol A (BPA), and phthalates have been found ubiquitously throughout our environment. Although exposure to EEDs has the ability to interfere with endocrine control of reproductive function and development in both humans and wildlife, inconsistent reports have made it difficult to draw conclusions concerning the hypothesized increased risk of breast cancer associated with EEDs. OBJECTIVES: The purpose of this study was to examine the cross-sectional relationship between exposure to PCBs, BPA or phthalates, and risk of breast cancer in U.S. women using the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) data between 1999 and 2002. METHODS: We analyzed data from participants (20 years of age and older) in the NHANES 1999-2000 and 2001-2002 cycles who had measurements of PCBs, BPA, and phthalates (= 1,493). Urinary concentrations of BPA, 11 PCB congeners, and 10 phthalate metabolites were measured. Logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CI) for the association between PCB, BPA or phthalate measurements and breast cancer. RESULTS: In age, race/ethnicity, and BMI-adjusted models, PCB138 was the only congener found to be significantly associated with breast cancer (OR of 1.36; 95% CI: 1.10-8.76). We also found the sum of non-dioxin-like PCBs (sum PCB) to be significantly associated with breast cancer (OR of 1.36; 95% CI: 1.10-8.76). Urinary concentrations of BPA, phthalates, and the sum of dioxin-like PCBs (sum DLC) were not significantly associated with breast cancer. CONCLUSIONS: Our results suggest a link between environmental exposures to PCB 138 and breast cancer. There were no significant associations between phthalates or BPA and breast cancers. These findings should be interpreted with caution because of the use of cross-sectional self-reported data and a small sample size of breast cancer subjects. Nonetheless, our finding emphasizes a need of comprehensive environmental molecular epidemiologic study to determine the potential role of environmental exposures to PCBs, phthalates, and BPA in the development of breast cancer.	Molecular and Cellular Endocrinology.2017;457(C):89-102	10.1016/j.mce.2016.10.003	27717745	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2885	Mouneimne Y et al.	2017	Bisphenol A urinary level, its correlates, and association with cardiometabolic risks in Lebanese urban adults	Bisphenol A (BPA) is an endocrine disruptor with multiple purported metabolic effects. This study aimed to measure BPA among Lebanese population, to identify its predictors, and to explore any link to metabolic syndrome (MetS) and its components. A cross-sectional study was conducted on 1,000 adults, randomly selected from Lebanese households. Socio-demographic, anthropometric, clinical, and laboratory markers of metabolic conditions (MC) and MetS data was divided into tertiles. A total of 80% of the subjects had detectable urinary BPA levels, with an overall median of 3.07 (< 0.75, µg/L) and a mean ± standard deviation of 3.96 ± 4.79 µg/g. There was a significant positive association with female gender and older age for being in the highest BPA tertile. BPA level was linked to metabolic syndrome (MetS), obesity, type 2 diabetes (T2D), hypertension, and dyslipidemia. After adjustment, the trend remained for BPA in association with MetS and T2D. Though urinary BPA in this Lebanese population was higher in older women, the levels were similar to world-reported figures. Our results suggest a link with metabolic disorders but not at a significant level. These findings call for longitudinal and broader sample measurements.	Environmental Monitoring and Assessment.2017;189(10):13	10.1007/s10661-017-6216-8	28942470	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2886	Park C et al.	2017	Associations between urinary phthalate metabolites and bisphenol A levels, and serum thyroid hormones among the Korean adult population - Korean National Environmental Health Survey (KoNEHS) 2012-2014	BACKGROUND: Phthalates and bisphenol A (BPA) have been used extensively in many consumer products, resulting in widespread exposure in the general population. Studies have suggested associations between exposure to phthalates and BPA, and serum thyroid hormone levels, but confirmation on larger human populations is warranted. METHODS: Data obtained from nationally representative Korean adults (≥ 6002) recruited for the second round of the Korean National Environmental Health Survey (KoNEHS) 2012-2014, were analyzed. These di-(2-ethylhexyl) phthalate (DEHP) metabolites, along with benzyl butyl phthalate (BBzP) and di-butyl phthalate (DBP) metabolites, and BPA were measured in subjects' urine. Thyroxine (T4), total triiodothyronine (T3), and thyroid-stimulating hormone (TSH) were measured in serum. The associations between urinary BPA, phthalate metabolites, and thyroid hormones were investigated using multivariate linear regression models. RESULTS: Urinary BPA was detected in 93.2% of the subjects. Increases of interquartile range (IQR) increases of mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) were associated with a 2.7% increase of TSH, and a 2.7% decrease of total T3 levels, respectively. When grouped by sex, urinary MEHHP levels were inversely associated with T3 only among males. Among females, mono-benzyl phthalate (MBzP) and mono-n-butyl phthalate (MnBP) levels were inversely associated with T3 level. CONCLUSIONS: In addition, negative associations between BPA and TSH was observed. CONCLUSIONS: Several phthalates and BPA exposures were associated with altered circulatory thyroid hormone levels among general Korean adult population. Considering the importance of thyroid hormones, public health implications of such alteration warrant further studies.	Science of the Total Environment.2017;584-585:949-957	10.1016/j.scitotenv.2017.01.144	28153396	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2887	Pornkunwilai S et al.	2015	Urinary bisphenol A detection is significantly associated with young and obese Thai children	Background: Bisphenol A (BPA), a xenoestrogenic monomer, is one of the most common industrial chemicals used in epoxy coatings for canned food and other consumer items. There is only limited information regarding BPA exposure in Thailand. Objectives: To determine urinary BPA concentrations in Thai children and to investigate the relationship between urinary BPA concentrations and anthropometric measurements, demographic characteristics, and BPA exposure risks in Thai children and adolescents. Methods: A cross-sectional study was conducted in 379 children and adolescents aged 7–18 years from kindergarten, elementary, and middle schools in Bangkok, Thailand. Urinary concentrations of total BPA were determined by liquid chromatography tandem mass spectrometry (LC–MS/MS). Anthropometric data and questionnaires regarding BPA exposure risks were collected. Results: BPA was detected in 58.1% of 379 urine samples (75.5%) in the creatinine-adjusted BPA (CAB) group. The median urinary BPA concentration was 2.1 ng/mL (1.1 ng/mg creatinine). Thirty-one participants (9%) were overweight and 34 (11%) were obese. The BPA detection rate was significantly higher in obese children (OR 5.42, 95% confidence interval (CI) 1.18 – 9.85, P = 0.02) compared with children of normal weight. BPA was detected more often in younger children (7–9 years) when compared with children (9–12 years) and adolescents (13–18 years). There were no significant associations between BPA levels and other demographic data or BPA exposure risks. Conclusions: BPA exposure in Thai children and adolescents may be lower than exposure in children from the United States, some European nations, and other Asian countries. Obese and younger children were significantly associated with BPA detection.	Asian Biomedicine.2015;9(3):363-372	10.5372/1905-7415.0903.405	-	ヒト	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

通帳性評価（動物）1：該当、0：該当しない　通帳性評価（疫学）1：該当、0：該当しない　通帳性評価（in vitro）1：該当、0：該当しない　通帳性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通帳性基準不適合と判断されるものは作成段階評価へ進め、当該物評価段階で原則に基づき排除。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と2用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通帳性評価基準通過（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2888	Przybyla J et al.	2018	A cross sectional study of urinary phthalates, phenols and perchlorate on thyroid hormones in US adults using structural equation models (NHANES 2007-2008)	BACKGROUND: Biomonitoring data shows that people are exposed to phthalates, phenols and perchlorate. Many of these compounds are endocrine disrupting compounds that affect thyroid hormone levels. Yet the effect of these compounds on thyroid hormone levels are often evaluated individually rather than as a mixture. Our objective was to examine the association between 11 urinary endocrine disrupting compounds and thyroid hormones using structural equation models. METHODS: Using data from the National Health and Nutrition Examination Survey 2007-2008, we fit a latent variable utilizing urinary measurements of N-compounds (N-CPDS) (perchlorate, nitrate, thiocyanate) and P-compounds (P-CPDS) (monobutyl phthalate, monoethyl phthalate, monomethyl phthalate, monobenzyl phthalate, mono-2-ethylhexyl phthalate, mono-isobutyl phthalate) and 3 compounds (triclosan, benzophenone-3, bisphenol A) as a latent variable with seven thyroid hormones (Total T4, Total T3, and Thyroid Stimulating Hormone) in two structural equation models. In both models, females (N = 752) and males (N = 860) over the age of 12 controlling for age, race, and urinary creatinine. RESULTS: In males, urinary endocrine disrupting compound levels were negatively associated with thyroxine binding globulin (TBG) (β = -0.07; 95% CI: -0.13, -0.01) and total triiodothyronine (TT3) (β = -0.07; 95% CI: -0.13, -0.01). In females, urinary endocrine disrupting compound levels were positively associated with TBG (β = 0.11; 95% CI: 0.04, 0.18). However, this association was not statistically significant. CONCLUSIONS: This cross-sectional analysis provides additional evidence that environmental exposure to phthalates and phenols is associated with endocrine-related processes. Furthermore, these results suggested sex-specific differences in exposure to endocrine disrupting mixtures, and the exposure-response between endocrine disrupting mixtures and thyroid hormone levels. Specifically, higher exposure to a mixture of endocrine disrupting compounds was associated with lower levels of total T4 in males, but not in females. While a structural methodological framework was used to assess these complex relationships, the cross-sectional nature of this analysis limits causal inference and further research is needed to determine the clinical significance of these findings.	Environmental Research.2018;163:26-35	10.1016/j.envres.2018.01.039	29426025	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2889	Radwan M et al.	2018	Urinary Bisphenol A Levels and Male Fertility	Bisphenol A (BPA) is a high production volume industrial chemical found in many consumer products. BPA is a suspected potent endocrine disrupter, with endocrine disrupting properties demonstrated in animal studies. Few human studies have investigated its exposure in relation to male fertility and the results are diverse. We aimed to investigate this association in a population-based male fertility. Bisphenol A urinary concentrations were measured using gas chromatography coupled with tandem mass spectrometry in 370 men under 35 years of age with normal sperm concentration (≥15 mln/ml) recruited from a general population between 2012 and 2015 as partners of pregnant women participating in the REPRO_PL cohort study. Semen samples were collected by masturbation after 2-5 days of sexual abstinence. In multivariate linear regression analysis identified a positive association between the urinary concentration of bisphenol A (BPA 50th percentile and total sperm per ejaculate fraction (β = 0.17; 95% CI: 0.02, 0.32). Also after mediation by continence, total sperm count, motile sperm count and sperm chromosome disomy (β = 0.17; 95% CI: 0.02, 0.32). Also after mediation by continence, total sperm count, motile sperm count and sperm chromosome disomy (β = .35). Urinary concentration of BPA also increase the percentage of immature sperm (HDS) (β = .020) and decrease motility (β = .35). The study provides evidence that exposure to BPA is associated with poorer semen quality. Future studies are needed to confirm these findings.	Am J Mens Health.2018;:1557988318799163	10.1177/1557988318799163	30261816	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2890	Rocha BA et al.	2018	Advanced data mining approaches in the assessment of urinary concentrations of bisphenols, chlorophenols, parabens and benzophenones in Brazilian children and their association to DNA damage	Human exposure to endocrine disrupting chemicals (EDCs) has received considerable attention over the last three decades. However, little is known about the influence of co-exposure to multiple EDCs on effect biomarkers such as oxidative stress in Brazilian children. In this study, concentrations of 16 EDCs were determined in urine samples collected from 300 Brazilian children of ages 6–10 years and data were analyzed by advanced data mining approaches. Urinary concentrations of bisphenol A (BPA), 2,4-dichlorophenol (2,4-DCP), 2,5-dichlorophenol (2,5-DCP), 2,6-dichlorophenol (2,6-DCP), 2,4,5-trichlorophenol (2,4,5-TCP), ethyl-paraben (EtP), propyl-paraben (PrP), 2,3-dihydroxybenzoic acid (2,3-DHB), methyl-paraben (MeP), ethyl-paraben (EtP), 2,4-dihydroxybenzoic acid (2,4-DHB), 3-hydroxy-4-methoxybenzophenone (BP-1), 2,2'-dihydroxybenzophenone (BP-8), bisphenol A (bis(2,3-dihydroxypropyl)-cystyl) ether (BADGE.2H2O), 2,4-dichlorophenol (2,4-DCP), and 2,4-dichlorophenol (2,5-DCP) were found in >50% of the samples. Data mining techniques, such as Self-Organizing Maps (SOM), Hierarchical Cluster Analysis (HCA) and Principal Component Analysis (PCA), revealed that exposure to mixtures of EDCs were associated with personal care product (PCP) use. Particularly significant associations were found between urinary concentrations of BPA, EtP, PrP, 2,5-DHB, 2,6-DHB, 2,4-DHB, 2,4,5-TCP, 2,4-DCP, and 2,5-DCP. After clustering the data on the basis of 3 EDCs (response levels), 6 demographic (age, gender and geographic location), and 10 BDMDE (effect), two distinct clusters of samples (cases/controls) BDMDE concentrations was the most critical parameter that differentiated the two clusters, followed by DP. When BDMDE was removed from the dataset, predictability of classical variables increased in the order of: DI+ EtP > DI+ MeP > ILA-DHB > BPA > ILA-DCP > MeP > TCS > EtP > BP1 > 2,5-DCP. Our results showed that co-exposure to DI+ EtP, DI+ MeP, ILA-DHB, BPA, 2,4-DCP, MeP, TCS, EtP, BP1, and 2,5-DCP were associated to DNA damage in children. This is the first study to report exposure of Brazilian children to a wide range of EDCs, and the data-mining approach further strengthened our findings of chemical co-exposure and biomarkers of effect.	Environment International.2018;116:269-277	10.1016/j.envint.2018.04.023	29704805	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2891	Santiago B et al.	2018	Evaluation of Dose Dependent Maternal Exposure to Bisphenol A on Thyroid Functions in Newborns	Bisphenol A (BPA) is an endocrine disrupting chemical compound that is mainly used in industrial products as packaging and plastics. It usually transmits to humans via oral route from food contact material. BPA has demonstrated to be found in body fluids with a higher amount of fetal tissues due to bio accumulation. Although it has been reported to affect the endocrine system, results on thyroid functions of newborns are conflicting. The aim of the present study is to demonstrate the effect of different levels of BPA in cord blood on the thyroid function of newborns, according to gestational age (GA). The study population included 48 newborns. The BPA levels, Thyroid stimulating hormone (TSH) and free thyroxine (FT4) levels of cord blood were measured. In addition, SPINA-GT (thyroid hormone capacity), TSH Index (TSHI), standardized TSH (sTSH) and free thyroxine index (FTI) were calculated. Results: BPA was detected in 100% of the samples. The mean BPA level was 1.2 ng/mL. Significant correlations were found between BPA and thyroid hormone levels, as well as, SPINA-GT, TSHI, sTSH in both genders. CONCLUSION: Although BPA has been shown to cross placental barrier, no significant effect was detected on thyroid hormones, SPINA-GT, TSHI and sTSH. Further investigations with larger study populations are warranted.	Journal of Clinical Medicine.2018;7(6):	10.3390/jcm7060119	29882905	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2892	Savastano S et al.	2015	Bisphenol-A plasma levels are related to inflammatory markers, visceral obesity and insulin-resistance: a cross-sectional study on adult male population	BACKGROUND: The current increase of obesity and metabolic syndrome (MS) focuses attention on bisphenol-A (BPA), "damager" endocrine disruptor, multicaloric component. Aim was to verify the role of BPA in metabolic alterations, insulin resistance, low grade inflammation and visceral obesity. METHODS: A cross-sectional study was performed in 76 net of 139 environmentally exposed adult males, unselected Caucasian subjects, enrolled by routine health survey in the "Federico II" University of Naples outpatient facilities. BPA plasma levels (0.1-6.0 ng/mL), metabolic risk factors, markers of insulin resistance (index, plasma resistin) chemoattractant protein-1, interleukin-6 (IL-6) and tumor necrosis factor-alpha were performed. Clinical and biochemical parameters have been compared with BPA and pro-inflammatory cytokines. RESULTS: BPA was detectable in 76 subjects (54.7%). Subjects with detectable BPA showed higher body mass index (BMI) (p = 0.001), waist circumference (p = 0.001), fasting glucose (p = 0.001), HOMA-IR (p = 0.001), IL-6 (p = 0.001) and C-reactive protein (CRP) (p = 0.001) levels. Moreover, BPA and pro-inflammatory cytokine levels were significantly higher in subjects with increased adiposity (BMI > 30) and MS. BPA correlated with BMI, triglycerides, glucose homeostasis and inflammatory markers. At the multivariate analysis WC, and IL-6 revealed the main predictors of BPA. CONCLUSIONS: Detectable BPA plasma levels have been found also in our population. The strictly association between BPA and WC, components of MS, and inflammatory markers, further supports the BPA role in visceral obesity-related low grade chronic inflammation.	Journal of Translational Medicine.2015;13:	10.1186/s12967-015-0532-y	26021871	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2893	Scinicariello and M F et al.	2016	Serum Testosterone Concentrations and Urinary Bisphenol A, Benzophenone-3, Triclosan, and Paraben Levels in Male and Female Children and Adolescents: NHANES 2011-2012	BACKGROUND: Exposure to environmental phenols (e.g., bisphenol A, benzophenone-3, and triclosan) and parabens is widespread in the population. Many of these chemicals have been shown to have anti-androgenic activity in animal studies. OBJECTIVES: We evaluated the cross-sectional associations between urinary concentrations of bisphenol A, benzophenone-3, triclosan, and parabens and serum testosterone in children and adolescents. METHODS: We used data from participants 6-19 years in the National Health and Nutrition Examination Survey (NHANES) 2011-2012. We performed multivariable linear regression to estimate associations between natural log-transformed serum TT and quartiles of urinary BPA, BP-3, TCS, and parabens. In male and female children (ages 6-11 years) and adolescents (ages 12-19 years). RESULTS: TCS and BPA were associated with significantly lower TT in male adolescents, and BPA was associated with significantly higher TT in female adolescents. TT was not consistently associated with TCS or total paraben in children or adolescents of either sex. CONCLUSIONS: To our knowledge, this is the first study to report an association of both BP-3 and BPA with serum TT in adolescents. Associations between BPA and TT differed according to sex in adolescents, suggesting that BPA may have different effects on androgen activity in males and females. Because of the cross-sectional design, further studies are needed to confirm and elucidate on our findings. Citation: Scinicariello F, Buser MC. 2016. Serum testosterone concentrations and urinary bisphenol A, benzophenone-3, triclosan, and paraben levels in male and female children and adolescents: NHANES 2011-2012. Environ Health Perspect 124:1888-1894; http://dx.doi.org/10.1289/EHP250.	Environmental Health Perspectives.2016;124(12):1898-1904	10.1289/EHP150	27383665	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2894	Shiue I et al.	2013	Urinary environmental chemical concentrations and vitamin D are associated with vision, hearing, and balance disorders in the elderly	BACKGROUND: Acute exposure to environmental chemicals can result in loss of consciousness and upon recovery neurological symptoms, but little evidence exists in large epidemiological human studies. Hence, it was hypothesized that urinary chemical concentrations, including bisphenol A (BPA), phthalates, and polycyclic aromatic hydrocarbon (PAH) biomarkers, are associated with vision, hearing, and balance disorders in a national population-based setting. METHODS: United States National Health and Nutrition Examination Survey is a national population-based multi-year cross-sectional study. Information on demographics and vision, hearing, and balance disorders was obtained by household interview, using questionnaires in the 2005-2006 cohort (aged 60 and above). Urinary environmental chemicals were detected by mass spectrometry. Logistic and multinomial logistic regression models, RESULTS: Urinary cotinine, molybdenum, and tungsten concentrations, which are commonly associated with chronic disease, were associated with vision disorder. Urinary 2,5-dichlorophenol and arsenic acid concentrations and circulating mono-n-butyl phthalate, mono-benzyl phthalate, and mono-(3-carboxypropyl) phthalate metabolites were associated with hearing disorder. Urinary 2,5-dichlorophenol, 2,4-dichlorophenol, and mono-benzyl phthalate concentrations, and circulating PAH were associated with balance disorder. Urinary cadmium was associated with tendency to have higher urinary benzene, 2,4-dichlorophenol, and mono-benzyl phthalate concentrations. CONCLUSIONS: Significant correlations were observed in urinary environmental chemicals and neurobehavioral impairment for the first time. However, the causation cannot be established due to its cross-sectional study design. Future studies with a longitudinal aspect and/or in clinical trials are warranted to clearly understand the biological mechanisms along the pathway before drawing a firm conclusion on these relationships.	Environment International.2013;53:41-48	10.1016/j.envint.2012.12.006	23314200	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2895	Spanier AJ et al.	2014	Bisphenol A Exposure Is Associated with Decreased Lung Function	OBJECTIVE: To examine the associations of bisphenol A (BPA) exposure with lung function measures and exhaled nitric oxide (FeNO) in children. STUDY DESIGN: We performed a cross-sectional analysis of a subsample of 15 children age 6-18 years who participated in the 2007-2010 National Health and Nutrition Examination Survey. We assessed univariate and multivariable associations of urinary BPA concentration with the predicted pulmonary function measures for age, sex, race/ethnicity, and height. Univariate outcomes in 1 unreliable (FVC), bronchial responsiveness (FEV1), bronchodilator response (FEV1), and exhaled NO (FeNO). RESULTS: Exposure and outcome data were available for 182 children. Median BPA was 2.4 ng/mL (IQR: 1.2, 4.5). In multivariable analysis, a larger urinary BPA concentration was associated with significantly decreased FVC (-0.08 L; 95% CI: -0.14, -0.02) and FEV1 (-0.07 L; 95% CI: -0.13, -0.01). Children in the highest BPA quartile had a 10% decrease in FVC and FEV1 (95% CI: -16, -3) and 3% decrease in %FVC/FVC (95% CI: -5, -1) compared to children in the lowest BPA quartile. In addition, children in the highest BPA quartile had a 20% decrease in %FEF25-75/FEV1 (95% CI: -31, -7) and 3% decrease in %FVC/FVC (95% CI: -5, -1). CONCLUSIONS: BPA exposure was associated with a modest decrease in %FEF25-75/small airways function and %FVC/FVC (pulmonary obstruction) but not FEV1, FVC, or FeNO. Explanation of the association cannot rule out the possibility of reverse causality.	Journal of Pediatrics.2014;164(6):1403-+	10.1016/j.jpeds.2014.02.026	24657123	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2896	Supornsilchai V et al.	2016	Increased levels of bisphenol A (BPA) in Thai girls with precocious puberty	BACKGROUND: Reports on the vascular toxicity of potential smart indicator exerted earlier start especially in girls. Bisphenol A (BPA), which possess estrogenic activity, might be a cause of advanced puberty. The objective of this study was to compare urinary BPA concentrations between girls with precocious puberty and normal girls. METHODS: Girls with precocious puberty (PP) and normal girls (NG) were recruited. Anthropometric measurements, estradiol, basal and gonadotropin-releasing hormone (GnRH)-stimulated follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels, uterine size, ovarian diameters, and bone ages were obtained. Urinary BPA concentrations were analyzed by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MSMS) with the lower limit of quantification (LLOQ) of 0.05 ng/mL. RESULTS: The median adjusted BPA concentration in advanced puberty group was higher than in control groups (1.8 vs. 0.9, p = 0.03). The positive BPA rate (%) in girls with precocious puberty (PP) was significantly higher than in normal girls (NG) (p = 0.04). We also found that the median adjusted BPA concentrations in girls with advanced puberty who were overweight/obese, was greater than in the normal pubertal overweight/obese girls (1.7 vs. 0.9 μg/g Cr, p=0.05), and was in the same trend among normal weight girls with advanced sexual puberty (0.8 vs. 0.6 μg/g Cr, p=0.09), but not statistically significant. CONCLUSIONS: The present findings suggest that BPA exposure appears to be related to an earlier age at onset of puberty especially in obese girls.	Journal of Pediatric Endocrinology & Metabolism.2016;29(11):1233-1239	10.1515/jpem-2015-0326	26812862	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2897	Tai and Y XC et al.	2016	Urinary bisphenol A concentrations positively associated with glycated hemoglobin and other indicators of diabetes in Canadian men	BACKGROUND: Bisphenol A (BPA), an endocrine disrupting chemical (EDC), may pose a risk to human health, including diabetes. However, epidemiological studies from the U.S., China and South Korea showed inconsistent results. OBJECTIVE: To examine the associations between BPA and indicators of diabetes in the general Canadian population. METHODS: The analysis was based on cross-sectional data from the Canadian Health Measures Survey (CHMS) Cycle 2 (2009-2011). We included 1824 participants with glycated hemoglobin (HbA1c) measurement and 3009 participants with serum glucose (SG) measurement aged 3-79 years. Urinary BPA was measured using online solid phase extraction coupled to high performance liquid chromatography-tandem mass spectrometry (LC-MS/MS). Multivariate linear regression models (ages 20-79 years) were conducted to evaluate the association between BPA and physician-diagnosed diabetes mellitus (DM). Bootstrap weights were applied to all the analyses to account for the complex survey design. RESULTS: The geometric mean of urinary BPA was 1.21 (+0.05 μg/L). Overall, a positive association was observed between urinary BPA quartiles and HbA1c levels in men after controlling for potential confounders (P=0.05), but not in women and children. Similar patterns were found for the associations of BPA with log-transformed SG levels and doctor-diagnosed DM. CONCLUSIONS: Higher urinary BPA levels were associated with adverse glucose homeostasis in Canadian men, independent of major covariates. Prospective studies with longitudinal design are needed to further investigate the causality.	Environmental Research.2016;147:172-178	10.1016/j.envres.2016.02.006	26890259	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2898	Teeguarden JG et al.	2015	24-hour human urine and serum profiles of bisphenol A: Evidence against sublingual absorption following ingestion in soup	Extensive first-pass metabolism of ingested bisphenol A (BPA) in the gastrointestinal tract and liver results in blood concentrations of bioactive BPA on <1% of total BPA in humans and non-human primates. Absorption of ingested BPA through non-metabolizing tissues of the oral cavity, recently demonstrated in dogs, could lead to the higher serum BPA concentrations reported in some human biomonitoring studies. We hypothesized that BPA in soup would be absorbed through the oral cavity in humans, and that the resulting higher systemic exposure to bioactive BPA would be reflected in greater urinary excretion of BPA bioavailability and higher serum BPA concentrations. Concurrent serum and urine concentrations of all BPA, and BPA glucuronide and sulfate conjugates, were measured in 6 adult men and women following ingestion of 30mcg 4C-BPA/kg body weight in soup. Absorption of all 4C-BPA was rapid (t1/2=0.49h) and elimination of the administered dose was complete (96-post ingestion, evidence against any bioactive BPA. The maximum serum 4C-BPA concentration was 0.26±0.at 1.4h after administration and represented <0.1% of total 4C-BPA. Pharmacokinetic parameters, pharmacokinetic model simulation, and the significantly faster appearance half-life of 4C-BPA glucuronide compared to 4C-BPA (0.29h vs 0.69h) are evidence against meaningful absorption of BPA in humans through any non-metabolizing tissue (<1%). This study confirms that typical exposures to BPA in food products presented in subpotencies serum BPA concentrations in humans, not all concentrations reported in some biomonitoring studies.	Toxicology and Applied Pharmacology.2015;288(2):131-142	10.1016/j.taap.2015.01.009	25620055	ヒト	-	-	-	-	-	-	-	-	臨床暴露試験	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	●	-	-
統合_2899	Verstraete SG et al.	2018	Bisphenol a increases risk for presumed non-alcoholic fatty liver disease in Hispanic adolescents in NHANES 2003-2010	BACKGROUND: Bisphenol-A (BPA) is a ubiquitous chemical and recognized endocrine disruptor associated with obesity and related disorders. We explored the association between BPA levels and suspected non-alcoholic fatty liver disease (NAFLD). METHODS: Unweighted analyses were used to study the relationship between urinary BPA levels and suspected NAFLD (alanine aminotransferase (ALT) > 30 U/L body mass index (BMI) > 95th percentile) in adolescents (12-19 years) participating in NHANES 2003-2010. Weighted analyses were used to estimate the prevalence of suspected NAFLD and to evaluate the risk with any detectable ALT. RESULTS: We included 882 adolescents with urinary BPA and fasting laboratory data from a total of 1988 adolescents. Mean age was 15.4 years. Detectable urinary BPA was found in a quarter of the sample (25.2 ng/mL) when compared to the first (< 1.4 ng/mL) (Odds Ratio (OR) 0.33, 95% Confidence Interval (CI) 0.16-0.67). The OR for the third and second quartiles were positive but did not reach statistical significance. The association was strongest in Hispanics (n = 344) with BPA levels in the second (OR 0.12, 95% CI 0.03-0.55) quartile and when limiting the analysis to obese adolescents (n = 332), in the second (OR 0.06, 95% CI: 1.26-35.06) and fourth BPA quartiles (OR 0.06, 95% CI: 1.07-36.23) compared to the first quartile. BPA levels were not associated with ALT elevation. CONCLUSIONS: The risk of suspected NAFLD is increased in participants in higher quartiles of BPA exposure, particularly in those of Hispanic ethnicity. Further studies are required to fully understand the potential role of BPA in non-alcoholic fatty liver disease.	Environmental Health.2018;17:	10.1186/s12940-018-0356-3	29391015	ヒト	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2900	Wan Y et al.	2018	Relationship between maternal exposure to bisphenol S and pregnancy duration	Bisphenol-S (BPS) has been progressively used due to the potential safety problems of bisphenol-A (BPA). Thus Human studies are needed to investigate the developmental effects of BPS. In this study, the impact of maternal BPS exposure on birth outcomes was evaluated with linear and logistic regression models. BPS was analyzed in each urine samples collected from 888 pregnant women at admission to labor. It was found in 90.7% of the urine samples with the specific gravity adjusted geometric mean concentration of 0.17 μg/L. Due to unit increase in urinary BPS was associated with a 0.72-day increase in pregnancy duration (95% CI: 0.16, 1.28). When stratified by fetal sex, each 1-unit increase in maternal urinary BPS was significantly correlated with increased gestational age (adjusted β = 1.02). With confidence intervals (CI) 0.47, 1.57) and increased odds of late-term birth (adjusted odds ratio = 1.29, 95% CI: 1.00, 1.67) in girls, but not significantly for boys. Including maternal urinary BPS and BPA in one model did not change the results. Associations of BPS with birth outcomes were similar to those of BPA. Our results suggested that maternal exposure to BPS, a substitute for BPA, was also significantly associated with increased gestational age, suggesting maternal BPS exposure may interfere with pregnancy duration. The findings require replication but reveal the possible risks posed by the development BPS exposure.	Environ Pollut. 2018 Jul;238:717-724.	10.1016/j.envpol.2018.03.057	29621731	ヒト	生殖発生	-	-	-	-	-	-	-	コホート研究	1	1	-	-	-	-	-	-	1	1	1	-	●	-	-	-	-	-	-	-	-	-

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	遺伝毒性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2901	Wang TG et al.	2015	Association of Bisphenol A Exposure With Hypertension and Early Macrovascular Diseases in Chinese Adults A Cross-Sectional Study	Bisphenol A (BPA) is an environmental endocrine disruptor that has been associated with cardiovascular outcomes in previous observational studies. We aimed to examine the relationships of urinary BPA levels with hypertension and early macrovascular diseases.This is a cross-sectional study. From June through August 2009, 3246 participants ages 50 years or older were enrolled from Baoshan District, Shanghai, China. Logistic regression models were used to examine the relationship of BPA with hypertension and carotid intima-media thickness (CIMT) and carotid plaque, 2 indicators of early macrovascular disease. We also performed stratification analysis by age and sex.The median (interquartile range) for BPA was 3.55 (2.66, 5.01) ng/mL, which is notably lower than previously reported in the United States and other Western countries. Urinary BPA concentrations were negatively associated with hypertension (multivariable-adjusted OR for the highest versus lowest BPA quartile = 0.61; 95% confidence interval [CI]: 0.48, 0.80). Similarly, BPA was inversely associated with CIMT (multivariable-adjusted OR = 0.68; 95% CI: 0.54, 0.87). The corresponding OR for PWV (50 versus lower) was not significant (OR = 0.88; 95% CI: 0.28, 2.80). The negative associations of BPA with hypertension, elevated CIMT, and arterial stiffness were consistent across 3 strata (sex and age) and robustness, and were stronger among participants ≥ 65 versus <65 years of age, and among women than men.In contrast with previous investigations, our study suggests negative associations of BPA exposure with hypertension and early macrovascular diseases among middle-aged and elderly Chinese. Future investigations are needed to draw more definite conclusions and generalize to other populations.	Medicine.2015;94(43):7	10.1097/MD.0000000000001814	26512580	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2902	Wang X et al.	2017	Urinary Bisphenol A Concentration and Gestational Diabetes Mellitus in Chinese Women	BACKGROUND: Bisphenol A (BPA) has been associated with variable metabolic effects in animal models. It is unknown whether BPA exposure affects glucose tolerance in pregnancy. We aimed to investigate whether urinary BPA concentrations were associated with gestational diabetes mellitus (GDM) in Chinese women.METHODS: Urinary BPA concentrations in 1,060 pregnant women from China's Healthy Baby Cohort Study were measured by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). GDM (n = 79) was diagnosed according to the criteria of the International Association of Diabetes and Pregnancy Study Groups. RESULTS: Multivariate regressions were used to explore the relationships of urinary BPA with GDM, plasma glucose levels in the 1-h 2-hour oral glucose tolerance test (OGTT), birth weight, and ponderosity. RESULTS: The geometric mean of BPA was 1.32 ng/mL. After adjustment for maternal age, education, husband smoking status, prepregnancy body mass index (BMI), and urinary creatinine concentration, plasma glucose at 2 hours in the 75 g OGTT was 0.38 mmol/L (95% confidence index [CI] = 0.73, 0.16) for women with urine BPA in the highest versus the bio tertile. For each unit increase in natural log-transformed BPA, the odds ratio for GDM was 1.49 (95% CI: 1.08, 2.06). Women with urine BPA in the highest versus the lowest tertile gained 0.63 kg/m2 more BMI (95% CI: 0.01, 1.26). BPA was decreased by 0.03 (95% CI: -0.05, -0.01) and 0.04 (95% CI: -0.06, -0.02) BMI units per doubling of urinary BPA concentrations, respectively. CONCLUSIONS: Higher maternal urinary BPA concentrations were associated with reduced risk of GDM and marginally lower birth weight and ponderosity.	Epidemiology.2017;28:541-547	10.1097/EDE.0000000000000730	29028674	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2903	Wang ZL et al.	2017	Urine bisphenol A and pubertal development in boys	BACKGROUND: Bisphenol A (BPA) is an environmental endocrine disruptor and is found in many consumer products. Animal studies suggest that BPA may perturb pubertal development in males, although studies in humans are limited.METHODS: We measured urinary BPA concentrations in 1,151 boys from Shanghai, China, and assessed pubertal development in 2014 and 2015. The boys were from three schools (one elementary, one middle, and one high school) in Shanghai were enrolled in a cross-sectional study. Tanner stages for genital and pubic hair development and testicular volume were assessed by a age-friendly trained physician. Information concerning carriers he was self-reported. Urine samples were collected to examine peripubertal BPA exposure levels. Associations between BPA exposure and pubertal development were examined using logistic regression models.RESULTS: The geometric mean urinary BPA concentration was 1.6 ng/mL. Boys with urine BPA in the highest tertile had 1.61 times the odds of pubic hair development (95% confidence intervals [CIs]: 1.02, 2.55) and 1.72 times the odds of testicular development (95% CI: 1.08, 2.73) compared with those in the lowest tertile. Further stratification showed that the BPA-associated ORs were 2.35 (95% CI: 1.03, 5.37) for pubic hair development in boys aged 10-11 years and 2.28 (95% CI: 1.02, 5.08) for testicular development in boys aged 12-13 years. No associations were observed in boys aged 14-15 years. Urine BPA was not associated with genital development.CONCLUSIONS: Our findings indicate an association between peripubertal BPA exposure and early pubertal onset, but delayed pubertal progression, in boys. Longitudinal studies of male pubertal development with periodic follow- up are needed to verify these results.	International Journal of Hygiene and Environmental Health.2017;220(1):43-50	10.1016/j.ijheh.2016.10.004	27769633	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2904	Yang CW et al.	2014	Visualized Gene Network Reveals the Novel Target Transcripts Sox2 and Pax6 of Neuronal Development in Trans-Placental Exposure to Bisphenol A	BACKGROUND: Bisphenol A (BPA) is a ubiquitous endocrine disrupting chemical in our daily life, and its health effect in response to prenatal exposure is still controversial. Early-life BPA exposure may impact brain development and contribute to childhood neurological disorders. The aim of the present study was to investigate molecular target genes of neuronal development in trans-placental exposure to BPA.METHODS:GEO (A meta-analysis of three public microarray datasets was performed to screen for differentially expressed genes (DEGs) in exposure to BPA. The candidate genes of neuronal development were identified from gene ontology analysis in a mammalian neuronal-cell network, and their gene expressions were determined using real-time PCR in 22-week-old fetal brains exposed to BPA. Immunofluorescent and Bromodeoxyuridine (BrdU) incorporation assays were used to examine the role of Sox2 and Pax6 in cell cycle progression of human neural progenitor cells (hNPCs).RESULTS: Among 96 neuronal transcripts, we found ten DAVID ontology clusters of 107 DEGs using the analysis of Bioconductor limma package, on-board two neuronal genes, we determining region of interest (ROI) and Pax6 in the cerebral cortex of human fetuses exposed to BPA. Knockdown of Sox2 and Pax6 in hNPCs by shRNA significantly reduced the BrdU-positive cells. Sox2 knockdown also induced cell cycle arrest at the G0/G1 phase, whereas Pax6 knockdown induced cell cycle arrest at the G2/M phase

別添-2　統合文献リスト

通格性評価（動物）1：該当、0：該当しない　　通格性評価（疫学）1：該当、0：該当しない　　通格性評価（in vitro）1：該当、0：該当しない　　通格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに通格性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。　　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	通格性評価基準適合（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2914	池野 みさ ら	2013	【乗原・薬物障害】 ビスフェノールA取扱業従事者に生じた白斑の2例	要約Abstract 化学物質 はフェノール化合物の一種である。 BPA 発泡樹脂容器 食品 の重合剤として利用 等 その 用 途 は 多 岐 に 渡 る。 BPA 発泡樹脂 は 、 主 に 食品 容器 、 BPA 発泡樹脂 は 、 主 に 食品 容器 、 BPA 発泡樹脂 は 、 主 に 食品 容器 、

別添-2 統合文献リスト

曝露性評価（動物）1：該当、0：該当しない

曝露性評価（疫学）1：該当、0：該当しない

曝露性評価（in vitro）1：該当、0：該当しない

曝露性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに曝露性基準不適合と判断されるもの以外を後続性評価へ進め、後続性評価段階で原著に基づき精査。

引用評価機関
●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	曝露性評価基準通過（1534報）	後続性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2927	Zheng LY et al.	2017	Environmental exposures and pediatric kidney function and disease: A systematic review	BACKGROUND: Environmental chemical exposures have been implicated in pediatric kidney disease. No appraisal of the available evidence has been conducted on this topic. METHODS: We performed a systematic review of environmental exposures and pediatric kidney function and disease in children and adolescents (≤ 21 years) using PubMed, Embase, Web of Science, and TOXLINE databases. We found 83 studies that met the search criteria and were included in this systematic review. Environmental exposures reviewed herein included lead, cadmium, mercury, arsenic, fluoride, aflatoxin, melamine, environmental tobacco, bisphenol A, dental procedures, phthalates, trichloroacetic acid, triclosan, and theTaishan Solution. Most studies assessed environmental chemical exposure via biomarkers but four studies assessed exposure via proximity to a hazardous source. There was mixed evidence of associations between metal exposures, and other non-metal environmental exposures, and pediatric kidney disease and other kidney disease biomarkers. The evaluation of causality is hampered by the small numbers of studies for each type of environmental exposure, as well as lack of study quality and limited prospective evidence. CONCLUSION: There is a need for well-designed epidemiologic studies of environmental chemical exposure and kidney disease outcomes.	Environmental research,2017;158:625-648	10.1016/j.envres.2017.06.029	28727988	ヒト	-	-	-	-	-	-	-	システマティックレビュー	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2928	Stahlhut RW et al.	2018	Experimental BPA exposure and glucose-stimulated insulin response in adult men and women	Context: Human cross-sectional and animal studies have shown an association of the chemical bisphenol A (BPA) with insulin resistance, type 2 diabetes, and other metabolic diseases, but no human experimental study has investigated whether BPA alters insulin/C-peptide secretion. Design: Men and postmenopausal women (without diabetes) were orally administered either the vehicle or a BPA dose of 50 microg/kg body weight, which has been predicted by US regulators (Food and Drug Administration, Environmental Protection Agency) to be the maximum safe daily oral BPA dose over the lifetime. Insulin response was assessed in two cross-over experiments using an oral glucose tolerance test (OGTT; experiment 1) and a hyperglycemic (HG) clamp (experiment 2). Main outcomes were the percentage change of BPA session measures relative to those of the vehicle session in incremental total area under the curve (iAUC) for insulin and C-peptide, the ratio of the C-peptide iAUC to the glucose iAUC (insulinogenic index), the Matsuda insulin sensitivity index, and the percentage change in the insulinogenic index (Supervisor - 1.00), an indicator of early-phase insulin response, and the equivalent C-peptide index (Pancan - 1.637), in the HG clamp study, focusing on the later-phase insulin response to a stable level of glucose. Several measures of insulin and C-peptide appeared suppressed during the BPA session relative to the control session; the change in insulin-motion concentration (Cmax) was negatively correlated with NOAEL and the Cmax of bioactive serum BPA. Conclusions: This exploratory study suggests that BPA exposure in a dose considered safe by US regulators may alter glucose-stimulated insulin response in humans.	J Endocr Soc. 2018 Sep 12;2(10):1173-1187.	10.1210/js.2018-00151	30302422	ヒト	代謝	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2929	Correia-Sá L et al.	2017	Exposure assessment to bisphenol A (BPA) in Portuguese children by human biomonitoring	Exposure to bisphenol A (BPA) is known to be widespread and available data suggests that BPA is not act as an endocrine disruptor. Diet is generally regarded as the dominant BPA exposure source, namely through leaching from food packaging. The aim of this study was to assess BPA exposure in Portuguese children by urinary BPA biomonitoring. A total of 120 children (6-9 years old) were recruited in Porto. Anthropometric weight (underweight children with no dietary control, the healthy diet group (n = 60) comprised children diagnosed for obesity/overweight but those other known associated diseases that were not on a healthy diet for weight control. First morning urine samples were collected and total urinary BPA was analysed after enzymatic hydrolysis via on-line SPE-LC-MS/MS, with isotope dilution quantification. Virtually all the children were exposed to BPA (LOD = 0.1 ng/mL; LOQ = 0.3 ng/mL; detection frequency = 99.2%). Median BPA concentrations were 1.1 ng/mL (creatinine corrected: 0.9 ng/mg creatinine; CI95: 0.7-1.2) and 1.0 ng/mL (creatinine corrected: 0.9 ng/mg creatinine) in the healthy diet group, but differences were not significant. Estimated daily intakes, however, were significantly higher in children of the regular diet group than in children of healthy diet group. Median (95th percentile) daily intakes amounted to 0.5 (0.07) ng/kg body weight/day in the regular diet group, and 23.2 (301) ng/kg body weight/day in the healthy diet group. Multiple logistic regression analysis revealed that children in the healthy diet group had 20% lower intakes than children in the regular diet group (aOR:0.81; 95% CI: 0.65-0.89). For both groups, however, urinary BPA levels and daily BPA intakes were within the range reported for other children's populations and were well below health guidance values such as the European Food Safety Authority (EFSA) temporary tolerable daily intake (t-TDI) of 5 mg/kg body weight/day. In addition, levels daily BPA intakes were even likely linked with the inherent dietary approach rather than with BPA itself or directly.	Environmental science and pollution research international,2017;24(35):27502-27514	10.1007/s11356-017-0358-7	28980160	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2930	Lu Y et al.	2016	Exposure of children to BPA through dust and the association of urinary BPA and triclosan with oxidative stress in Guangzhou, China	Both bisphenol A (BPA) and triclosan (TCS) are phenolic compounds widely used in a variety of household applications. These compounds could be released into the environment, enter the human body and cause a variety of potential health hazards. Children are sensitive and susceptible to these contaminants. To investigate the potential oxidative DNA damage from exposure to BPA and TCS, ninety-six urine samples of children (aged 3-6 years) were collected from Guangzhou, China, in December 2013. Urinary BPA and TCS were analyzed by high-performance liquid chromatography-tandem mass spectrometry. Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) was determined using a bench chromatography-tandem mass spectrometer. The geometric mean concentrations of urinary BPA, TCS and 8-OHdG were 1.08 μg/g Cr (1.1-28 μg/L), 2.1 and 1.96 μg/g Cr (1.1-28 μg/L), respectively. The results showed that both BPA and TCS exposure, were associated with oxidative damage. Significant dose-effects existed between the urinary BPA, TCS levels, and the 8-OHdG concentrations. Multiple linear regression analysis showed that one percent increase in BPA and in TCS could generate 0.35% and 0.281% increase in 8-OHdG in urine for children in Guangzhou. We also determined the concentrations of BPA in dust using high performance liquid chromatography. The mean concentration of BPA was 336 μg g(-1) in indoor dust and 2.21 μg g(-1) in outdoor dust. The dust contributes approximately 4.25% to the urinary BPA exposure for the children. In conclusion, BPA and TCS exposure correlates with oxidative DNA damage.	Environmental science. Processes & impacts,2016;18(12):1492-1499	10.1039/c6em00472e	27808329	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2931	Xie M et al.	2016	Exposure to bisphenol A and the development of asthma: A systematic review of cohort studies	BACKGROUND: There is conflicting evidence about the association between bisphenol A (BPA) exposure and childhood asthma risk. We aimed to review the epidemiological literature on the relationship between prenatal or postnatal exposure to BPA and the risk of childhood asthma between 1870-2015. The PubMed database was systematically searched, and additional studies were found by searching reference lists of relevant articles. RESULTS: Six studies fulfilled the eligibility criteria. Three studies found that prenatal BPA exposure is associated with an increased risk of childhood asthma, while another study reported a reduced risk of wheeze. Two studies found that postnatal BPA exposure is associated with an increased risk of childhood asthma. The evidence for the association between BPA exposure and childhood asthma is inconsistent. Besides, the influence of BPA exposure during the second trimester of pregnancy on the prevalence of childhood asthma was inverted. Further studies are urgently needed to explore the underlying mechanisms about adverse effect of BPA exposure on childhood wheeze/asthma.	Reproductive toxicology (Elmsford, N.Y.),2016;65:224-229	10.1016/j.reprotox.2016.08.007	27542534	ヒト	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2932	LaKind JS et al.	2019	Factors affecting interpretation of national biomonitoring data from multiple countries: BPA as a case study	INTRODUCTION: The use of biomonitoring data as an indicator of national levels of human exposure to environmental chemicals has grown in importance and prevalence. Nationally representative urinary bisphenol A (BPA) data are now available for Canada, the United States and Korea. Here we address the following questions: Are urinary BPA data from these countries comparable? What can be discerned regarding geographic and/or temporal similarities or differences? Are there generalizable lessons to be learned regarding comparison of biomonitoring results from different countries? METHODS: We examined underlying methods and resultant urinary BPA data from national surveys of three countries: Canada (Canadian Health Measures Survey, CHMS, 2009-2015); United States (National Health and Nutrition Examination Survey, NHANES, 2009-2014); and Korea (Korean National Environmental Health Survey, KoNEHS, 2012-2014). RESULTS: Urinary BPA data from Canada, Korea and the US are not directly comparable due to differences in methods for analyzing urine samples for BPA and participants in national surveillance sampling and subsequent results. Total BPA data are only used in the CHMS program. There were geographic differences in fasting times of participants. Median urinary BPA levels in Canada remained relatively constant over the three cycles (1.2-1.3 ng/mL), while US levels decreased from 1.3 to 1.0 ng/mL and Korean levels increased from 0.7 to 1.3 ng/mL over similar time periods. The most recent survey year data indicate that levels in all three substantially across countries. Canadian urinary BPA levels have been stable; non-significant decreases in males may be due to higher body weight in the more recent Canadian surveys. In contrast, the decrease in intakes in the US appears to be due to decreases in urinary BPA as body weights in the US have been stable. Korean urinary BPA levels have increased substantially over the survey years. DISCUSSION: Differences in urinary BPA levels between countries may be due to differences in methodological differences, methods for dilution adjustment, and population characteristics should be carefully considered when interpreting biomonitoring data. Despite the plethora of publications describing issues with use of creatinine levels for urinary dilution adjustment, there have been no major methodological advances that could assist in interpreting urinary chemical data. A combination of biomonitoring and traditional exposure assessment approaches may be needed to fully assess human exposures to BPA and other chemicals. CONCLUSIONS: National biomonitoring surveys provide important information on population levels of chemicals such as BPA and can assist in understanding temporal and geographic similarities, differences, and trends. However, caution must be exercised when using these data to draw anything but broad conclusions. Even when methodological differences are considered, it is difficult to compare urinary BPA data from different countries. Urinary BPA data from Canada, the US and Korea are not directly comparable. Only the national-scale monitoring of BPA described here, they must be considered when comparing data for other chemicals measured as part of both national and smaller scale biomonitoring based research as well as for BPA data from other studies.	Environmental research,2019;173:318-329	10.1016/j.envres.2019.03.047	30951958	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2933	Nahar MS et al.	2015	In utero bisphenol A concentration, metabolism, and global DNA methylation across matched placenta, kidney, and liver in the human fetus	While urine has been an easily accessible and feasible matrix for human biomonitoring, analytical measurements in internal tissues and organs can provide more accurate exposure assessments to understand disease etiology. This is especially important for the endocrine active compound, bisphenol A (BPA), where studies investigating internal doses at sensitive periods of human development are currently lacking. Herein, BPA concentrations, BPA-specific metabolizing enzyme gene expression, and global DNA methylation were characterized across three matched tissues from elective pregnancy terminations of 2nd trimester human fetuses: the placenta, liver, and kidney (N= 22 each; 76-106 days). Compared to liver (geo. mean 0.65 ng/g), 4.1, 89% concentrations were lower in matched placenta (2.69 (15.6) ng/g; 17) and kidney (11.8 (1.1) ng/g; 21) samples. BPA-specific metabolism gene expression of UGT2B, UGT2B15, STS, and SULT1A1 differed across each tissue type; however, conjugation and deconjugation expression patterns were similar across the tissues. Average DNA methylation was highest in placenta (74.2%), followed by liver (73.2%) and kidney (72.2%). Methylation of repetitive elements LINE-1 and Alu was significantly correlated between placenta and liver (Alu: rho = 0.47, p = 0.03; LINE-1: rho = 0.47, p = 0.03), but not between placenta and kidney or liver and kidney. Placental BPA concentrations were positively associated with global methylation for the placenta only using the LINE-1 assay (p value 0.001) and GLOBAL content (p value <0.001). Total BPA concentrations were positively associated with global methylation for the placenta only using the LINE-1 assay (p value 0.002), suggesting organ-specific biological effects after fetal exposure. Utilizing sensitive human clinical specimens, results are informative for BPA toxicokinetics and toxicodynamics assessment in the developing human fetus.	Chemosphere,2015;124:54-60	10.1016/j.chemosphere.2014.10.071	25434263	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2934	Sangani S. DA et al.	2016	Integrated exposure and risk characterization of bisphenol-A in Europe	The current study aims at a comprehensive risk characterization of bisphenol A (BPA) supported by an integrated exposure modelling framework that comprises for field and near-field exposure modelling coupled to a dynamic lifetime PBPK model. Exposure analysis was done on European data of BPA food residues and human biomonitoring (HBM). The latter were further assimilated through an advanced exposure reconstruction modelling framework to estimate the corresponding external and internal systemic dose of BPA and its metabolites. Special attention was paid on the assessment of exposure to BPA during critical developmental life-stages such as gestation by modelling the mother-fetus toxicokinetic interaction. Our findings showed that current exposure levels in Europe are below the temporary Tolerable Daily Intake (t-TDI) of 4 μg/kg_bw/d proposed by EFSA. Nevertheless, the risk characterization ratios indicated a potential risk for high exposed consumers, which was also confirmed by the margin of exposure (MoE) approach. The MoE values were below 1000, indicating more toxicological effects when BMDL modelling from toxicology the BMDL temporary level daily intake (t-TDI) was equivalent internal dose. Use of the ToxCast/Tox21 Biological Pathway Altering Dose (BPAD) as an alternative internal exposure reference value, resulted in increased margins of safety compared to the conventional exposure/risk characterization scheme.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association,2016;98(Pt B):134-147	10.1016/j.fct.2016.10.017	27769850	ヒト	-	-	-	-	-	-	暴露推定	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2935	Jin H et al.	2018	Occurrence and Partitioning of Bisphenol Analogues in Adults' Blood from China	Widespread human exposure and associated adverse health effects led to regulations on the usage of bisphenol A (BPA). Several bisphenol analogues, BPs have been introduced as BPA alternatives in various applications. However, these BPs have been shown to exhibit similar or even stronger endocrine-disrupting activities, compared with that of BPA. Currently, information on the human exposure to BPs alternatives remains limited. In this study, nine BPs were quantified in 82 pairs of plasma and red blood cell (RBC) samples from Chinese participants, to human plasma, the predominant BPs was BPA, bisphenol S (BPS), and bisphenol AF (BPAF) were frequently detected in RBC fraction. Estimated total daily intake (EDI) of BPA was in the range of 0.0008-0.79 μg/kg bw/day for the participants, and adults aged >50 years had comparatively lower EDI. To our knowledge, this is the first study to assess the occurrence and partitioning of BPA alternatives in normal human plasma and RBCs from the Chinese general population.	Environmental Science and Technology,2018;52(2):812-820	10.1021/acs.est.7b03958	29243481	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2936	Myridakis A et al.	2015	Phthalate esters, parabens and bisphenol-A exposure among mothers and their children in Greece (Rhea cohort)	Exposure to endocrine disruptors, used as additives, preservatives, plasticizers and solvents in numerous consumer products, might cause adverse health effects. Humans exposed to these chemicals, metabolized and excrete them mainly via urine. Urinary metabolite concentrations are used as biomarkers of exposure. We evaluated the exposure of 1 month pregnant women enrolled in a prospective birth cohort in Greece (Rhea cohort) to phthalates, parabens and bisphenol A. Concentrations of eight phthalate metabolites, six parabens and bisphenol A were measured in 238 mother–child pairs of the "Rhea" cohort in Greece. Concentration levels in mother and children were comparable with corresponding concentrations in other countries worldwide. Low Spearman correlation coefficients (r(s) ≤ 0.3, p-value < 0.01) were observed for all the phthalates (DEP, di-n-butyl phthalate (DnBP), butyl benzyl phthalate (BBP) and ethyl paraben (EPB) between mothers and their children. We observed higher median daily intake (DIs) for mothers (e.g. di-ethyl phthalate 8.9 μg kg(-1) bw(-1)) than for their children (1.2 μg kg(-1) bw(-1)) for all detected compounds, except for di-2-ethylhexyl phthalate (DEHP) and bisphenol A. Principal component analysis (PCA) revealed that the main sources of exposure (diets related and personal care products) for phthalates, parabens and bisphenol A. Differences in DEHP metabolites were observed among mothers–children and female–male children.	Environment international,2015;83:1-10	10.1016/j.envint.2015.05.014	26072145	ヒト	-	-	-	-	-	-	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2937	Sayci IU et al.	2019	Preliminary study on bisphenol A levels and possible exposure history of mother and exclusively breastfed infant pairs	The aims of this study were to determine bisphenol A (BPA) levels in breast milk and urine specimens of healthy mother and exclusively breastfed infant pairs lasting six times BPA exposure, and also to examine the relationship between BPA levels and possible BPA exposure history. Forty mothers and their 1-3 month-old exclusively breastfed infant were included in the study. The questionnaire about sociodemographic characteristics and possible BPA exposure history were filled out. Breast milk and urine samples were taken. BPA analyses of these samples were conducted using high performance liquid chromatography coupled with fluorescence detection. The limit of detection (LOD) and limit of quantification (LOQ) were 0.1 and 0.3 ng/mL, respectively. Mean BPA levels were found as 0.5 ± 0.2 ng/mL (0.3-0.9 ng/mL) and 0.6 ± 0.3 ng/mL (0.3-1.1 ng/mL) in breast milk and urine samples, respectively. Infants' mothers were consuming yoghurt in plastic containers had significantly higher urinary BPA levels (p = 0.02). Mothers' mothers had beverages in plastic glass showed higher breast milk BPA levels (p = 0.02). There were no statistical associations between BPA levels and the use of plastic materials and tools (p > 0.05).Conclusion: The measurable BPA concentrations in breast milk and urine samples of exclusively breastfed infant-mother pairs were not found to have any adverse effect on their delivery outcome. Nonetheless, breastfed healthy infants' mothers have considerable exposure to BPA from their mothers through breastfeeding. What is known: • Humans, animals, and infants are exposed to BPA from their mothers through placental transfer and breastfeeding. • Breast milk is considered a continuous low-level exposure to BPA. What is New: • BPA was detected in 100% of maternal urine, infant urine, and breast milk samples in healthy mother-infant pairs having no known BPA exposure. • The measurable amount of BPA in breast milk and infant urine may reflect possible BPA exposure of mother-infant pairs.	Eur J Pediatr. 2019 Apr;178(4):541-550.	10.1007/s00431-019-03329-4	30707364	ヒト	ADME	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2938	Philippat C et al.	2019	Prenatal Exposure to Select Phthalates and Phenols and Associations with Fetal and Placental Weight among Male Births in the EDEN Cohort (France)	BACKGROUND: The placenta performs crucial physiological functions to ensure normal fetal development. Few epidemiological studies investigated placental weight sensitivity to phthalates and phenols. OBJECTIVE: Our goal was to explore whether maternal exposure to certain phthalates and phenols is associated with changes in placental weight at birth and in placental to birth weight ratio (PBR). METHODS: Placental weight and birth weight were available for 373 mother–son pairs in the EDEN (Etude des Déterminants pré-et postnatals du développement et de la santé de l'Enfant) cohort for whom 9 phenols, 11 di-/monophenols, 11 phthalates, and 5 phthalate substitutes were measured in maternal urine samples collected around 24 wk of gestation. We used linear regressions and Bayesian kernel machine regressions (BKMR) to model placental weight, birth weight, and PBR. Structural equation models (SEMs) were used to explore potential mediation by placental weight. RESULTS: The multipollutant BKMR model for placental weight retained four biomarkers: triclosan and monocarboxy-isononyl phthalate (MCPP), which were negatively associated with placental weight, and benzophenone-3 and the sum of parabens, which were positively associated with this outcome. The BKMR model for PPI revealed two associations: benzophenone-3 (BP3) and monocarboxy-isooctyl phthalate (MCPP), which were negatively associated with this outcome. DISCUSSION: The positive association between the sum of parabens and placental weight was consistent with results on a fetal growth biomarker, insulin-like growth factor 3 (IGF3), measured in cord blood in a subsample of 130 boys. The SEM suggested that IGF3 may mediate 10% of the association between BP3 and PPI. These associations were not reported in previous studies and should be seen as hypothesis generating. Studies relying on repeated assessments of exposure to properly characterize critical windows are needed to substantiate the plausibility of the hypotheses generated by our results. https://doi.org/10.1289/EHP3523.	Environ Health Perspect. 2019 Jan;127(1):17002.	10.1289/EHP3523	30624098	ヒト	生殖発生	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2939	Christensen KL et al.	2015	Reconstruction of bisphenol A intake using a simple pharmacokinetic model	Bisphenol A (BPA) is used in the manufacture of a range of consumer products, and human biomonitoring studies suggest that exposure to BPA is nearly ubiquitous. We constructed and calibrated a simple pharmacokinetic model to predict urinary concentrations of BPA based on a known BPA dose. This also tested a rather new physiologically based model that three compartments: "Lumped Gut," "Slowly" and "Rapidly" We calibrated and validated the model parameters using blood and urine measurements from nine volunteers who consumed 5 mg of d(3)-BPA. We then applied the model to a second group of eight persons, who supplied full volumes of urine over 7 consecutive days and a diary identifying times and types of food and beverage consumed, to "reconstruct" the time and mass of BPA intakes. These reconstructed daily intakes ranged on average from 60 to 180 ng/kg bw, within the range of, but slightly higher than, those summed from other studies. Basal low-levels of intakes occurred within an hour of reported food or drink consumption, supporting the hypothesis that diet is the main pathway of exposure to BPA. However, one-third of all measured external intakes took place outside this time window, suggesting that other sources of BPA exposure may also be relevant.	Journal of exposure science & environmental epidemiology,2015;25(3):240-8	10.1038/jes.2013.81	24252884	ヒト	-	-	-	-	-	-	PBPKモデル	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

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別添-2　統合文献リスト

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性基準不適合と判断されるものは作成段階評価へ進め、当該物質評価段階で原著に基づき精査。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2953	Kasper-Sonnenberg M et al.	2014	Phthalate metabolites and bisphenol A in urines from German school-aged children: results of the Duisburg birth cohort and Bochum cohort studies	Some phthalates and also bisphenol A (BPA) interfere with the human endocrine system and are labelled as reproductive toxicants. Children's exposure to these contaminants is suspected to be associated with developmental disorders and other health impairments. We provide biomonitoring data on 25 urinary phthalate metabolites and BPA levels in first morning urine of 8–10 year old children. Participants were children born between 2002 and 2004 in Duisburg (DUI) and Bochum (BOC), Germany. Creatinine-adjusted concentrations of BPA and phthalate metabolites were measured by GC-MS/MS and LC-MS/MS. The geometric mean (GM) maternal urinary concentration of total BPA, ascertained for specific gravity, was 0.86 (95% CI 0.79–0.95) μg/L. Almost 88% of the women had detectable urinary concentrations of BPA. An analysis of urinary concentrations of BPA by maternal characteristics with specific gravity as a covariate in the linear model showed that the geometric mean concentrations (1) decreased with increasing maternal age, (2) were higher in current smokers or women who quit during pregnancy compared to never smokers, and (3) tended to be higher in women who provided a fasting urine sample and who were born in Canada and had lower income and education. Several of the phthalate metabolites analyzed were not prevalent in this population (MCHP, MEHP, MEHHP, MEOP), while percentages detectable at less than 25%. The phthalate DEHP metabolites MEHHP and MEOHP were detectable in 50.4% and 46.1% of the children, respectively. Urinary concentrations of BPA were significantly higher than those of the DEHP metabolites, which is remarkable since the DEHP metabolites tended to be higher in older women and when the urine was collected later in the day. This study provides the first biomonitoring results for the largest population of pregnant women sampled in the first trimester of pregnancy. The results indicate that exposure among this population of pregnant women to these chemicals is comparable to or even lower than that observed in a Canadian national population-based survey.	Int J Hyg Environ Health. 2014 Nov;217(8):830-8.	10.1016/j.ijheh.2014.06.001	24986699	ヒト	発達神経	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2954	Arbuckle TE et al.	2014	Phthalate and bisphenol A exposure among pregnant women in Canada--results from the MIREC study	Bisphenol A (BPA) and phthalates are endocrine disruptors possibly linked to adverse reproductive and neurodevelopmental outcomes. These chemicals have commonly been measured in urine in population surveys; however, such data are limited for large populations of pregnant women, especially for the critical first trimester of pregnancy. The aim of the study was to measure BPA and phthalate metabolites in first trimester urine samples collected in a large national cross-sectional pregnancy cohort study and to identify major predictors of exposure. Approximately 2000 women were recruited in the first trimester of pregnancy from ten cities across Canada during 2008-2011 (the MIREC Study). Spot urine samples were collected at the first prenatal visit (median 11 weeks gestation) and analyzed for BPA and 11 phthalate metabolites by HPLC-MS/MS. The geometric mean (GM) maternal urinary concentration of total BPA, accounted for specific gravity, was 0.86 (95% CI 0.79-0.95) μg/L. Almost 88% of the women had detectable urinary concentrations of BPA. An analysis of urinary concentrations of BPA by maternal characteristics, with specific gravity as a covariate in the linear model showed that the geometric mean concentrations: (1) decreased with increasing maternal age, (2) were higher in current smokers or women who quit during pregnancy compared to never smokers, and (3) tended to be higher in women who provided a fasting urine sample and who were born in Canada and had lower income and education. Several of the phthalate metabolites analyzed were not prevalent in this population (MCHP, MEHP, MEHHP, MEOP), while percentages detectable at less than 25%. The phthalate DEHP metabolites MEHHP and MEOHP were detectable in 50.4% and 46.1% of the children, respectively. Urinary concentrations of BPA were significantly higher than those of the DEHP metabolites, which is remarkable since the DEHP metabolites tended to be higher in older women and when the urine was collected later in the day. This study provides the first biomonitoring results for the largest population of pregnant women sampled in the first trimester of pregnancy. The results indicate that exposure among this population of pregnant women to these chemicals is comparable to or even lower than that observed in a Canadian national population-based survey.	Environ Int.2014;68:55-65.	10.1016/j.envint.2014.02.010	24709781	ヒト	バイオモニタリング	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2955	Pollard SH et al.	2019	Male exposure to bisphenol A (BPA) and semen quality in the Home Observation of Periconceptional Exposures (HOPE) cohort	BACKGROUND: Exposure to (or uptake) A (BPA) has been associated with reduced semen quality. The objective of this study was to examine associations between BPA measured in urinal daily first morning urine samples and semen quality parameters among men trying to conceive. METHODS: This prospective, preconception cohort included 661 men ages 18-40 without known subfertility. Men collected daily, first morning urine during their female partner's fertile window. Semen samples were collected through intercourse after the fertile window. RESULTS: Samples from 661 men were analyzed. Median (IQR) BPA exposures (ng/mL) were found among men with abnormal sperm tail morphology (OR = 1.12, 95% CI = 1.00, 1.26) compared to men with normal morphology findings. OR = 1.39, 95% CI = 1.17, 1.70). There was no association with sperm count. CONCLUSION: Higher exposure to BPA was associated with abnormal sperm tail morphology in this prospective, pre-conception cohort.	Reprod Toxicol. 2019 Dec;90:82-87.	10.1016/j.reprotox.2019.08.014	31445078	ヒト	精巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2956	Bansal A et al.	2019	In utero bisphenol A exposure is linked with sex specific changes in the transcriptome and methylome of human amniocytes	CONTEXT: Prenatal exposure to bisphenol A (BPA) is linked to obesity and diabetes but the molecular mechanisms driving these phenomena are not known. Alterations in deoxyribonucleic acid (DNA) methylation in amniocytes exposed to BPA in utero represent a potential mechanism leading to metabolic dysfunction later in life. OBJECTIVE: To profile changes in genome-wide DNA methylation and expression in second trimester human amniocytes exposed to BPA in utero. DESIGN: A nested case-control study was performed in amniocytes matched for offspring sex, maternal race/ethnicity, maternal age, gestational age at amniocentesis, and gestational age at birth. Cases had recorded in food BPA measuring ≥0.25 to 25 ng/mL. Sex-specific genome-wide DNA methylation analyses and RNA sequencing (RNA-seq) were performed. SETTING: Urine samples were collected from pregnant women undergoing routine second trimester genetic amniocentesis at the University of Massachusetts, Amherst. PARTICIPANTS: Pregnant women with BPA exposure. Ingenuity pathway analysis was performed to identify biologically relevant pathways enriched after BPA exposure. In vitro H-C1-2-1 cell line was used to validate the effect of BPA on cell viability and proliferation. RESULTS: Maternal urine BPA concentrations were 0.25 to 25 ng/mL (median, 0.5 ng/mL). Pathways related to metabolic dysfunction, collagen signaling, and adipogenesis. Thirty-six DMRs were identified in male BPA-exposed amniocytes, and 10 in female amniocyte analysis (q < 0.05). H-C1 analysis identified interactions between DMRs and 32 genes with expression changes in male amniocytes and 12 in female amniocytes (P < 0.05). CONCLUSION: A unique trajectory of human amniocytes exposed to BPA in utero, sex-specific analysis identified gene expression changes in pathways associated with metabolic disease and novel DMRs with potential clinical regulatory functions.	J Clin Endocrinol Metab. 2020 Feb 1;105(2):453-467.	10.1210/clinem/dgz037	31536135	ヒト	代謝	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2957	Adesman A et al.	2017	Formula Feeding as a Risk Factor for Attention-Deficit/Hyperactivity Disorder: Is Bisphenol A Exposure a Smoking Gun?	OBJECTIVE: Breastfeeding during infancy is associated with a lower risk of attention-deficit/hyperactivity disorder (ADHD). Although this is presumably due to breast milk's nutritional advantages, formula-fed infants have, until recently, also been exposed to bisphenol A (BPA), a neurotoxic chemical previously used to manufacture baby bottles and formula cans. Our goal was to examine the association between formula feeding and ADHD, controlling for BPA exposure. METHODS: Data were analyzed from the 2011-2012 National Health and Nutrition Examination Survey (NHANES) for children aged 6 to 15 years (N = 5563). Logistic regression was used to model parent-based ADHD diagnosis as a function of breastfeeding, adjusting for 12 possible confounding variables using a propensity score. RESULTS: In the 2011 data set (weighted n = 9,630,000), formula-fed subjects had a 9-fold increased odds of ADHD compared with breastfed subjects (adjusted odds ratio [aOR] 9.08, 95% confidence interval [CI] 2.18-14.61). In the 2012/12 data set (n = 5,723,000), there was no significant association between feeding and ADHD (aOR 1.05, 95% CI 0.60-1.84). This is despite an increase in the percentage of formula-fed children (2011-2012 data set: 16.8% ± 2.1% [SE] vs 2012-2013 data set: 20.7 ± 0.9%). Urine BPA concentrations were 89% exposed among breastfed infants, ADHD was more common among formula-fed infants. In the 2007 but not the 2011/12 sample, where exposure to BPA was markedly reduced. These findings suggest that the reduced prevalence of ADHD among breastfed infants may not be due to the nutritional benefits of breast milk, but rather early exposure to BPA, a neurotoxic chemical previously found in infant formula.	J Dev Behav Pediatr. 2017 Sep;38(7):545-551.	10.1097/DBP.0000000000000468	28727611	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2958	Fastoni A et al.	2019	Fetal exposure to bisphenol A: Presence of bisphenol A in urine of pregnant women assisted in a hospital in the City of Buenos Aires, Year 2013	Introduction: Bisphenol A (BPA) is an endocrine disrupter (ED) possibly linked to adverse reproductive and neurodevelopmental effects that is used as an additive in food and beverage containers. There are no data of BPA levels in the Argentine population. The objective of this study was to measure BPA in the urine of pregnant women. Methods: Cross-sectional study. Detection of BPA in pregnant women of the Hospital Italiano de Buenos Aires, Argentina, who were assisted in the prenatal clinic between January and March 2013. Urine samples were collected in the first trimester of pregnancy. Demographic and clinical data were also collected. Results: 108 pregnant women, average age 32 years (Standard Deviation (S.D.) 5.4). 89% (S.D.) 9.6) BMI by tertiles and 82.7% (89/1.2) 1.7 BMI were university or higher education. 86.3% (95% CI 78-73.07 of BPA in urinary samples were quantifiable, with a median BPA of 3.1ng/mg Cr (IR 3.2-4.7). Conclusions: This study shows that exposure to BPA during the process of embryonic development in a sector of the population of Argentina is widespread. In Argentina, the use of this ED is only regulated in baby bottles.	Rev Fac Cien Med Univ Nac Cordoba.2019;76(2):86-91.	10.31053/1853.0605.v76.n2.22806	31216162	ヒト	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2959	Mansouri V et al.	2019	Exposure to phthalates and bisphenol A is associated with higher risk of cardiometabolic impairment in normal weight children	Some obese individuals have normal metabolic profile, and some normal weight persons have impaired metabolic status. Our hypothesis was that one of the potential underlying factors for such differences is exposure to phthalates and BPA. We investigated the associations of urinary phthalates and BPA with cardiometabolic risk factors in normal weight children and adolescents. A cross-sectional study was conducted on a subsample of 220 participants of a national school based surveillance program in Iran. We measured urine BPA and phthalate metabolites by gas chromatography-mass spectrophotometry. We compared them in children and adolescents with and without excess weight and those with and without cardiometabolic risk factors (MetS group). We categorized the concentrations of chemicals in tertiles, and then we applied logistic regression models after adjustment for potential confounding factors. The concentrations of BPA and some metabolites of phthalates were significantly different in the four groups studied. MEHP concentration was associated with higher odds ratio of cardiometabolic risk factors in participants with normal weight (OR 95% CI: 1.08, 3.45 for the highest tertile). MEHP, MEHHP, MEOHP, and BPA were significantly associated with increased risk of excess weight (OR 95% CI: 1.08, 3.45; 1.08, 3.45; 1.08, 3.45; and 1.08, 3.45, respectively). This study showed that the association of BPA and phthalates with cardiometabolic risk factors is independent of the weight status. Our findings suggest that the metabolic impairment in some normal weight children and normal metabolic profile of some obese children can be, in part, related to exposure to these environmental chemicals. Graphical abstract	Environ Sci Pollut Res Int. 2019 Jun;26(18):18604-18614.	10.1007/s11356-019-05123-z	31055746	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2960	Zhang W et al.	2019	Exposure to Bisphenol a Substitutes and Gestational Diabetes Mellitus: A Prospective Cohort Study in China	Background: The associations of bisphenol A (BPA) and gestational diabetes mellitus (GDM) has been investigated in only a small number of studies, and research on the associations between BPA substitutes and GDM is scarce. Objective: We aimed to investigate the associations of four bisphenols (bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF)) levels in urine sample with the risk of gestational diabetes mellitus (GDM) and fasting plasma glucose (FPG) levels in pregnant women. Methods: A prospective cohort study was conducted in Wuhan, China, from 2013 to 2016. Concentrations of four bisphenols (BPA, BPF, BPS, BPAF) were measured in first-trimester urine samples using Ultra-high performance liquid chromatography-quadrupole-quadrupole-linear ion trap tandem mass spectrometry (UHPLC-TQ/MS). An oral glucose tolerance test (OGTT) was performed at 26-28 gestational weeks and GDM was diagnosed post hoc using International Association of Diabetes and Pregnancy Study Groups criteria. We used multivariable logistic regression models to examine the associations of urinary bisphenols with the risk of GDM, and multiple linear regression models to examine the associations of bisphenols exposure with plasma glucose levels. Results: Urinary BPAF was associated with increased odds of GDM among women with normal pre-pregnancy BMI (adjusted odds ratio (aOR): 1.75 (95% CI: 1.08, 2.83) for the highest group compared to the lowest group). Urinary BPA was associated with increased odds of GDM (aOR: 1.71 (95% CI: 1.06, 2.76)) among women with pre-pregnancy BMI ≥ 24 kg/m2. Urinary BPAF was associated with increased FPG (adjusted β: 0.06 mmol/L (95% CI: 0.01, 0.11)) among women with pre-pregnancy BMI ≥ 24 kg/m2 and GDM. Concurrent with the result of GDM, women in the highest BPAF category had a mean of 0.06 mmol/L (95% CI: 0.01, 0.11) higher fasting plasma glucose (FPG) levels than women in the lowest category. For BPA and plasma glucose, non-linear associations were observed between urinary BPA and FPG and the sum of the FPG z-score among women who were overweight (a-for-non-linear association < 0.05). We also found that BPA per unit increase in natural log transformed specific gravity-adjusted BPA (ln-SG-adj-BPA) was associated with a 0.03 mmol/L (95% CI: 0.01, 0.06) increase in FPG levels and the associations might be modified by baseline β for interaction = 0.05). Among women with female fetus, a per unit increase in ln-SG-adj-BPA was associated with a 0.04 mmol/L (95% CI: 0.02, 0.06) increase in FPG, a 0.11 mmol/L (95% CI: 0.04, 0.17) increase in FPG and a 0.19 mmol/L (95% CI: 0.08, 0.30) increase in the sum of FPG z-score. Conclusions: Our results provide evidence that BPAF and BPS might be potential risk factors of GDM, which require to be studied further.	Front Endocrinol (Lausanne). 2019 Apr 30:10:262.	10.3389/fendo.2019.00262	31114544	ヒト	生殖(妊娠糖尿病)	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-
統合_2961	Murphy L et al.	2019	Exposure to bisphenol A and diabetes risk in Mexican women	Bisphenol A (BPA) is an endocrine disrupting chemical widely used in the production of polycarbonate plastics and epoxy resins, which has been previously linked to diabetes among non-Hispanic populations. As part of a case-control study for breast cancer, only controls with BPA information were included in this report. The final sample size comprises 75 self-reported diabetics and 301 non-diabetics. Urinary free bisphenol A (BPA-F) (ng/L) was determined by solid-phase extraction and HPLC-FLD analysis. Logistic regression models were used to evaluate the association between BPA-F and self-reported diabetes. After adjusting by age, urinary BPA-F (LOG (10.0 ng/g creatinine) was associated with diabetes: exposure (OR = 1.80; 95% CI: 1.06, 3.06) compared with women in the reference category (547-635 ng/g creatinine). BPA may be an environmental inducer of diabetes. More studies are needed to confirm this result, especially in Hispanic populations.	Environ Sci Pollut Res Int. 2019 Sep;26(25):26332-26338.	10.1007/s11356-019-05731-9	31286379	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2962	Wang B et al.	2014	Exposure to bisphenol A among school children in eastern China: a multicenter cross-sectional study	Bisphenol A (BPA) is one of the highest production and consumption volume chemicals in the world. Although exposure of children to BPA has been studied in Western countries, little is known about its level in China. In this study, we measured urinary BPA concentrations in children from eastern China and assessed the exposure characteristics. Spot urine samples were collected from 1,469 children aged 3-11 years. Urinary BPA was measured by ultra-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) method and used for the measurement and estimation of BPA were presented as unadjusted (ng/mL), creatinine-adjusted (ng/g creatinine) and specific gravity (SG)-adjusted (ng/mL) forms. BPA was detected in 98.9% of urine samples with their unadjusted concentrations ranging from 0.1 to 326.8 ng/mL (0.023–67.66 ng/g/d), indicating that the exposure of BPA was common for school children living in eastern China. The geometric mean and median of BPA was 1.11 ng/ml (creatinine-adjusted: 1.07 ng/g creatinine; SG-adjusted: 1.17 ng/ml) and 1.85 ng/ml (creatinine-adjusted: 2.01 ng/g creatinine; SG-adjusted: 1.87 ng/ml), respectively. The highest urinary BPA level was found in the age group of 10 years with GM concentration of 1.95 ng/ml, and it decreased with the rising age (11 year: 1.18 ng/ml; 8 years: 1.08 ng/ml; 9 years: 1.07 ng/ml; 3 years: 1.06 ng/ml; 7 years: 1.05 ng/ml; 6 years: 1.04 ng/ml; 4 years: 1.03 ng/ml; 5 years: 1.02 ng/ml). Our results indicate that the tolerable daily oral reference dose of 50 mg/kg bw/day recommended by either the European Food Safety Authority or the US Environment Protection Agency. There was no significant difference in urinary BPA concentrations between children who were overweight or obese and those with normal weight ($P>0.05$), whereas BPA daily intake was unexpectedly higher among normal weight children ($P<0.001$). Compared with creatinine correction, this exercise method of specific gravity is preferred to evaluate BPA exposure for children.	J Expo Sci Environ Epidemiol. 2014 Nov;24(6):657-64.	10.1038/jes.2014.36	24866264	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2963	Ji H et al.	2018	Exposure of environmental Bisphenol A in relation to routine sperm parameters and sperm movement characteristics among fertile men	Although several human studies have examined bisphenol A (BPA) exposure in relation to routine sperm parameters, evidence of BPA's effects on sperm movement characteristics is limited. We examined associations of BPA exposure with sperm movement characteristics including sperm movement characteristics using tertile tests. This cross-sectional study was conducted in Sanda County, Suzhou Province, China. Subjects provided semen samples analyzed by computer-aided sperm analysis. ELISA system and urine samples for BPA assay. They were invited to complete an in-person interview with a structured questionnaire to obtain demographics, lifestyle factors, and medical history. Multivariate linear regression models were used to estimate associations between urinary BPA concentrations and sperm parameters. Median urinary BPA concentration was detected in 73.0% of urine samples, with a geometric mean of 1.65 mg/g of creatinine. Compared with subjects in the lowest tertile of BPA, subjects with detected BPA had increased viscosity (1.26, beta: 2.18, 95% confidence interval (CI): 0.37, 4.01; Straightness: 0.78, beta: -1.67, 95% CI: 0.38, 2.75), Wobble (WOB, beta: 1.75, 95% CI: 0.36, 3.16), reduced amplitude of lateral head displacement (ALH, beta: -0.26, 95% CI: -0.5, -0.02) and linear-angular displacement (LIN2, beta: -1.17, 95% CI: -2.22, -0.11). Subjects in the highest tertile of creatinine-adjusted BPA group had lower sperm concentration than those with undetected BPA. Dose-response relationships of BPA with LIN, WOB, ALH, VAP, and sperm concentration were demonstrated by statistically significant trends across tertiles of creatinine-adjusted BPA concentrations. Similar results were obtained when modeling BPA as a continuous variable. Repeated measurement BPA would decrease sperm concentration and sperm swing characteristics (ALH and WOB), and increase sperm velocity (slow, SLOW, and WOB), which might mediate further effects on impaired male fecundity.	Sci Rep. 2018 Dec 3;8(1):17548.	10.1038/s41598-018-35787-5	30510208	ヒト	精巣	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2964	Liu J et al.	2018	Exposure and dietary sources of bisphenol A (BPA) and BPA-alternatives among mothers in the APrON cohort study	Diet is regarded as the main source of bisphenol A (BPA) exposure, but comparatively little is known about dietary sources of BPA alternatives. Here we measured exposure of BPA and BPA-alternatives among pregnant women in Canada, estimated their 24-h intakes and examined the importance of various dietary sources. Free and total BPA, bisphenol S (BPS) and bisphenol F (BPF) were measured in 437 second-trimester maternal urine samples, and in 69 paired samples collected at three months postpartum. Linear regression was used to evaluate associations between urinary concentrations of bisphenols and 24-h dietary recall data. The geometric means of total BPA in second trimester and postpartum are 1.2 and 0.9ng/mL, respectively (urine N = 71) now higher than corresponding total BPA (0.8 and 0.7ng/mL). The detection frequency of BPF was 2.3%. BPA and BPS were detected in 99.5% and 97.5% of second trimester urine samples, respectively. The 95th percentile of 24-h intake was 1.4 and 0.2μg/kg bw/day for BPA and BPS, respectively. Free BPA was more detectable when total BPA or BPF concentrations were higher, always at ≤ 1% of the total concentration. The tolerable daily intake for total BPA (i.e. 50ng/kg bw/day) was not exceeded, but for BPS the estimated 24-h intake was as high as 10ng/kg bw/day (95th percentile: 0.2ng/kg bw/day), and for BPF was even higher among the highest centile of exposure (maximum and 99th percentile: 36, 0.8ng/kg bw/day). Canned food consumption was associated with higher total BPA, but was not associated with BPS. For BPF, mustard consumption may be an important exposure source, particularly among the highest exposed. Relatively high exposure to BPS and BPF in a minority of pregnant women highlights the need to better understand the associated health risks and exposure sources of BPA alternatives.	Environ Int. 2018 Oct;119:319-326.	10.1016/j.envint.2018.07.001	29990952	ヒト	その他	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

適格性評価（動物）1：該当、0：該当しない　適格性評価（疫学）1：該当、0：該当しない　適格性評価（in vitro）1：該当、0：該当しない　適格性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに適格性基準不適合と判断されるものは除き後続性評価へ進め、当該性評価段階で原則に基づき除外。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2965	Philips EM et al.	2019	Early pregnancy bisphenol and phthalate metabolite levels, maternal hemodynamics and gestational hypertensive disorders	STUDY QUESTION: Are early pregnancy urinary bisphenol and phthalate metabolite concentrations associated with placental function markers, blood pressure (BP) trajectories during pregnancy and risk of gestational hypertensive disorders?SUMMARY ANSWER: Early pregnancy bisphenols and phthalate metabolites were not consistently associated with maternal BP changes or gestational hypertensive disorders, but subclinical, placental dysfunction may be associated with certain phthalate metabolites.WHAT IS KNOWN ALREADY: Exposure to endocrine disrupting chemicals (EDCs) during pregnancy may disrupt early placental development and affect the risk of gestational hypertensive disorders. Previous studies investigating effects of bisphenols and phthalate metabolites on gestational hypertensive disorders reported inconsistent results and did not examine placental function or BP throughout pregnancy.STUDY DESIGN, SIZE, DURATION: In a population-based prospective cohort study, bisphenol and phthalate metabolite concentrations were measured in a spot urine sample in early pregnancy among 1006 women whose children participated in perinatal follow-up measurements. PARTICIPANTS/MATERIALS, SETTING, METHODS: Main mechanism of women-drilled any BP measurement or with pre-existing hypertension, 1002 women were included in the analysis. Urinary bisphenol and phthalate metabolite concentrations were measured in early pregnancy (median 9 GW). Maternal BP was measured at 16, 20, 24, 28, 32 and 36 GW. Placental function was assessed by uterine artery pulsatility index (PI), uterine artery resistance index (RI), notching and placental weight1, and maternal BP were measured in different trimesters. Information on gestational hypertensive disorders was obtained from medical records. MAIN RESULTS AND THE ROLE OF CHANCE: During mid-pregnancy increases in MMP phthalate metabolites was associated with a 0.6 (CI 95% 0.1; 1.1), 0.5 (CI: higher early pregnancy of PI, 1.7 MAP ratio (range in total sample 9 MAD. This association was driven by more (CI: carboxymethyl)hexyl)phthalate. In the repeated measurements regression models, each log-unit increase in bisphenol A was associated with a 0.5 (CI: 0.1; 0.9) mmHg higher MAP, 0.4 (CI: 0.1; 0.7) mmHg higher MAP and 0.4 (CI: 0.1; 0.7) mmHg higher MAP in the second, third and fourth trimester, respectively. Bisphenols and phthalate metabolites showed no consistent associations with any other outcomes. LIMITATIONS, REASONS FOR CAUTION: Information on a large number of potential confounders was available but was partly self-reported. Bisphenols and phthalate metabolites, which typically have a half-life of 24-28 h, were measured via a single spot urine sample. In early pregnancy. In addition, as the current sample size, the study was powered to detect an odds ratio of 1.57 for gestational hypertensive and 1.79 for pre-eclampsia, but was underpowered to perform multivariable analyses for these outcomes. Further studies combining data from different cohorts may be necessary to increase power. These limitations are possible sources of bias. WIDER IMPLICATIONS OF THE FINDINGS: Our findings suggest that bisphenols and phthalate metabolites are not consistently associated with maternal BP changes or gestational hypertensive disorders, but subclinical placental dysfunction may be associated with certain phthalate metabolites in the first half of pregnancy in the general population. Our results are therefore more supportive of an association of early pregnancy bisphenols and phthalate metabolites with risk for pre-eclampsia than with gestational hypertension. STUDY FUNDING/COMPETING INTEREST(S): This analysis was supported by Erwin RIEGER PO from the National Institutes of Health, USA. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health. The authors report no conflicts of interest.	Hum Reprod. 2019 Feb 1;34(2):365-373.	10.1093/humrep/dey364	30576447	ヒト	心血管	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2966	Martinez MA et al.	2018	Comparing dietary and non-dietary source contribution of BPA and DEHP to prenatal exposure: A Catalonia (Spain) case study	Bisphenol A (BPA) and Di-(2-ethylhexyl) phthalate (DEHP) are two wide-spread chemicals classified as endocrine disruptors (ED). The present study aims to estimate the non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP for a pregnant women cohort. In addition, to assess the prenatal exposure for the fetus, a physiologically based pharmacokinetic (PBPK) model was used. It was adapted for pregnancy in order to assess the internal dosimetry levels of ED's (BPA and DEHP) in the fetus. Estimates of exposure to BPA and DEHP from all pathways along with their relative importance were provided in order to characterize exposure. The non-dietary exposure was estimated using urinary biomarkers. Urine samples (n = 129) were collected from pregnant women participating in the Spanish birth cohort Infancia y Medio Ambiente (INMA) as a continuous exposure over. Total non-dietary mean values were 0.6(Dermal)+(high)+(low) for BPA (0.0002(Dermal)+(high)+(low) for BPA and 90th percentile, respectively) and 0.6(Dermal)+(high)+(low) for DEHP (0.6(Dermal)+(high)+(low) for BPA and 0.8(Dermal)+(high)+(low) for 50th and 90th percentile, respectively) for DEHP. Indoor environments, and especially dust ingestion were the main non-dietary contributors to the total exposure of BPA and DEHP in both EDs and EDs. However, on an exposed, diet showed the higher contribution to total exposure with >90% for BPA and 60% for DEHP. Although diet was considered the primary source of exposure to BPA and phthalates, it must be taken into account that in non-dietary sources the first (pre-metabolism) is lacking, so these may be of equal or even higher toxicological relevance than dietary sources. The present study is in the framework of "Health and environmental risk assessments based on large population surveys" (HEALIS) project (PTF-16-00842).	Environ Res. 2018 Oct;166:25-34.	10.1016/j.envres.2018.05.008	29859370	ヒト	ADME	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2967	Kim HK et al.	2019	Body fluid concentrations of bisphenol A and their association with in vitro fertilization outcomes	Bisphenol A (BPA) is an endocrine-disrupting chemical thought to mimic the action of estrogens. There have been reports suggesting an association between BPA exposure and infertility in humans. In this prospective study, we investigated the concentrations of BPA in follicular fluid (FF), serum, and urine collected from 70 women undergoing in vitro fertilization (IVF). The median (interquartile range) BPA concentrations were 2.4 (1.2–4.6) ng/mL in FF, 2.2 (1.2–4.6) ng/mL in serum, and 1.2 (0.6–2.2) ng/mL in urine. The mean ± SD of BPA in all participants was 3.7 ng/mL. In the logistic regression models, BPA concentrations in FF, but not in serum or urine, were significantly associated with female body phenols, follicular fluid, and semen) did not significantly affect the outcomes such as pregnancy, presence of good-quality embryo, or the proportion of normally fertilized oocytes. In the multiple linear regression models, BPA concentrations of body fluids did not significantly affect the parameters such as number of retrieved oocytes, peak E2 level, sperm concentration, and sperm motility. In conclusion, BPA concentrations in body fluids were not significantly associated with IVF outcomes such as pregnancy, good-quality embryo, normally fertilized oocytes, number of retrieved oocytes, peak E2 level, sperm concentration, and sperm motility. Therefore, we could not find the evidence that the non-occupational low dose exposure to BPA affects IVF outcomes.	Hum Fertil (Camb). 2021 Jul;24(3):199-207.	10.1080/14647273.2019.1612104	31099279	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2968	Philips EM et al.	2018	Bisphenol and phthalate concentrations and its determinants among pregnant women in a population-based cohort in the Netherlands, 2004-5	BACKGROUND: Exposure to bisphenols and phthalates in pregnancy may lead to adverse health effects in women themselves and their offspring.OBJECTIVE: To describe first trimester bisphenol and phthalate urine concentrations, including bisphenol and phthalate replacements, and determine nonfactional, socio-demographic and lifestyle related determinants.METHODS: In a population based prospective cohort of 1,786 mothers, we measured first trimester bisphenol, phthalate and creatinine urine concentrations.Samples collected in 2004-2006, median gestational age 12.9 weeks (inter quartile range (IQR) 12.1- 13.7). We examined associations of potential determinants with log transformed bisphenol and phthalate concentrations. Outcomes were log transformed. Statistical analyses were performed with linear regression models. In the final models, only the First Frequency Questionnaire was aimed at Dutch housewives. RESULTS: Bisphenol A, bisphenol F, and bisphenol F were detected in 79.2%, 67.8% and 82.2% of the population, respectively. Urine or butylphthalate, mono-(3-carboxypropyl) phthalate, mono-carboxyoctyl phthalate and mono-(2-ethyl-5-carboxypentyl) phthalate were detected in 99.9%, 99.9% and 98.9% of the population, respectively. Non-smoking was applied. Dietary was associated with higher high-molecular-weight phthalate concentrations and the lack of folic acid supplement use with higher di- or monoesters. Irrespective most differences were 68.7(mean)(95% CI 0.6-69.72) and 1.28(mean)(1.15-1.39)). CONCLUSION: Bisphenol A and F exposure was highly prevalent in pregnant women in the Netherlands as early as 2004-5. Although associations of dietary and other key factors with bisphenol and phthalate concentrations were limited, adverse lifestyle factors including obesity and the lack of folic acid supplement use were to be associated with higher phthalate concentrations in pregnant women. The major limitation was the availability of only one urine sample per participant. However, since phthalates are reported to be quite stable over time, results concerning determinants of phthalate concentrations are expected to be robust.	Environ Res. 2018 Feb;161:562-572.	10.1016/j.envres.2017.11.051	29245124	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2969	Ha. C et al.	2019	Bisphenol A, Chlorinated Derivatives of Bisphenol A and Occurrence of Myocardial Infarction in Patients with Type 2 Diabetes: Nested Case-Control Studies in Two European Cohorts	A positive association between Bisphenol A (BPA) exposure and coronary heart disease has been shown, but not in patients with type 2 diabetes (T2D). During the treatment of drinking water, chlorination leads to the formation of chlorinated derivatives of Bisphenol A (ClxBPA), a more lipophilic estrogenic activity than BPA. No evidence exists for a relationship between exposure to ClxBPA and myocardial infarction in patients with T2D. The objective of this study was to evaluate the relationship between exposure to BPA, ClxBPA and the occurrence of myocardial infarction (MI) in patients with T2D. Two nested case-control studies in two prospective cohorts (SURDIAGENE, France, and ESTHER, Germany) were conducted. In SURDIAGENE, 1,000 patients with T2D were followed for 9 years and 151 developed MI. Urinary concentrations of BPA and of ClxBPA and isolated MI was determined. Exposure to BPA was 70% in the ESTHER cohort and 58% in the SURDIAGENE cohort. In a meta-analysis of the two studies, concentrations of BPA were significantly associated with urine BPA elimination adjusted OR = 1.97 (1.20-3.78), p = 0.04. Exposure to ClxBPA significantly differed in the SURDIAGENE and ESTHER studies (10% and 4%, respectively; p = 0.0009). It was only strongly associated with MI in the SURDIAGENE cohort with an adjusted odds ratio (OR) of 12.33 (2.77-72.48) but this association was not evaluated in the ESTHER study. adjusted OR 0.17 (0.01-1.23). Whether these results may be explained by different water chlorination processes in France and Germany, resulting in different ClxBPA exposure levels, requires further investigation.	Environ Sci Technol. 2019 Aug 20;53(16):9876-9883.	10.1021/acs.est.9b02963	31310111	ヒト	心血管(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2970	Manfo FPT et al.	2019	Bisphenol A differentially affects male reproductive function biomarkers in a reference population and agro pesticides users from Djuttisa, Cameroon	The consequences of bisphenol A (BPA) exposure on male reproductive function were studied in two populations from Cameroon, farmers using agro pesticides in Djuttisa (rural area) and boatmen in Yaoundé (urban area, Centre region). Urinary BPA concentration from all participants was measured, and the values were correlated with biochemical markers of male reproductive function. The data showed that BPA could be detected in 100% of the urine samples from Djuttisa and Yaoundé. The median BPA concentration was 1.5 times higher in Djuttisa than in Yaoundé (1.5 and 1.0 μg/L, respectively). Despite the higher urinary concentration, the BPA average daily intake was estimated to be 0.38 – 0.05 mg/kg bw/day (0.5 mcrog/day/person) in the Cameroon population. Interestingly, free and bioavailable testosterone concentrations and estradiol/testosterone ratio correlated with BPA levels in the overall population. When data were analysed according to residency, BPA correlated with total testosterone levels (+/- 0.030) and estradiol/testosterone ratio (+/- 0.038) in the urban residents only, while the rural population exhibited significant increases in sex hormone binding globulin with increased BPA exposure. Our data showed that the rural Cameroon population is exposed to BPA but that increased BPA association to endocrine reproductive markers suggests that other environmental factors in combination with BPA exposure might influence testicular function.	Toxicol Ind Health. 2019 Apr;35(4):324-335.	10.1177/0748233719838437	30983554	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2971	Rodriguez-Carrillo A et al.	2019	Bisphenol A and cognitive function in school-age boys: Is BPA predominantly related to behavior?	BACKGROUND: Bisphenol A (BPA) has been associated with impairments in children's behavior, but few studies have investigated its relationship with cognitive functions.OBJECTIVE: To investigate the association of urinary BPA concentrations with cognitive domains and intelligence quotient (IQ) in Spanish boys. METHODS: BPA levels were quantified by liquid chromatography-tandem mass spectrometry in 2,480 ABO mini-sort urine sample from 369 boys of the INMA-Granada cohort, in their follow-up at 9-11 years of age. Cognitive function was evaluated by a trained psychologist using a comprehensive neuropsychological test battery (Wechsler Intelligence Scale for Children-IV, Conners' Continuous Performance Test-II, Trail Making Test, Stroop Color and Word Test). Behavior was assessed by the Child Behavior Checklist. Verbal, performance and total IQ scores were derived. Multiple linear regression models adjusted for socioeconomic and lifestyle confounders were fitted.RESULTS: Median (p25, p75) urinary BPA concentrations were 1.9 (0.9, 3.7) ng/mL and 1.75 (0.75, 3.2) mcg/g of creatinine (Cr). Boys in the third and fourth quartile of volume-based BPA concentrations showed better processing speed scores than boys in the first quartile (beta = 5.37, 95%CI: 1.6, 9.4 and beta = 3.83, 95%CI: -0.2, 7.9, respectively) and boys in the third quartile showed better inhibitory control (beta = 3.8, 95%CI: -0.2, 7.9) and impulsivity (beta= -4.2, 95%CI: -9.0, 0.5). In contrast, boys in the fourth quartile showed poorer working memory scores than those in the first quartile (beta: -3.6, 95%CI: -7.1, -0.1). All these associations were attenuated when Cr-standardized BPA concentrations were considered. Cr-based BPA concentrations were also associated with a higher risk of being below the 25th percentile of working memory scores (OR(q4 v 1)=1.99,95%CI: 1.01, 3.91). CONCLUSIONS: Our findings do not support an association between urinary BPA concentrations and cognitive function in 9 among boys, except for working memory. BPA was previously found to be associated with behavior problems in the same study population, suggesting that BPA may predominantly affect the behavior of children rather than their cognitive function, in line with previous epidemiologic studies.	Neurotoxicology. 2019 Sep;74:162-171.	10.1016/j.neuro.2019.06.006	31238050	ヒト	発達神経	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2972	Huang S et al.	2019	Bisphenol A and bisphenol S exposures during pregnancy and gestational age - A longitudinal study in China	Bisphenol A (BPA) and its substitute bisphenol S (BPS) are endocrine disrupting chemicals and metabolized rapidly in human body. BPA exposure in late pregnancy has been suggested to be associated with preterm birth (PTB), but the associations of interest BPA and BPS exposures with gestational age have been rarely studied. We aimed to examine maternal urinary BPA and BPS concentrations across pregnancy in relation to gestational age and PTB. A prenatal cohort study was conducted between 2013 and 2015 in Wuhan, China. Maternal urinary BPA and BPS concentrations were measured in a complete series of urine samples collected from 1,236 pregnant women in each trimester. Gestational age was calculated based on the last menstrual period (LMP) and confirmed by ultrasound examination. Linear mixed models were used to examine the associations between maternal urinary BPA and BPS concentrations across pregnancy (i.e. exposure) with a 1-SD rise increase in gestational BPA (1.126, 1.048) and/or adjusted odds ratios of 1.19 (95%CI: 1.00, 1.42) for PTB. Higher BPA concentrations in late trimesters were also negatively associated with gestational age and positively correlated with PTB. In contrast, only a positive association of third-trimester BPS with gestational age was found, but the significant association disappeared in the adjusted models. Both maternal trimester and averaged BPA exposure across pregnancy were significantly associated with shortened gestation and increased risk of PTB. However, the results showed little evidence of a relationship between BPS and PTB.	Chemosphere. 2019 Dec;237:124426.	10.1016/j.chemosphere.2019.124426	31362131	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-
統合_2973	Mustieles V et al.	2019	Bisphenol A and adiposity measures in peripubertal boys from the INMA-Granada cohort	INTRODUCTION: Childhood obesity is one of the most serious public health challenges of our times. Although an important body of experimental evidence highlights the obesogenic potential of endocrine disruptors, such as bisphenol A (BPA), the epidemiological evidence remains inconclusive and limited. OBJECTIVE: To assess associations between urinary BPA concentrations, and several adiposity measures in peripubertal boys from the Environment and Childhood (INMA) cohort in Granada, Spain. MATERIAL AND METHODS: BPA concentrations were determined in spot urine samples from 356 boys, aged 9-11, and their weight, height, waist circumference, and triceps and subscapular skinfolds were measured. Body mass index (BMI) z-score, fat mass index (FMI), and waist-to-height ratio (WHtR) were also calculated. Linear regression models were used to examine associations between urinary BPA concentrations (as a continuous and multivariable Tertile) and logistic regression models, BPA(LT3) (in tertiles) models, each natural log-unit increase in urinary BPA concentrations was associated with higher BMI z-score (beta= 0.03; 95%CI: -0.03, 0.11) and increased odds of overweight/obesity (OR= 1.06; 95%CI= 1.00, 1.28). Children with higher BPA concentrations had higher WHtR values (beta= 0.007; 95%CI: -0.001, 0.015), and BPA was associated with a greater risk of abdominal obesity (OR= 1.09; 95%CI= 1.00, 1.18). No associations were found with % body fat mass. CONCLUSIONS: BPA may exert an obesogenic effect in peripubertal boys, potentially increasing the risk of overweight/obesity, especially abdominal obesity. However, these results should be interpreted with caution given the modest sample size and the possibilities of reverse causality and residual confounding by diet and lifestyle patterns.	Environ Res. 2019 Jun;173:443-451.	10.1016/j.envres.2019.03.045	30974370	ヒト	代謝	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2974	Chang CH et al.	2019	Associations between prenatal exposure to bisphenol a and neonatal outcomes in a Taiwanese cohort study: Mediated through oxidative stress?	This study determined whether maternal bisphenol A (BPA) exposure influences birth outcomes through oxidative stress and estimated the daily intake of BPA through breast milk to infants. One hundred and eighty-six pregnant women without pregnancy complications were enrolled and maternal urine was collected in the third trimester. Postnatal breast milk was collected in the first and third months after delivery. Concentrations of BPA and 8-hydroxy-2'-deoxyguanosine (8-OHdG) were measured by high-performance liquid chromatography-tandem mass spectrometry and enzyme-linked immunosorbent assay, respectively. Structural equation model were employed to determine the effects of BPA exposure and oxidative stress levels on birth outcomes. A causal mediation analysis was conducted to verify the mediated effects of oxidative stress due to maternal BPA exposure on birth outcomes. The daily intake of BPA in breast milk was calculated using probabilistic risk assessment methods. The geometric means (geometric standard deviation) of BPA levels for maternal urine and first- and third-month breast milk were 2.34 (3.08) μg/g creatinine, 1.38 (3.01) ng/g, and 0.57 (3.97) ng/g, respectively. No significant mediation effects between BPA exposure, oxidative stress level, and neonatal head circumference. Three percent of 1-month-old babies and 1% of 3-month-old babies exceeded the BPA tolerable daily intake of 4 μg/kg bw/day proposed by the European Food Safety Authority. Results indicated that BPA exposure and/or its pregnant women and infants in northern Taiwan. The marginally significant correlation between maternal BPA exposure and neonatal head circumference should be considered.	Chemosphere. 2019 Jul;226:290-297.	10.1016/j.chemosphere.2019.03.093	30933738	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2975	Chin HB et al.	2019	Association of urinary concentrations of early pregnancy phthalate metabolites and bisphenol A with length of gestation	BACKGROUND: Environmental exposure to phthalates and bisphenol A (BPA) may have endocrine disrupting effects that alter length of gestation. We assessed the association between the urinary concentrations of 11 phthalate metabolites and BPA with length of gestation in a cohort of women followed from before conception until delivery.We assessed the associations between urinary concentrations of 11 phthalate metabolites and BPA with length of gestation in a cohort of women followed from before conception until delivery. METHODS: Pre-pregnancy and first trimester urine samples were collected from 501 women who conceived spontaneously and delivered singleton live births. Urinary concentrations were used to estimate the hazard of birth among 125 naturally conceived, singleton live births with screening for medical interventions that artificially shortened pregnancy. RESULTS: Higher concentrations of mono-(2-ethyl-5-hydroxyhexyl) phthalate (a metabolite of di-(2-ethylhexyl) phthalate (DEHP)) during the pre-implantation window were associated with reduced probability of birth, i.e., longer gestational hazard ratio (HR): 0.93, 95% CI: 0.87, 0.98; p = 0.01). The HR for the molar sum of the four DEHP metabolites measured showed a similar association (HR: 0.67, 95% CI: 0.43, 1.05). Higher concentrations of mono-(3-carboxypropyl) phthalate (MCPP) were associated with longer gestation (HR: 1.08, 95% CI: 1.01, 1.16). Neither monoethyl phthalate nor BPA were associated with gestational length. MBzP, MiBP, MnBP, MCPP, and MEP were associated with risk of earlier birth, i.e., shorter length of gestation. HR: 1.05, 1.11, 1.02, 1.08, 1.04 (CI: 1.00-1.09, 1.04-1.18, 0.96-1.08, 1.00-1.08). Early gestational exposure to DEHP and possibly other high molecular weight phthalates, (as reflected by urinary MCPP concentrations) may influence the length of pregnancy. Such effects could have consequences for neonatal and maternal health.	Environ Health. 2019 Aug 30;18(1):80.	10.1186/s12940-019-0522-2	31470855	ヒト	生殖発生	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_2976	Dalkan C et al.	2020	Association of cord blood bisphenol A (BPA) with cord blood adiponectin, leptin, fetal growth; adiposity and neoantal complications in a newborn cohort	Objective: To evaluate the relation between cord blood bisphenol A (BPA), leptin, adiponectin, birth weight, height, skin thickness, and perinatal results.Method: This study was performed in near East University Medical Faculty, Nicosia, Cyprus with 150 healthy mothers, Cord blood leptin, adiponectin, BPA levels were measured by ELISA and birth weight, heights and back, scalp, and arm skin thickness were measured and perinatal problems noted.Results: One hundred eighty-seven newborns were included in the study. Mean ± SD of BPA, adiponectin, leptin levels were 48.3 ± 2.22 ng/mL, 46.82 ± 15.29 μg/mL and 3.08 ± 2.08 ng/mL. Mean birth weight, height, head circumference were 3306.76 ± 386.06g, 48.34 ± 2.63cm, 34.31 ± 1.72cm. The association anthropometric measurements, BPA, leptin, and adiponectin levels were not statistically significant (p>.05). The relation between cord blood leptin, adiponectin, and BPA levels and small for gestation, large for gestation and average for gestation groups were not significant (p>.05). Moreover, relation between leptin, adiponectin, BPA levels and perinatal complications were not significant (p>.05). Conclusion: Cord blood BPA, adiponectin, leptin levels were not related to birth weight, height, head circumference, skin thickness, scalp, and arm skin thickness. Contrary to previous studies, higher BPA levels were associated with small for gestational age (SGA) births; however, this relation was not noted in our study. Furthermore, there is no relation between adiponectin, BPA, leptin, and adiponectin. This difference may be as a result of higher cord BPA levels compared with previous studies.	J Matern Fetal Neonatal Med. 2020 Aug;33(15):2588-2593.	10.1080/14767058.2018.1555808	30606068	ヒト	生殖発生	-	-	-	-	-	-	横断研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価へ進め、当該時評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2977	Braun JM et al.	2019	Association between gestational urinary bisphenol a concentrations and adiposity in young children: The MIREC study	BACKGROUND: Bisphenol A (BPA) is a high production volume chemical and because of its use in many consumer products, exposure is ubiquitous. Gestational BPA exposure has been associated with excess adiposity in rodent studies, but not consistently in human studies. We investigated the relation between gestational BPA exposure and early childhood adiposity in a prospective cohort study of 719 mother-child pairs. METHODS: We measured BPA concentrations in urine collected during pregnancy and in early childhood (median: 3.2 years, 95% range: 1.9-5.3). We estimated covariate-adjusted associations of log2-transformed BPA concentrations with child adiposity measures and examined whether these associations differed in boys and girls. RESULTS: Median BPA concentrations were 0.8 ng/mL (95% 0.3-3). Among both boys and girls, each doubling of gestational BPA concentration was associated with higher waist-for-height z-score (boys: 0.03, 95% CI: 0.001, 0.060). The association of BPA with waist circumference and subscapular skinfold thickness was modified by sex (sex×BPA interaction p-values 0.1). In girls, each 2-fold increase in BPA concentration was associated with a 2.0 cm (95% CI: 0.2, 3.9) and 0.3 mm (95% CI: 0.03, 0.58) increase in waist circumference and subscapular skinfolds, respectively. Associations were generally null or slightly inverse in boys. CONCLUSIONS: In this cohort, gestational urinary BPA concentrations were associated with subtle increases in girls' central adiposity during early childhood.	Environ Res. 2019 May;172:454-461.	10.1016/j.envres.2019.02.038	30831435	ヒト	代謝	-	-	-	-	-	-	コホート研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2978	Rashidi BH et al.	2017	A case-control study of bisphenol A and endometrioma among subgroup of Iranian women	BACKGROUND: Endometriosis is a multifactorial hormonally-related complex disease with unknown etiology. Epidemiologic data were suggested the possible effects of endocrine disrupting chemicals such as bisphenol A (BPA) on endometriosis. BPA is similar to endogenous estrogen and has the ability to interact with estrogen receptors and stimulate estrogen production. Our aim was to evaluate the relationship between urinary BPA concentrations in women with endometrioma. METHODS: A BIO-MATHODS: This case-control study consisted of fifty women who have been referred to gynecology and infertility center with endometrioma and were candidate for operative laparoscopy and ovarian cystectomy as cases. Fifty women who had not any evidence of endometrioma in clinical and ultrasound evaluation and came in the same clinic for routine check up were selected as controls. The urinary BPA concentrations were measured by high performance liquid chromatography (HPLC). Data were analyzed using logistic regression model. RESULTS: The median urinary BPA level in the case group was 1.4 ng/ml, while in the control group was 0.35 ng/ml, using the Mann-Whitney U test. The median urinary BPA level was significantly higher in the case group than in the control group (P < 0.001). The multivariate logistic regression method and detection limit was 0.25 ng/mL. RESULTS: Percentage of urine samples containing BPA was 86% in cases, and 82.5% in control. Urinary BPA showed a right skewed distribution. The mean concentration of BPA was 5.01 ± 3.67 ng/ml, and 1.01 ± 1.17 ng/ml, in endometriosis and control group, respectively (P < 0.001, Mann-Whitney U test). The logistic regression showed that the odds ratio of the BPA was 13.1 (95% confidence interval: 1.83-7.14) after adjustment of age, parity, body mass index (BI), and educational status. CONCLUSION: This study showed a positive association between urinary BPA concentrations and endometrioma. However, further larger-scale studies are needed to confirm this hypothesis.	J Res Med Sci. 2017 Jan 27;22:7.	10.4103/1735-1995.199086	28400829	ヒト	子宮	-	-	-	-	-	-	症例対照研究	1	1	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
統合_2979	Amin DM	2019	Role of copeptin as a novel biomarker of bisphenol A toxic effects on cardiac tissues: biochemical, histological, immunohistological, and genotoxic study	Copeptin is a precursor for arginine vasopressin which is usually elevated in acute stress and cardiac emergencies. Bisphenol A (BPA) is an ideal plasticizing factor used in manufacturing of plastics and epoxy resins. To evaluate the cardiotoxicity of bisphenol A and to access copeptin as a cardiac toxic diagnostic and prognostic biomarker in Wistar rats. Sixty Wistar rats were classified into three groups group1: rats's group received regular diet and water; group 2: rat's group administered corn oil; and group 3: rat's received BPA daily with 138 mg/kg bw (LC). After 3 weeks, blood samples were collected for estimating serum copeptin levels, liver and kidney functions. Histological examination of liver, kidney, and heart tissues was performed. Immunohistochemical staining for caspase-3 was done for heart tissues. Bisphenol A induced a significant increase in mean values of serum copeptin level. Histopathological changes in the liver and kidney of BPA-treated rats showed severe congestion of blood vessels and extensive cytoplasmic degeneration in the examined tissues. Ultrasonically, disordered indented nuclei, focal loss of myofibrils, normal cross striations loss, mitochondrial swelling, and interrelated disks distortion were noticed. Immunohistochemical study showed a significant increase in TUNEL immunoreactions in the myocytes of BPA administered rats. In addition, current study showed that bisphenol A exposure produced DNA damage in cardiac cells. We concluded that bisphenol A has deleterious effects on cardiac tissues mass, while copeptin is a good diagnostic and prognostic biomarker.	Environmental Science and Pollution Research, 26, 36037–36047	10.1007/s11356-019-06855-8	31713131	動物	-	1	0	1	1	0	30 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2980	Badding MA, Barraj L, Williams AL, Scrafford C and Reiss R	2019	CLARITY-BPA Core Study: analysis for non monotonic dose-responses and biological relevance	The results of a large 2-year bisphenol A (BPA) rat study conducted by the NTP, called the CLARITY-BPA Core Study, were recently released. This study addressed some of the toxicological issues associated with BPA, including potential non-monotonic dose-response (NMDR) findings reported in the literature. The CLARITY-BPA Core Study found no NMDRs for any of the 38 endpoints examined. Our Key Findings based on the primary statistical tests from the Core Study were evaluated using a previously published methodology that relies upon six characteristics commonly observed in studies that have a tendency for a NMDR. Failure to meet the majority of the characteristics indicates limited evidence of NMDR. The analysis found that only 7 of the 40 findings met at least 3 of the characteristics an increase in percent benefit/risk in dose-dose formats and decreased total fetal scale to step dose scales. However, these findings are not consistent with those of other BPA data. Importantly, none of the endocrine related or reproductive endpoints fulfilled at least 1 of the characteristics. This analysis found limited evidence for NMDR associated with BPA treatment in the study. These results are consistent with the conclusions reached in the Core Study report.	Food Chem Toxicol. 2019 Sep;131:110554.	10.1016/j.fct.2019.06.001	31207305	動物	一般毒性(用量反応性解析)	1	1	1	SD rat：1	5用量：1	2.5, 25, 250, 2500,25000 μg/kg；1 and 25,000 μg/kg;1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-	-
統合_2981	Balabanic D, Filipič M, Klevenz A and Žegura B	2021	Genotoxic activity of endocrine disrupting compounds commonly present in paper mill Effluents	In the present study we evaluated cytotoxic and genotoxic activities of endocrine disrupting compounds (EDCs), including dimethyl phthalate (DMP), diethyl phthalate (DEP), benzyl butyl phthalate (BBP), di(2-ethylhexyl) phthalate (DEHP), bisphenol A (BPA), and nonylphenol (NP), which have been previously identified in effluents from two paper mills with differentiated paper production technologies (virgin or recycled fibres). Moreover, we evaluated genotoxic activity of the effluents from these two paper mills and compared it to the activity of artificial complex mixtures consisting of the mean EDCs at concentrations detected in corresponding paper mill effluents. None of the EDCs, even genotoxic in Salmonella typhimurium (OECD test guideline 471), induced DNA damage in human hepatocellular carcinoma (HepG2) cells (comet assay). Out of exposure genotoxic effects were determined at concentrations ≥ 1 μg/L for BBP and DEHP, ≥ 32 μg/L for DMP, DBP, DBP, and BPA, and ≥ 100 μg/L for NP, while after 25 h of exposure DNA damage occurred at ≥ 0.32 μg/L for BBP, DEHP, and BPA, ≥ 1 μg/L for DMP, DBP, and NP, and ≥ 10 μg/L for DEP. Genotoxic activity of effluents was significantly higher compared to activity of artificial mixtures in HepG2 cells, while the effluents and corresponding artificial mixtures for the paper mill that uses recycled fibre were genotoxic. Genotoxic activity of effluents was significantly higher compared to corresponding artificial mixtures suggesting the presence of further unknown compounds contributing to the effect. Wastewater monitoring based on chemical analysis is limited to determination of targeted compounds and does not take into account possible interactions between chemicals in mixtures. Therefore, it does cannot provide an adequate information on potential toxic effects required for the assessment of genotoxic activity of real environmental samples and their potential threats to the environment and human health.	Sci Total Environ. 2021 Nov 10:794:148489.	10.1016/j.scitotenv.2021.148489	34217092	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2982	Bansal R and Zoeller RT	2019	CLARITY-BPA: Bisphenol A or propylthiouracil on thyroid function and effects in the developing male and female rat brain	The CLARITY-BPA experiment, a large collaboration between the National Institute of Environmental Health Sciences, the National Toxicology Program, and the US Food and Drug Administration, is designed to test the effects of bisphenol A (BPA) at a variety of endocrine systems and endpoints. The specific aim of this subproject was to test the effects of BPA exposure on thyroid functions and thyroid hormone action in the developing brain. Timed pregnant National Center for Toxicological Research Sprague-Dawley rats (strain code 23) were dosed by gavage with vehicle control (0.3% carboxymethylcellulose) or one of five doses of BPA (2.5, 25, 250, 2500, or 25,000 μg/kg/day) from gestation day (GD) 6 through postnatal day (PND) 20. Propylthiouracil (PTU; 3 mg/kg/day) was used as a positive control for thyroid disruption. Offspring were euthanized on PND 21 and 70 (n = 10/sex/dose/time point). Serum thyroid hormone concentrations were measured by radioimmunoassay. Brains were collected, and the cerebellum was cryosectioned and processed for immunohistochemistry. Data were analyzed by ANOVA and Dunnett's post hoc test. Exposure to PTU, but not BPA, significantly reduced serum T4 and T3 concentrations in both sexes on PND 21 and 70. Serum TSH was significantly elevated in PTU-exposed males on PND 21 and 70 and in females on PND 21. Cerebellar histology was normal in all BPA exposure groups. Quantification of PCNA-positive cells revealed a significant increase in the number of proliferating cells in the external granular layer of PTU-exposed males on PND 21 and 70 and females on PND 21. Exposure to BPA did not affect serum thyroid hormone or thyroid hormone-sensitive end points in the developing brain at PND 21. In contrast, propylthiouracil (PTU)-induced severe T4 insufficiency in the exposed pups (80% male/level and elevated serum TSH) had effects at PTU were observed in the male brain and were in the female brain. As a result, it is difficult to interpret the negative effects of BPA on the thyroid in this rat strain because the thyroid system appears to respond differently from that of other rat strains.	Endocrinology. 2019 Aug 1;160(8):1771-1785.	10.1210/en.2019-00121	31135896	動物	甲状腺	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	1	-	-	-	-	●
統合_2984	Chen M, Li S, Hao M, Chen J, Zhao Z, Hong S, Min J, Tang J, He M and Hong L	2020	T-type calcium channel blockade induces apoptosis in C2C12 myotubes and skeletal muscle via endoplasmic reticulum stress activation	Loss of T-type calcium channel (TCC) function has been reported to result in decreased cell viability and impaired muscle regeneration, but the underlying mechanisms remain largely unknown. We previously found the expression of TCC is reduced in aged pelvic floor muscle of multiple vaginal delivery mice, and this is related to endoplasmic reticulum stress (ERS) activation and autophagy flux blockade. In the present work, we further investigated the role of TCC in regulating ERS and skeletal muscle apoptosis. Mibefradil, a TCC blocker, was used to treat C2C12 myotubes and skeletal muscle in vivo. Western blot, qPCR, and flow cytometry were performed to detect the apoptosis and ERS. Co-immunoprecipitation was used to identify the interaction between TCC and ERS sensor protein. Overexpression of TCC inhibited mibefradil-induced ERS and the mitochondrial membrane potential (MMP), reduced mitochondrial reactive oxygen species (ROS) generation, and enhanced expression of mitochondrial apoptosis proteins. Functional inhibition of TCC induced ERS, resulting in disorder of Ca^{2+} homeostasis. In endoplasmic reticulum, and ultimately leading to cell apoptosis in C2C12 myotubes. Tibialis anterior muscles of T-type α 1H channel knockout mice displayed a smaller skeletal muscle fiber size and elevated ERS-mediated apoptosis signaling. Our data point to a novel mechanism whereby TCC blockade leads to ERS activation and terminal mitochondrial-related apoptotic events in C2C12 myotubes and skeletal muscles.	FEBS Open Bio. 2020 Oct;10(10):2122-2136.	10.1002/2211-5463.12965	32865339	動物	骨格筋	1	0	0	0	0	0	-	-	-	-	-	-	-	1	1	-	1	●	-	-	-	-	-	-	-	-	-	-
統合_2985	Di Pietro P, D'Auria R, Viggiano A, Ciaglia E, Maccarello R, Russo RD, Puca AA, Vecchione C, Nori SL and Santoro A	2020	Bisphenol A induces DNA damage in cells exerting immune surveillance functions at peripheral and central level	Bisphenol A (BPA) is a synthetic xenoestrogen diffused worldwide. Humans are chronically exposed to low doses of BPA from food and drinks, thus BPA accumulates in tissues posing human health risk. In this study, we investigated the effects of BPA on peripheral blood mononuclear cells (PBMC) from human healthy donors, and in glia and microglial cell offspring at perinatal day 17 (CTRO) from pregnant females who received BPA exposure after coupling and during lactation and weaning. Results indicated that BPA affected PBMC immunological functions. Indeed, it increased PBMC proliferation causing an S-phase cell cycle accumulation or reversible reversible ROS-like ones, without interfering with mitochondrial membrane potential. Moreover, BPA induced chromosome aberrations and the appearance of shattered cells characterized by high number of fragmented and pulverized chromosomes, micronuclei, and nuclear buds, which are indicative of genomic instability. Consistently, BPA induced DNA damage, as shown by the increase of γH2AX foci. Cell death induced by BPA was mediated by the increase of CTBK1/2 phosphorylation, p21/WAF1 and PARP1 protein expression. Intriguingly, we observed for the first time that BPA-induced effects were associated to an specific modulation of IL-4 and IFNβ in human PBMC. Immunofluorescence analysis of rat hippocampus corroborated in vitro findings showing that BPA-induced pCHK1 phosphorylation in microglia and astrocytes, by decreasing DNA- expression within the dentate gyrus. Overall these results suggest that BPA can alter immune surveillance functions at both peripheral and central level with a potential risk for cancer, neuroinflammation and neurodegeneration.	Chemosphere. 2020 Sep;254:126819.	10.1016/j.chemosphere.2020.126819	32334263	in vitro	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	●	-	-	-	-	-	-	-	-	-	-
統合_2986	Escarda-Castro E, Herraez MP and Lombó M	2021	Effects of bisphenol A exposure during cardiac cell differentiation	Heart development requires a precise temporal regulation of gene expression in cardiomyocytes. Therefore, the transcriptional changes in differentiating cells can lead to congenital heart diseases. Although the genetic mutations underlie most of these alterations, exposure to environmental contaminants, such as bisphenol A (BPA), has been recently considered as a risk factor as well. In this study we investigated the genotoxic and epigenetic effects of BPA throughout cardiomyocyte differentiation. Hl-1 cells (cardiomyocyte) were exposed to 10 and 50 μM BPA before and during the last two days of cardiac stem cell differentiation. Then, we analyzed the phenotypic and molecular modifications (at transcriptional, genetic and epigenetic level). The results showed that treated myoblasts developed a skeletal muscle cell-like phenotype. The transcriptional analysis revealed that BPA induced the overexpression of cardiac progenitor markers (*Isl1*, *Nkx2.5*, *Gata4*, *Mef2c*, *Tbx5*, *Hand1* and *Hand2*), whereas mature cardiac markers (*Tnnt2*, *Myh6*, *Myh7*, *Cx43*, *Cx45*, *Kcnj2*, *Scn5a*, *Ryr2*, *Atp2a2*, *Pln*, and *Kcnh2*). Additionally, significant effects on some observed regarding DNA damage and histone acetylation levels after the two periods of BPA exposure: in cells exposed to the lowest the percentage of DNA repair foci (formed by the co-localization of γ-H2AX and 53BP1) increased in a dose-dependent manner, whereas the treatment with the lowest triggered a decrease in the epigenetic marks H3K9ac and H3K12ac. Our in vitro results revealed that BPA seriously interferes with the process of cardiomyocyte differentiation, which could be related to the reported in vivo effects of this toxicant on cardiogenesis.	Environ Pollut. 2021 Oct 1:286:117567.	10.1016/j.envpol.2021.117567	34126515	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	10 μM および30 μM	1	-	-	-	●	-	-	-	-	-	-	-	-	-	-
統合_2987	Frankyn H, Budiawan B, Handayani S and Dwi	2020	Study of urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) in rats (Rattus norvegicus) due to bisphenol A (BPA) exposure based on fenton-like reaction	This study was conducted to analyze the formation of DNA adduct 8-OHdG due to oxidative damage of DNA caused by Bisphenol (BPA) and chromium (VI) exposure. The in vivo study was conducted to the rat (Rattus norvegicus) as a model animal. The rats were divided into 4 groups, namely the control group, the BPA exposure group, the chromium exposure group, and the BPA and chromium exposure group. The formation of 8-OHdG in urine samples was analyzed using LC-MS/MS with internal phase chromatography. Mixture of acetonitrile:acetate pH 6.8 (20:80) and acetonitrile:water:acetic acid as mobile phase in LC-MS/MS for an elution gradient. The results showed that the exposure of BPA, the mixture of BPA and Cr (VI) might cause the formation of urinary 8-OHdG in rats. The longer exposure time causes the increase levels of urinary 8-OHdG formation. The study also showed that urinary 8-OHdG concentration increases due to synergistic effect between BPA and Cr (VI) exposure.	Proceedings of the IOP Conference Series: Materials Science and Engineering, 763, 012024	10.1088/1757-899X/763/1/012024	-	動物	-	1	1	1	不明	0	2 mg/kg BW	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2988	Gonzalez-Cadavid NF	2019	Cellular-molecular signature and mechanism of BPA effects on Penile erection – CLARITY-BPA grantee study results		-	10.22427/NTP-DATA-018-00009-0001-000-9	-	動物	-	1	1	1	1	1	[illegible]	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2989	Hanioka N, Isobe T, Tanaka-Kagawa T and Ohkawara S	2020	Wogonin glucuronidation in liver and intestinal microsomes of humans, monkeys, dogs, rats, and mice	Wogonin, one of the flavonoids isolated from Scutellaria baicalensis, exhibits some beneficial bioactivities, including anti-inflammatory and anticancer effects, and is metabolized into glucuronide by UDP-glucuronosyltransferase (UGT) enzymes in humans. In the present study, wogonin glucuronidation was examined in the liver and intestinal microsomes of humans, monkeys, dogs, rats, and mice using a kinetic analysis. The kinetics of wogonin glucuronidation by liver microsomes followed the Michaelis–Menten model for all species examined. CLint values in hepatic microsomes were in the order of humans > monkeys > mice > dogs > rhesus. The kinetics of intestinal microsomes fit the Michaelis–Menten model for humans, monkeys, rats, and mice and the substrate inhibition model for dogs. CLint values were rats > monkeys > mice > dogs > humans. The tissue dependence of CLint values was liver microsomes > intestinal microsomes for humans, dogs, and rats, and liver microsomes = intestinal microsomes for monkeys and mice. These results demonstrated that the metabolic abilities of UGT enzymes toward wogonin in the liver and intestines markedly differ among humans, monkeys, dogs, rats, and mice, and suggest that species differences are closely associated with the biological effects of wogonin.	Xenobiotica, 50, 906-912	10.1080/00498254.2020.1725180	32005083	動物	-	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-	-
統合_2990	Hercog K, Maisanaba S, Filipič M, Solinar-Dolenc M, Kač L and Žegura B	2019	Genotoxic activity of bisphenol A and its analogues bisphenol S, bisphenol F and bisphenol AF and their mixtures in human hepatocellular carcinoma (HepG2) cells	The use of bisphenol A (BPA) in manufacturing of plastics is being gradually replaced by presumably safer analogues, such as bisphenol S (BPS), bisphenol F (BPF) and bisphenol AF (BPAF). Despite their widespread occurrence in the environment, there is a knowledge gap in their toxicological profiles. We investigated cytotoxic/genotoxic effects as well as changes in the expression of selected genes involved in the xenobiotic metabolism, response to oxidative stress and DNA damage upon exposure to BPS and their mixtures in human hepatocellular carcinoma HepG2 cells. BPA, BPS, BPF and BPAF induced cytotoxicity (MTT assay) and genotoxicity (comet assay) in HepG2 cells. The lowest BPA concentration that induced the formation of DNA double-strand breaks determined with γ-H2AX assay was 0.01 μg/mL (i.e. 44 nM). All four BPs up-regulated the expression of *CYP1A1* and *GSTA1*, while BPS up-regulated and BPAF down-regulated the expression of *GSTT1*. Only BPA up-regulated oxidative stress responsive gene *SOD2*, while BPAF up-regulated the expression of *CDKN1A* and *GADD45a*. At concentrations relevant for human exposure (ng/mL range) BPA and its analogues as individual compounds and in mixtures did not exert genotoxic activity, whereas BPA and BPAF as well as the mixtures up-regulated the expressions of *CYP1A1* and *GSTA1*.	Sci Total Environ. 2019 Oct 15:687:267-276.	10.1016/j.scitotenv.2019.05.486	31207516	in vitro	-	-	-	-	-	-	-	-	-	-	1	1	ヒト一次肝細胞の増殖と分化（log10用量）	1	-	-	-	●	-	-	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100nM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_2991	Herzog K, Şören A, Makarasta S, Filipic M and Žegura B	2020	Plastics in cyanobacterial blooms—genotoxic effects of binary mixtures of cylindrospermopsin and bisphenols in HepG2 cells	Ever-expanding environmental pollution is causing a rise in cyanobacterial blooms and the accumulation of plastics in water bodies. Consequently, exposure to mixtures of cyanotoxins and plastic-related contaminants, such as bisphenols (BPs), is of increasing concern. The present study describes genotoxic effects induced by or exposure to one of the emerging cyanotoxins—cylindrospermopsin (CYN)—10.5 µg/mL and BPs (bisphenol A (BPA), BPF, BPS, BPAF, BPZ, BPAP, BPB, BPC, BPE, BPG, BPP, BPTMC, BPM, BPZP, BPFL, BPAD, BPC2, BPPH, BPBP, BPA-DE, BPA-DG, BPA-DM, BPA-DP, BPA-DPG, BPA-DPP, BPA-DPP, BPA-DPP

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	透明性評価基準適合（1534報）	信頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_3005	Pan D, Feng D, Ding H, Zhang X, Ma Z, Yang B and Xie M	2020	Effects of bisphenol A exposure on DNA integrity and protamination of mouse spermatozoa	Background: Bisphenol A is widely used in the manufacture of polycarbonate plastics and has caused increasing concern over its potential adverse impacts on spermatogenesis. However, the effect of bisphenol A on spermatogenesis is yet to be explored. Objectives: To evaluate whether bisphenol A has adverse effects on DNA integrity and protamination of spermatogenic cell. Materials and methods: Newborn male mice were subcutaneously injected with bisphenol A (0.1, 5 mg/kg body weight) or 1 ml corn oil (control group, n = 20) daily from post-natal day 1 until 39. At post-natal day 70, epididymis caudal spermatozoa were collected for sperm quality analysis. Testicular sperm were collected for DNA integrity and protamination analysis. The ultrastructural features of testicular sections were examined under a transmission electron microscope. Western blot and RT-PCR were used to detect the expression levels of transition protein (Tnp1 and Tnp2, protamine (Prm1 and Prm2 protein, and mRNA in mice testes. Results: Bisphenol A significantly reduced sperm counts, impaired sperm motility, and increased the percentage of malformed spermatozoa. Poor sperm chromatin integrity and increased TUNEL-positive spermatogenic cells were also observed in mice exposed to bisphenol A. Ultrastructural analysis of testes showed that bisphenol A exposure caused incomplete chromatin condensation, retention of residual cytoplasm, and abnormal acrosome formation. In addition, the relative expression levels of Tnp2 and Prm2 in mice testes decreased significantly in bisphenol A groups. Discussion and conclusion: Our findings identified that neonatal bisphenol A exposure may negatively contribute to the sperm quality in adult mice. Mechanistically, we showed that bisphenol A induced sperm chromatin integrity along with increased DNA damage, which may be due to poor protamination of spermatozoa.	Andrology, 8, 486-496	10.1111/andr.12694	31489793	動物	-	1	0	1	不明	0	0.1、5 mg/kg 体重	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3006	Pandpatil VV, Kumari D, Chatterjee A, Kumar S, Bhaskar V, Polasa K and Ghosh S	2020	Protective effect of turmeric against bisphenol - A induced genotoxicity in rats	In this study, the protective role of turmeric on genotoxic effects of Bisphenol A exposure in Wistar rats by in vivo experiment were investigated. Bisphenol A is a known endocrine disrupter and suspected carcinogen, that comes that through plastics for food packaging and food processing. In this study, rats were divided into three groups of twelve animals each and were administered with Bisphenol A by oral gavage at 0 levels, at 0, 50 and 100 µg /kbt of the animals. Israeli group were fed with food which contained 5% turmeric (w/w/w), for a period of 3 wk, while the rest of the rats received the same diet treatment without the addition of turmeric. In the present study, the DNA damage was assessed using Alkaline Comet Assay. Significant increase in DNA damage was observed in Bisphenol A exposed groups as compared to control group. In the micronucleus assay, the formation of micronuclei was assessed using Mann Whitney U test. Significant decrease in serum malondialdehyde and urinary 8-hydroxy-2' -deoxyguanosine levels were observed in Bisphenol A exposed groups as compared to Bisphenol A groups. Bisphenol A groups exhibited significantly higher mean levels of DNA damage in liver and kidney as compared to the untreated control group. Bisphenol A group showed significant increase in the formation of micronuclei which was approximately threefold higher as compared to the control group. A significant decrease in DNA migration was observed in Bisphenol A co-treated groups in liver and kidney. Turmeric feeding significantly inhibited the micronuclei formation induced by Bisphenol A. The study results indicate that turmeric can protect against Bisphenol A induced genotoxicity in rats.	Journal of Nutritional Science and Vitaminology, 66, S336-S342	10.3177/jnsv.66.S336	33612621	動物	-	1	1	1	不明	0	0, 50 and, 100 µg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3007	Plank AC, Frey S, Basedow LA, Solati J, Carneiro F, von Horsten S, Kratz O, Moll GH and Golub Y	2021	Prenatally traumatized mice reveal hippocampal methylation and expression changes of the stress-related genes Crhr1 and Fkbp5	In our previous study, we found that prenatal trauma exposure leads to an anxiety phenotype in mouse pups, characterized by increased corticosterone levels and increased anxiety-like behavior. In order to understand the molecular mechanisms underlying this phenotype, we here investigated the hippocampal methylation and expression changes of the stress-related genes Crhr1 and Fkbp5 in prenatally traumatized mice. Pregnant C57BL/6J mice were exposed to a combination of predator sound and restraint stress on gestational days 16 and 17. Hippocampal methylation levels of several regulatory gems of the stress axis in the dorsal hippocampus (DHPC) and ventral hippocampus (VHPC) of PT-offspring and adult mice. We detected increased corticosterone levels following homotypic restraint (CORT) and decreased FKBP protein levels in PT-adult mice. These alterations were accompanied by a decreased methylation status of the Crhr1 promoter and an increased methylation status of the Fkbp5 promoter, respectively. Interestingly, the changes in Fkbp5 and Crhr1 mRNA levels were not detected in the embryonic (hPPC of PT mice. Together, our findings provide evidence that prenatal trauma has a long-term impact on stress axis function and anxiety phenotype associated with altered Crhr1 and Fkbp5 transcripts and promoter methylation.	Translational Psychiatry, 11, 183	10.1038/s41398-021-01293-y	33758173	動物	-	1	不明	0	1	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3008	Qiu B, Xu Y, Wang J, Liu M, Dou L, Deng R, Wang C, Williams KE, Stewart RB, Xie Z, Ren W, Zhao Z, Shi-xu W, Liang T and Yang W	2019	Loss of FKBP5 affects neuron synaptic plasticity: an electrophysiology insight	FKBP5, FK506 binding protein 5, which acts as a co-chaperone of heat-shock protein 90 (HSP90) and negatively regulates GR, its association with mental disorders has been identified, but its function in disease development is largely unknown. Long-term potentiation (LTP) is a functional measurement of neuronal connection and communication, and is considered one of the major cellular mechanisms that underlies learning and memory, and is closely related to mental diseases. In this study, a reduction (~ 30%) of FKBP5 protein was observed in the hippocampus (HPC) of Fkbp5 knockout (KO) mice was observed when compared with control wild-type (WT) littermates. Furthermore, the glutamatergic and GABAergic signaling pathways. The frequency of mEPSCs was decreased in KO hippocampus, indicating a decrease in excitatory synaptic activity. While no differences were found in levels of glutamatergic neurotransmission, the frequency of mIPSCs was significantly increased in KO hippocampus, indicating an increase in inhibitory synaptic activity. Moreover, the amplitude of mIPSCs was also increased. Immunofluorescence GABA was found to be enhanced in Fkbp5 KO hippocampus. Further investigation suggested that increased expression of GAD65, but not GAD67, accounted for this increase. Additionally, a profound GABAergic alteration was observed in the form of increased mIPSC frequency in the KO hippocampus, indicating an increase in presynaptic GABA release. Our findings uncover a novel role for Fkbp5 in neuronal synaptic plasticity and highlight the value of Fkbp5 KO as a model for studying its role in neurological function and disease development.	Neuroscience, 402, 23-36	10.1016/j.neuroscience.2019.01.021	30685540	動物	-	1	不明	0	0	不明	不明	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3009	Ramos C, Ladeira C, Zeferino S, Dias A, Faria I, Cristovam E, Gomes M and Ribeiro E	2019	Cytotoxic and genotoxic effects of environmental relevant concentrations of bisphenol A and interactions with doxorubicin	Bisphenol A (BPA) is one of the most widely utilized endocrine disruptors, to which humans are exposed, particularly through ingestion. BPA is an estrogenic compound with a putative association to tumorigenesis. Although extensively studied in estrogen-responsive cells, information regarding its effects on cells from the upper gastrointestinal tract exposed to free/active forms of BPA is still scarce. Similarly, BPA interactions with other drugs have been neglected, although it has been suggested to have a potential role in doxorubicin (DOX) chemoresistance. This study is intended to assess potential cytotoxic and genotoxic effects of BPA, as well as its interactions with DOX, in human epithelial type 2 cells (Hep-2) originated from a human laryngeal carcinoma and in a DNA damage-responsive cell line, the human lung fibroblasts (MRC-5). Cell viability was assessed by the neutral red uptake assay, and the genotoxic potential was evaluated by the micronucleus assay and the comet assay. Cytotoxicity was observed in Hep-2 cells exposed to BPA (≥ 50 µM) and DOX (≥ 0.5 µM). The comet assay and micronucleated cells and mitotic disruption was evaluated cytologically by fluorescent microscopy with DAPI staining. Cytotoxicity analysis revealed that exposure to BPA per se does not affect cellular viability. Nevertheless, the genotoxic analysis showed that BPA induced an increase of DNA damage in the Hep-2 cell line and in oxidative damage in the MRC-5 cell line. An increase of micronuclei was also observed in both cell lines following BPA exposure. BPA and DOX co-exposure suggested that BPA acts as an antagonist of DOX effects in both cell lines. The interaction with DOX appears to be cell type dependent, exhibiting a non-monotonic response curve in MRC-5 cells, a BPA-experiencing cell line. Our study emphasizes the need for a deeper knowledge of BPA interactions, particularly with chemotherapeutic agents, in the context of risk assessment and public health.	Mutat Res Genet Toxicol Environ Mutagen. 2019 Feb;838:28-36.	10.1016/j.mrgentox.2018.11.009	30678825	in vitro	-	-	-	-	-	1	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3010	Sahu C, Charaya A, Singla S, Dwivedi DK and Jana G	2020	Zinc deficient diet increases the toxicity of bisphenol A in rat testis	Zinc (Zn) plays an important role in maintaining the process of spermatogenesis and reproductive health. Bisphenol-A (BPA), an endocrine disrupting chemical is known to be a reproductive toxicant in different animal models. The present study was designed to study the effect of low Zn utmost detrimental factors (Zn deficient condition and influence of toxicant BPA) on germ cell growth and overall male reproductive health in rats. Male Wistar rats (n = 24) were divided into four groups (n = 6) and treated orally for 60 days as follows: Group I (control) received 0.5 ml/kg b.w. of 0.5% carboxymethyl cellulose (CMC), Group II received 100 mg/kg b.w. zinc deficient diet (ZDD) fed rats (ZDD), Group III received BPA (100 mg/kg b.w./day) and Group IV received ZDD + BPA (100 mg/kg b.w./day) for 60 days. After 60 days of treatment, epididymides, and prostate were investigated. Testicular deoxyribonucleic acid (DNA) damage was evaluated by Halo and Comet assay, apoptosis of sperm and testis were quantified by TUNEL assay. Serum protein electrophoretic patterns and testicular protein expressions such as Nrf-2, catalase, PCNA, and Hsp2 were analyzed by Western blot analysis. The results showed that BPA significantly increased the testicular, epididymal, and prostate toxicity in dietary Zn deficient condition due to testicular hypersomnia, hypogonadism, increased cellular and DNA damage, apoptosis, as well as perturbations in protein expression.	Journal of Biochemical and Molecular Toxicology, 34	10.1002/jbt.22549	32609952	動物	-	1	1	1	不明	0	100 mg/kg/日	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
統合_3011	Song RH, Wang B, Yao QM, Li Q, Jia X and Zhang JA	2019	The impact of obesity on thyroid autoimmunity and dysfunction: a systematic review and meta-analysis	Background: To help inform decision making in the clinical setting, we carried out a systematic review and meta-analysis to estimate the association of thyroid disease risks with obesity. Methods: Pubmed, Embase, Web of Science, Cochrane database and Google Scholar electronic databases were searched from inception to October 31, 2018 without language restrictions to explore the relationship between thyroid disorders and obesity. The relative risk (RR) or odds ratio (OR) for thyroid disorders were calculated using the DFSE and the DTSTG software. Results: A total of 22 studies were included in the study. (1) Meta-analysis showed that obesity was significantly associated with an increased risk of hypothyroidism (RR = 1.80, 95% CI 1.63-2.11, P < 0.001). Meta-analyses after stratification further showed that obese population had increased risks of overt hypothyroidism (RR = 3.31, 95% CI 2.52-4.36, P < 0.001) and subclinical hypothyroidism (RR = 1.76, 95% CI 1.57-1.93, P < 0.001). (2) Further meta-analysis also showed obesity was closely associated with Hashimoto's thyroiditis (RR = 1.91, 95% CI 1.41-2.52, P < 0.001), but not with Graves' disease. (3) In the meta-analysis of antibodies, obesity was correlated with positive thyroid peroxidase antibody (TPOAb) (RR = 1.43, 95% CI 1.12-1.81, P = 0.001), but not with positive thyroglobulin antibody (TGAb). Conclusions: Obesity was significantly related to hypothyroidism, HT, and TPOAb, implying that prevention of obesity is crucial for thyroid disorders.	Front Immunol. 2019 Oct 1:10:2349.	10.3389/fimmu.2019.02349	31681268	ヒト	代謝(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	1	1	1	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3012	Su KZ, Li YR, Zhang D, Yuan JH, Zhang CS, Liu Y, Song LM, Lin Q, Li MW and Dang J	2019	Relation of circulating resistin to insulin resistance in Type 2 diabetes and obesity: a systematic review and meta-analysis	Background: Resistin, a cysteine-rich polypeptide encoded by the RETN gene, which plays an important role in many mechanisms in violent studies, including lipid metabolism, inflammation and insulin resistance. Nevertheless, the relationship between resistin and insulin resistance in humans is under debate. The present study was designed to clarify the correlation between resistin and insulin resistance. Methods: A systematic literature search was performed using PubMed, Embase and Cochrane Library until March 3, 2018 with the keywords "resistin" and "insulin resistance." 7 event plots and Egger's test were used to detect publication bias. A random effects model was used to calculate the pooled effect size. Subgroup analysis and meta-regression was performed to identify the sources of heterogeneity. Results: Fifteen studies were included in our systematic review. Among them, 13 studies with Pearson coefficients were used for meta-analysis. We found resistin levels were weakly correlated with insulin resistance in those with T2DM and obesity (r = 0.21, 95% CI: 0.09-0.33, I2 = 59.7%, P = 0.003). Nevertheless, subgroup analysis suggested that circulating resistin levels were significantly positively correlated with insulin resistance in Asians (r = 0.29, 95% CI: 0.17-0.41, I2 = 0.0%, P < 0.001) but not in Caucasians (r = 0.04, 95% CI: -0.08-0.16, I2 = 0.0%, P = 0.492). Moreover, circulating resistin and insulin resistance in those with normal circulating resistin levels (<12.8 ng/ml) (r = 0.02, 95% CI: -0.02-0.8,I2 = 0.0%, P = 0.000). Publication bias was insignificant (Egger's test, P = 0.992). Conclusion: In T2DM and obese individuals, resistin levels were positively correlated with insulin resistance in those with hyperresistinemia, but not in those with normal circulating resistin levels.	Front Physiol. 2019 Nov 19:10:1399.	10.3389/fphys.2019.01399	31803062	ヒト	代謝(メタアナリシス)	-	-	-	-	-	-	メタアナリシス	1	1	-	-	-	-	-	1	1	1	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3014	Yang L, Baumann C, De La Fuente R and Viveiros MM	2020	Mechanisms underlying disruption of oocyte spindle stability by bisphenol compounds	Accurate chromosome segregation during meiotic division depends on the assembly of a bipolar spindle apparatus and formation of correct chromosome-microtubule (MT) interactions (Chiodal et al. 2010). Thus, exposure to spindle-disrupting compounds can promote meiotic errors, which in turn lead to aneuploidy in oocytes and genomic instability in developing embryos upon fertilization (Eichenlaub et al. 2012). The adverse effects caused by environmental toxicants on gamete quality and function is a growing concern. In the current study, we tested the effect of bisphenol compounds, including bisphenol A (BPA) and bisphenol F (BPF), on assembled meiotic spindle organization in isolated MII oocytes, a critical stage prior to fertilization. Bisphenol A, widely used in plastics manufacture, is recognized as a potent endocrine disrupter with estrogen-like activity as it can bind to intracellular ERα, ERβ1 and cell surface GPR30 estrogen receptors to affect cell signaling and proliferation (Acconcia et al. 2015). Due to its widespread use, increasing evidence suggests that BPA has significant detrimental effects on human and animal health (Gore et al. 2015; Patisaul et al. 2018), which has prompted some restrictions on its use. Yet, it remains highly prevalent. Moreover, the use of replacement analogs, such as bisphenol S (BPS) and bisphenol F (BPF), has increased in recent years. However, these bisphenol analogs have been shown to exhibit similar estrogenic activity as BPA (Rochester and Bolden 2015; Rochester et al. 2015; Rochester and Bolden 2015; Pelch et al. 2019). Studies demonstrate that BPA adversely affects various aspects of the reproductive system in males and females, including germ cell development and function (Peretz et al. 2014). In females, maternal exposure to environmentally relevant doses of BPA has been shown to disrupt early oocyte/follicle development (Hunt et al. 2012; Berger et al. 2016) and promote increased rates of oocyte meiotic abnormalities, including aneuploidy (Hunt et al. 2003; Susiarjo et al. 2015; Rousseaux et al. 2018). Meiotic abnormalities in oocytes are also evident following in vitro culture with continuous exposure to BPA (Lenie et al. 2016). While the endocrine disrupting activity of BPA is well documented, studies also point to damaging effects on microtubule (MTs) that are less understood. Microtubule and spindle defects have been reported in response to BPA exposure during meiotic division in diverse systems, including somatic cells (Pinchin et al. 1987), plant cells (Adamakis et al. 2016), and sea urchin embryos (Zhang et al. 2018). Meiotic abnormalities in mammalian oocytes following maternal in vivo exposure (Hunt et al. 2003) or ovarian follicle culture (Lenie et al. 2016), with BPA were frequently associated with meiotic spindle MT disruption. Notably, exposure to BPA or common replacement analogs during in vitro meiotic maturation has been shown to hinder the progression to metaphase II (MII) as well as disrupt meiotic spindle assembly and organization/increase (Can et al. 2005; Eichenlaub-Ritter et al. 2008; Lenie, Delbaeresse et al. 2017; Lenie, Campen et al. 2018), and human (Machtinger et al. 2018) oocytes. Nevertheless, the underlying mechanisms of bisphenol-mediated spindle MT disruption remain unclear. Here, we investigated the effects of bisphenol compounds, BPA, BPS, and BPF, on the assembled meiotic spindle in mouse MII oocytes following in vitro maturation (IVM) in the absence/presence of BPA exposure. We also tested whether bisphenol exposure in MII oocytes affected the distribution of meiotic chromosomes. Moreover, newly investigations used oocytes cell-enclosed oocytes interesting BPA exposure in vitro, raising the question as to whether meiotic abnormalities might also be partially attributable to bisphenol effects on the surrounding granulosa cells (Peretz et al. 2014; Marcus et al. 2017). In the current study, we exposed matured oocytes to BPA and a common replacement analog, BPF, to gain a better understanding of the direct effects of bisphenols on MTs and spindle organization. The aim was to test the hypothesis that bisphenol exposure during meiotic maturation disrupts spindle MT assembly and chromosome alignment in mouse oocytes. Our findings indicate that BPA and BPF are detrimental to oocyte spindle organization and stability as well as spindle-associated factors. Moreover, we show differences in BPA and BPF action on MTs, as well as, identify an important link between bisphenol-mediated MT disruption and Aurora Kinase A activity.	Reproduction. 2020 Apr;159(4):383-396.	10.1530/REP-19-0494	31990668	in vitro	-	-	-	-	-	1	1	5, 25, 50 µg/ml	1	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3015	Yang Y, Liu C, Yang J, Yuan F, Cheng R, Chen R, Shen Y and Huang L	2021	Impairment of sirtuin 1-mediated DNA repair is involved in bisphenol A-induced aggravation of macrophage inflammation and atherosclerosis	Bisphenol A (BPA), an environmental pollutant, has received considerable attention worldwide for its hazardous effects of promoting atherosclerosis and increasing the risk of cardiovascular diseases (CVDs). However, the mechanisms involved are unclear. We aimed to investigate the mechanisms underlying BPA-aggravated atherosclerosis and potential preventive treatments. Four-week-old male Ldlr-/- C57BL/6 mice were administered 250 µg/L BPA via drinking water for 10 weeks with or without a Nicotinic acid and/or resveratrol (SIRT1 for 12 weeks. Chronic BPA exposure significantly aggravated atherosclerosis, enhanced the production of inflammatory cytokines but not lipid levels, promoted macrophage infiltration into plaque areas. Moreover, BPA exposure decreased, performed in macrophages. Isolated from BPA-exposed mice, BPA exposure also promoted inflammatory phenotype in response to cholesterol crystal treatment than those from control mice. The current assay revealed that the DNA repair capacity of BPA-exposed macrophages was impaired, and sensors binding showed that BPA exposure inhibited the activity of sirtuin 1 (SIRT1), a histone deacetylase. Mechanistically, BPA exposure decreased SIRT1 activity, thereby increasing the acetylation of Ku70 and impairing its DNA binding ability and its ability to recruit DNA-dependent protein kinase catalytic subunit (DNA-PKcs). Consequently, BPA-induced impairment of DNA repair and apoptosis, as indicated by phosphorylated H2AX expression and cleaved PARP expression. Moreover, BPA administration significantly ameliorated BPA-aggravated NLRP3 inflammasome activation, as indicated by decreased ASC speck formation and interleukin-1β production, which were abolished by NAD1 knockdown. Furthermore, NAD1 administration prevented BPA-induced aggravation of atherosclerosis. Our findings indicate that impairment of sirtuin 1-mediated DNA repair is involved in BPA-induced aggravation of macrophage inflammation and atherosclerosis and that NAD1 might be a promising preventive and therapeutic agent for BPA-related CVDs.	Chemosphere, 265, 128997	10.1016/j.chemosphere.2020.128997	33239236	動物	-	1	1	1	Ldlr-/- C57BL/6	0	250 µg/L	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3016	Yin L, Siracusa JS, Mascot E, Guan X, Eberfeld C, Liang S and Yu X	2020	High-content image-based single-cell phenotypic analysis for the testicular toxicity prediction induced by bisphenol a and its analogs bisphenol S, bisphenol AF, and tetrabromobisphenol A in a three-dimensional testicular cell Co-culture model	Emerging data indicate that structural analogs of bisphenol A (BPA) such as bisphenol S (BPS), tetrabromobisphenol A (TBBPA), and bisphenol AF (BPAF) have been introduced into the market as substitutes for BPA. Our previous study compared in vitro testicular toxicity using murine C18-4 spermatogonial cells and found that BPAF and TBBPA exhibited higher spermatogonial toxicity as compared to BPA and BPS. Recently, we developed a novel in vitro three-dimensional (3D) testicular cell co-culture model, enabling the classification of reproductive toxic substances. In this study, we applied the testicular cell co-culture model and employed a high-content image (HCI)-based single-cell analysis to further compare the testicular toxicities of BPS and its analogs. We also developed a machine learning (ML)-based HCA pipeline to examine the complex phenotypic changes associated with testicular toxicities. We found donor- and time-dependent changes in a wide spectrum of adverse endpoints, including nuclear morphology, DNA synthesis, DNA damage, and cytoskeletal rearrangement. Our results revealed that BPAF and TBBPA induced significant changes in the cell population, whereas BPS and BPA showed minimal effects. Furthermore, single-cell based analysis not only observed the trends of the averaged population, but also revealed changes in the sub-population. Machine learning-based phenotypic analysis revealed that treatment of BPS and its analogs resulted in the loss of spatial cytoskeletal structure, and an accumulation of G0 phase cells in a dose- and time-dependent manner. Furthermore, treatment of BPAF induced multinucleated cells, which were associated with altered DNA damage response and impaired cellular F-actin filaments. Overall, our demonstrated cross-and effective means to evaluate multiple toxic endpoints in the testicular co-culture model through the combination of ML and high-content image-based single-cell analysis. This approach provided an in-depth analysis of the multi-dimensional HCA data and provided an unbiased quantitative analysis of the phenotypic alterations.	Toxicological Sciences, 173, 313-335	10.1093/toxsci/kfz233	31750923	in vitro	-	-	-	-	-	1	0	25, 50, 100, 200, and 400 µM	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-	-	-

別添-2　統合文献リスト

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_3017	Yu H, Chen Z, Hu K, Yang Z, Song M, Li Z and Liu Y	2020	Potent clastogenicity of bisphenol compounds in mammalian cells — human CYP1A1 being a major activating enzyme	Bisphenols (BPs) are environmental pollutants with released DNA damage in human population however, they are generally inactive in standard mutagenicity assays, possibly due to insufficient metabolic activation. In this study, induction of micronuclei and double-strand DNA breaks by 8 BPs, BPF, and BPS in Chinese hamster V79 derived cell lines expressing various human CYP enzymes and a human hepatoma (C3A) metabolism-competent cell line were investigated. Molecular docking of BPs to human CYPs indicated some substrate-enzyme potentials, including CYP1A1 for each compound, which did not induce micronuclei in V79-derived cell lines without human CYPs. BPF, BPS, and BPB induced micronuclei in V79-derived cell lines with CYP1A1, CYP1A2, and CYP3A4, but not in those with CYP2A6 and CYP2E1. However, in cells co-exposed to 1-aminobenzotriazole (a CYP inhibitor) or ketoconazole (a CYP3A4 inhibitor) or furafylline (a CYP1A2 inhibitor), the micronuclei induction by each compound, with thresholds lowered from 2.5–5.0 to 0.6–1.2 μM. Immunofluorescence staining of γ-H2AX foci, a DNA double-strand break marker, and inhibition of topoisomerase II activity by each compound, with thresholds lowered from 2.5–5.0 to 0.6–1.2 μM. Immunofluorescence staining of γ-H2AX foci, a DNA double-strand break marker, and inhibition of topoisomerase II activity by each compound, with thresholds lowered from 2.5–5.0 to 0.6–1.2 μM. Immunofluorescence staining of γ-H2AX foci, a DNA double-strand break marker, and inhibition of topoisomerase II activity by each compound indicated poor clastogenic effects. In conclusion, BPs are potently clastogenic in mammalian cells, which requires activation primarily by human CYP1A1 and are negatively modulated by phase II metabolism. Copyright © 2020 American Chemical Society.	Environ Sci Technol. 2020 Dec 1;54(23):15267-15276.	10.1021/acs.est.0c04808	33201683	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	1	不明	1	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3018	Yuan J, Kong Y, Ommati MM, Tang Z, Li H, Li L, Zhao C, Shi Z and Wang	2019	Bisphenol A-induced apoptosis, oxidative stress and DNA damage in cultured rhesus monkey embryo renal epithelial Marc-145 cells	Bisphenol A (BPA) is widely used in the production of epoxy resins and polycarbonate plastics. Under harsh situations, these plastics likely decant BPA, which then can seep into the environment. Various concentrations of BPA have been detected in many biological fluids. However, there is paucity of information on the detrimental effects of BPA and its subsequent cellular events in chronic kidney disease (CKD). Hence, in this in vitro study, we aimed to investigate the effects of BPA on renal epithelial cell activation, apoptosis, and DNA damage. Rhesus monkey embryo renal epithelial Marc-145 cells were exposed to 10 −1, 10 −2, 10 −3, 10 −4, 10 −5, 10 −6, and 10 −7 M BPA concentrations for 24 h. Cell viability was assessed by MTT assay. Our results showed that BPA induced cytotoxicity in Marc-145 cells in a dose-dependent manner. At the LOAEL level, cells concentration increases in apoptosis-related indices, lactate dehydrogenase (LDH) activity, reactive oxygen species (ROS) generation, malondialdehyde, and nitric oxide (NO) content, and the ratio of comet Marc-145 cells with a dose-dependent manner. The data indicated that increased oxidative stress, apoptosis, and DNA damage in epithelial Marc-145 cells might play a pivotal role in the mechanism of BPA-induced nephrotoxicity.	Chemosphere. 2019 Nov;234:682-689.	10.1016/j.chemosphere.2019.06.125	31234085	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	1	- - - - - - - - - - - - - - - - - - - -	1	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3019	Yuan J, Che S, Zhang L, Li X, Yang J, Sun X and Ruan Z	2021	Assessing the combinatorial cytotoxicity of the exogenous contamination with BDE-209, bisphenol A, and acrylamide via high-content analysis	Food is often exposed to multiple types of contaminants, and the coexistence of contaminants may have antagonistic, additive or synergistic effects. This study investigated the combinatorial toxicity of the three most widespread exogenous contaminants, decabromodiphenyl ether (BDE-209), bisphenol A (BPA), and acrylamide (ACR) to HepG2 cells. A mathematical model (Chou−Talalay) and high-content analysis (HCA) were employed to evaluate the combinatorial effects of the contaminants. The results showed that BDE-209, BPA, and ACR induced cytotoxicity in HepG2 cells. Furthermore, the cytotoxicity induced by BDE-209, BPA, and ACR, and binary combination of contaminants exhibited additive synergistic effects. In general, combining multiple contaminants significantly increased the cellular reactive oxygen species (ROS), Ca2+ flux, DNA damage and Caspase-3, and decreased mitochondrial membrane potential (MMP) and nuclear roundness, indicating that the additive or synergistic mechanism of the combined contaminations was disturbance in multiple organelles. This study emphasizes the complexity of human exposure to food contaminants and provides a scientific basis for formulating strict regulatory standards.	Chemosphere. 2021 Dec;284:131346.	10.1016/j.chemosphere.2021.131346	34217936	in vitro	-	-	-	-	-	-	-	-	-	-	-	不明	1	不明	1	-	-	-	-	-	●	-	-	-	-	-	-	-	-
統合_3020	Zahra Z, Khan MR, Majid M, Manjum S and Sajid M	2020	Gonadoprotective ability of Vincetoxicum arnottianum extract against bisphenol A-induced testicular toxicity and hormonal imbalance in male Sprague Dawley rats	Vincetoxicum arnottianum (Wight) of family Apocynaceae is a rich source of therapeutic alkaloids, phenolics and flavonoids. Study aims to evaluate the protective potential of methanol extract of Vincetoxicum arnottianum (VAME) on bisphenol A (BPA)-induced testicular toxicity in male Sprague Dawley rat. Quantitative analysis of VAME for total phenols (TPC), total flavonoid (TFC) and total alkaloid content (TAC) along with HPLC analysis for polyphenolics was carried out. BPA induced testicular toxicity was determined through analysis of sperm parameters, DNA damage, serum testicular toxicological biomarkers along with histopathological examination of testis. VAME was constituted of TPC 300.58 ± 1.67 μg GAE/mg, TFC 295.17 ± 0.60 μg RE/mg, TAC 136.4 ± 5.092, Results exist at 22.000 μg/mg) and vanillic acid (12.048 μg/mg). VAME co-administration to BPA-treated rats significantly (p < 0.05) improved sperm parameters, testicular biomarkers, testosterone level, and histopathological changes in testis. Co-administration of VAME with BPA significantly (p < 0.05) reduced CAT and SOD and restricts under in testis tissues of BPA-induced toxicity were significantly recovered by VAME. Histological and comet assay studies also overlooked the protective potential of VAME in BPA-intoxicated rats. The presence of polyphenols and alkaloids might contribute towards the scavenging and ameliorative potential of VAME in testicular toxicity induced by BPA.	Andrologia. 2020 Jul;52(6):e13590.	10.1111/and.13590	32293051	動物	精巣	1	0（腹腔内）	1	1	0	不明	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-
統合_3021	Zhang S, Bao J, Gong X, Shi W and Zhong X	2019	Hazards of bisphenol A — blocks RNA splicing leading to abnormal testicular development in offspring male mice	This study was conducted to investigate the effects of maternal exposure to BPA on testicular development in offspring mice. Pregnant Kunming mice were randomly divided into 7 groups with 10 mice in each group. Group A was the control group and the mice were given distilled water orally. Mice in groups B, C, D, E, F, G received BPA orally at a dose of 0.09 mg/kg, 0.9 mg/kg, 9 mg/kg, 30 mg/kg, 60 mg/kg, 90 mg/kg, 120 mg/kg, respectively. Pups were exposed to BPA for 35 days from gestation day 0 to lactation day 21. The mice were sacrificed on weaning (postnatal day 21). Histological observation of testicular development in male offspring mice was carried out. The testicular organ index increased significantly when the BPA and exposure dose was above 30 mg/kg/d (P < 0.05). BPA contents in serum of F1 male mice increased significantly when the BPA exposure dose was above 30 mg/kg/d (P < 0.05). Testosterone secretion in the testis of F1 male mice was significantly inhibited when the BPA exposure dose was above 9 mg/kg/d. The transcription of BPA in the testis was significantly increased when BPA was above 30 mg/kg/d (P < 0.05). Transcriptome sequencing showed that the Sertoj 38 which encoding 14-3-3ζ/δ subunit was significantly up-regulated in spliceosome pathway, and the Hmga1a 63 encoding splicing external protein component was significantly down-regulated. The blockage of spliceosome might be one of the reasons why BPA affects testicular development.	Chemosphere. 2019 Sep;230:432-439.	10.1016/j.chemosphere.2019.05.044	31121507	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	●	-	-	-	-	-	-
統合_3022	Zhang H, Wang Z, Meng L, Kuang H, Liu J, Lv X, Pang Q and Fan R	2020	Maternal exposure to environmental bisphenol A impairs the neurons in hippocampus across generations	Humans from fetal to adult stages are chronically and specially exposed to bisphenol A (BPA, an endocrine disruptor) due to its ubiquitous existence in daily life. To investigate the long-term neurotoxicity of maternal exposure to BPA, female mice were exposed to BPA (0.5 mg/kg/day) from 7 days before pregnancy to 21 days after delivery. Offspring mice (F1 generation) were fostered by dams without exposure to BPA. Then, a figure of BPA was kept until weaning. Then, the first-generation (F1) mice were used to generate the F2 mice. The offspring of mice not exposed to BPA served as the control groups. The F1 mice were sacrificed on weaning (postnatal day 21). Histological observation of neurodevelopment damages in hippocampus was carried out. The testicular organ index increased significantly when the BPA and exposure dose was above 30 mg/kg/d (P < 0.05). BPA contents in serum of F1 male mice increased significantly when the BPA exposure dose was above 30 mg/kg/d (P < 0.05). Testosterone secretion in the testis of F1 male mice was significantly inhibited when the BPA exposure dose was above 9 mg/kg/d. The transcription of BPA in the testis was significantly increased when BPA was above 30 mg/kg/d (P < 0.05). Transcriptome sequencing showed that the Sertoj 38 which encoding 14-3-3ζ/δ subunit was significantly up-regulated in spliceosome pathway, and the Hmga1a 63 encoding splicing external protein component was significantly down-regulated. The blockage of spliceosome might be one of the reasons why BPA affects testicular development.	Toxicology. 2020 Feb 28;432:152393.	10.1016/j.tox.2020.152393	32027964	動物	神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3024	Barberio L., Paulesu L., Canesi L., Grasselli E., and Mandalà M	2021	Bisphenol a Interferes with Uterine Artery Features and Impairs Rat Feto-Placental Growth	Bisphenol A (BPA) is a widespread environmental contaminant, found in human fluids and tissues. Maternal BPA exposure is associated with alterations in pregnancy outcomes. Because maternal uterine circulation plays a crucial role in normal placenta and fetal growth, we hypothesized that BPA compromises the function of uterine arteries (UAs) and fetoplacental development. Female rats were orally administered with BPA (10, 25 or 50 µg/kg/day) from 3 days before mating to gestational day (GD) 20. Pregnancy outcomes, UA reactivity, and placental and fetal features were evaluated at GD20. BPA did not affect maternal uterine UAs. Uterine arteries isolated and examined by pressure myography (Bowman, Ontario, Canada) from antimesenteric veins weighted a positive and dose-of-exposure-dependent vasodilation. In UAs of BPA-treated rats, lower diameter, acetylcholine relaxation and expression of endothelial nitric oxide synthase 3 (NOS3), estrogen receptor α (ERα) and peroxisome proliferator-activated receptor γ (PPARγ) were reduced. Conversely, an increase was observed in NOx. BPA treatment also reduced placental weights, while fetal weights were increased. For the first time, our results indicate that UAs represent a specific target of BPA during pregnancy and provide insight into the molecular mechanisms that underlie its negative effects on pregnancy outcomes.	Int J Mol Sci. 2021 Jun 27;22(13):6912.	10.3390/ijms22136912	34199136	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	●	-	-	-	-	-	-	-	-
統合_3025	Bruno K.A., Mathews J.E., Yang A.L., Frisancho J.A., Scott A.J., Greyner H.D., Molina F.A., Greenaway M.S., Cooper G.M., Bucalo A., Morales-Lara A.C., Hill A.R., Mease A.A., Di Florio D.N., Saurez J.M., Conrado A.C., Stafford A.R., and Fairweather D.	2019	BPA Alters Estrogen Receptor Expression in the Heart After Viral Infection Activating Cardiac Mast Cells and T Cells Leading to Perimyocarditis and Fibrosis	Myocarditis is an inflammatory heart disease that leads to dilated cardiomyopathy (DCM) and heart failure. Sex hormones play an important role in the development of myocarditis with testosterone driving disease in males and estrogen being cardioprotective in females. The human population is widely exposed to the endocrine disruptor bisphenol A (BPA) from plastics such as water bottles, plastic food containers, soup paper, and receipts. Several clinical and numerous animal studies have found an association between elevated BPA levels and cardiovascular disease. A recent report found elevated levels of BPA in the serum of patients with DCM compared to healthy controls. In this study, we examined whether exposure to BPA for 3 weeks prior to infection with coxsackievirus B3 (CVB3) and throughout disease in female mice would increase myocarditis. Female A/J mice were fed plastic cages laden with bisphenol A (BPA) or control cages and then infected with CVB3. Mice were euthanized and examined by pressure myography. Moreover, the uterine arteries were weighted a positive and dose-of-exposure-dependent vasodilation. In UAs of BPA-treated rats, lower diameter, acetylcholine relaxation and expression, of endothelial nitric oxide synthase 3 (NOS3), estrogen receptor α (ERα) and peroxisome proliferator-activated receptor γ (PPARγ) were reduced. Conversely, an increase was observed in NOx. BPA treatment also reduced placental weights, while fetal weights were increased. For the first time, our results indicate that UAs represent a specific target of BPA during pregnancy and provide insight into the molecular mechanisms that underlie its negative effects on pregnancy outcomes.	Front Endocrinol (Lausanne). 2019 Sep 4;10:598.	10.3389/fendo.2019.00598	31551929	動物	心臓	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3026	Cao T., Cao Y., Wang H., Wang P., Wang K., Nu H., and Shao C	2020	The Effect of Exposure to Bisphenol A on Spermatozoon and the Expression of Tight Junction Protein Occludin in Male Mice	Although bisphenol A (BPA) has been associated with impaired spermatogenesis, the mechanisms remain unclear. Tight junction occludin plays important roles in spermatogenesis. The objective of the present study was to explore the effects of BPA exposure in adolescent mice. Male mice were orally treated with two doses of BPA (50 mg/kg/d, middle dose; 0.5 mg/kg/d, or high dose; 5 mg/kg/d) or with oil from pre-weaned day (PND) 21 to 83. Animals were killed on PND 84 and PND 125. On PND 84, the sperm count, sperm motility, and the expression of occludin showed a dose-related decline. On PND 125, the sperm count, sperm motility, and the expression of occludin were in recovery. However, there remained significant decreases. In these parameters in the 50 mg/kg/d group on PND 125 compared with the control. The dose-related effects on the measured parameters and occludin expression suggest an early suppressive or damaging effects on the blood–testis barrier followed by recovery after dosing ceased. At a BPA dose of 50 mg/kg/d, recovery did not occur, suggesting that higher doses of BPA may cause irreversible damage to reproduction in male mice.	Dose Response. 2020 May 18;18(2):1559325820926745.	10.1177/1559325820926745	32523488	動物	精子	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3027	Dobrzyńska M.M., Gajowik A., and Radzikowska J.	2020	The impact of preconceptional exposure of F0 male mice to bisphenol A alone or in combination with X-rays on the intrauterine development of F2 progeny	Bisphenol A (BPA) is used for the production of polycarbonates and epoxy resins. Exposure to chemical and physical environmental factors may influence the health of exposed individuals, and of the next generations. The aim of the study was to investigate the effect of BPA administered to male mice (F0) alone at doses 0.05 mg/kg bw, 0.5 mg/kg bw, 5 mg/kg bw, 50 mg/kg bw, 500 mg/kg bw or in combination with X-rays at 0.5 Gy in two doses (0.05 Gy + 0 mg/kg bw, 0.05 Gy + 5 mg/kg bw, 0.5 Gy + 0 mg/kg bw, 0.5 Gy + 5 mg/kg bw) on the course of pregnancy in female mice (F1) and their offspring (F2). Pregnant females were sacrificed on day 18 of pregnancy, and the number of implantations, live fetuses, as well as early and late post-implantation deaths. The fertility of males and the percentage of pregnant females in each group were also assessed. The results showed that the number of implantations in the offspring of male mice exposed to BPA at the highest dose (500 mg/kg bw) was significantly reduced in the groups of 10 mg/kg bw and 50 mg/kg bw of BPA, whereas the number of live fetuses and F0 males in the groups of 5 mg/kg bw and 50 mg/kg bw of BPA was significantly increased. The frequency of early resorptions in all the experimental groups were found. The results observed in regard to prenatal development of the F2 generation suggest that sperm of the sons of F0 paternal males exposed to BPA contains genetic defects that affect the possibility of fertilization. The results of both pubescent and mature males exposed to BPA showed that fertilized eggs died before implantation, probably due to defects induced in the sperm. This confirmed that BPA induced transgenerational effects in male gene cells.	Mutat Res Genet Toxicol Environ Mutagen. 2022 Jun;878:503480.	10.1016/j.mrgentox.2022.503480	35649674	動物	生殖毒性	1	1：飲水	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3030	Gao L., Luo D., Wu D., Sun Q., Liu Y., Wen D., and Jia L.	2022	Effects of mammalian target of rapamycin and aryl hydrocarbon receptor-mediating autophagy signaling on the balance of Th17/Treg cells during perinatal bisphenol A exposure in female offspring mice	Bisphenol A (BPA)'s immunotoxic properties have received increasing interest, which can lead to immune dysfunction and related disease development. However, the mechanism is not completely clear. A growing body of evidence suggests that autophagy has important roles in innate immunity, inflammatory response, and adaptive immunity. This study aimed to investigate the possible mechanisms of mammalian target of rapamycin (mTOR), and hydrocarbon receptor (AHR), and autophagy in Th17/Treg imbalance induced by perinatal BPA exposure. Our results showed that the number of Th17 cells in the spleen of offspring female mice significantly increased, while the number of Treg cells decreased significantly, which was consistent with the expression levels of our regulation of RORγt protein and a down-regulation Foxp3 protein. The levels of mTOR, p-mTOR, and p-mTOR/mTOR were significantly increased, while the levels of AHR, ARNT, and Beclin1 were significantly decreased in the spleen of offspring female mice. However, there was no significant change in the levels of AHR protein, and the ratio of p-mTOR and mTOR protein levels. We conjectured that the potential mechanism of the imbalance of Th17/Treg upon perinatal exposure to BPA was probably associated with autophagy dysfunction. Proper autophagy plays an important role in maintaining the homeostasis of the thymic and spleen immune system.	Environ Toxicol. 2022 Jul;37(7):1781-1789.	10.1002/tox.23525	35357751	動物	免疫	1	1	0	1	0	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3031	Gao T., Yin Z., Wang M., Tang Z., Zhong K., Li J., Hu Y., Wu D., Jiang K., and Xu X	2020	The effects of pubertal exposure to bisphenol-A on social behavior in male mice	Puberty is a crucial developmental period for structural modifications of brain and activation of the neural circuits underlying sex differences in social behavior. It is possible that pubertal exposure to bisphenol A (BPA), a ubiquitous endocrine disruptor, could affect social behavior in male mice. Male C57BL/6J mice were exposed to BPA (0, 0.05, 0.5, 5, 50 mg/kg/day) by oral gavage from postnatal day (PND) 21 to PND 60. Social behavior was assessed in the three-chamber test. Our results showed that pubertal BPA exposure decreased social play behavior and affected the dominance index and sociability of adolescent male mice. Further, pubertal BPA exposure reduced sociability and social novelty preference of adult males. BPA-inhibited social interactions with opposite-sex but increased social sexual exploration and the low intensity mating behavior (mounting) with same-sex in adult males. In residential intruder test, BPA-exposed males showed increased aggressive behavior and decreased social investigation toward the intruder. Moreover, we found that BPA-induced changes were significantly in the levels of AHR protein, and the ratio of p-mTOR and mTOR protein levels. We conjectured that the potential mechanism of the imbalance of Th17/Treg upon perinatal exposure to BPA was probably associated with autophagy dysfunction. Proper autophagy plays an important role in maintaining the homeostasis of the thymic and spleen immune system.	Chemosphere. 2020 Apr;244:125494.	10.1016/j.chemosphere.2019.125494	31812767	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	-
統合_3032	Hanioka N., Isobe T., Tanaka-Kagawa T., Jinno H., and Ohkawara S	2022	In vitro glucuronidation of bisphenol A in liver and intestinal microsomes: interspecies differences in humans and laboratory animals	Bisphenol A (BPA) is an endocrine-disrupting chemical, and is predominantly metabolized into glucuronide in mammals. The present study was conducted in order to examine the hepatic and intestinal glucuronidation of BPA in humans and laboratory animals such as monkeys, dogs, rats, and mice to an in vitro system using microsomal fractions. For, three, and CLint values in human liver microsomes were 736 μL/(1.7 min)/mg protein, and 7.36 mL/min/kg protein, respectively. CLint values in liver microsomes of monkey, dogs, rats, and mice were 1.9-, 3.2-, 1.7- and 8.2-fold that of humans, respectively. In intestinal microsomes, For, times, and CLint values in humans were 39.3 μL/(8 min)/mg protein, and 622 mL/min/kg protein, respectively. The relative levels of CLint in monkey, dogs, rats, and mice to that of humans were 7.0-, 12-, 30-, and 19-fold, respectively. Although CLint values were higher in liver microsomes than in intestinal microsomes in all species, and marked species difference in the ratio of liver to intestinal microsomes was observed as follows: humans < monkeys < dogs < rats < mice. These results suggest that the functional roles of UDP-glucuronosyltransferase (UGT) enzymes expressed in the liver and intestines in the metabolism of BPA enormously differ among humans, monkeys, dogs, rats, and mice.	Drug Chem Toxicol. 2022 Jul;45(4):1565-1569.	10.1080/01480545.2020.1847133	33187449	in vitro	-	-	-	-	-	-	-	-	-	-	-	1	0	不明	1	-	-	-	-	-	●	-	-	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成者間評価への進め、当該時評価段階で原著に基づき精査。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準通過（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_3034	Kamtekar P.C., Ahn J.S., Kim Y.H., Jung S.E., Kim B.J., Lee H.S., and Ryu B.Y	2020	Gestational exposure to bisphenol a affects testicular morphology, germ cell associations, and functions of spermatogonial stem cells in male offspring	Exposure to bisphenol A (BPA) in the gestational period damages the reproductive health of offspring; detailed evidence regarding BPA-induced damage in testicular germ cells of offspring is still limited. In this study, pregnant Sprague–Dawley rats were gavaged daily with 0 (CON), 0.05 (BPA-L), 5 (BPA-H), or 50 (BPA-P) μg/kg/day BPA from gestational day 0 to postnatal day 21. Testicular histology and germ cell apoptosis were evaluated in male offspring at 3 and 6 weeks (wk) of age. Sertoli cell (SC) and Leydig cell (LC) numbers were counted by immunofluorescence staining for transcription factor SOX9 and 3β-hydroxysteroid dehydrogenase (3β-HSD), respectively. Spermatogonial stem cell (SSC) frequency was determined by transplantation of testicular cells into recipient mice. Transcriptomic analysis was performed on testicular cells from 3-wk-old male offspring. Serum testosterone levels were significantly decreased in the BPA-P group at 3 wk (0.82 ± 0.07 ng/mL) and 6 wk (1.67 ± 0.13 ng/mL) compared to the CON group (3 wk: 1.32 ± 0.08 ng/mL; 6 wk: 3.04 ± 0.21 ng/mL; p < 0.05). Testicular histology revealed that BPA-P exposure at 3 wk induced abnormalities in seminiferous epithelial stages and testis morphology. These effects were eradicated in the next (7 and 7.5 gestations. Moreover, there was an alteration in the ratio of germ cell population and the apoptosis rate in germ cells increased in 7-wk-old offspring at the 3 kGy dose. However, the total number of spermatogonia remained unchanged. Finally, a reduction in the stemness properties of spermatogonial stem cells in F1 offspring was observed upon 3 kGy exposure. Therefore, we provide evidence of BPA-induced disruption of physiology and functions in male germ cells during the gestational period. This may lead to severe reproductive health issues and infertility in offspring.	Int J Mol Sci. 2020 Nov 17;21(22):8644.	10.3390/ijms21228644	33212759	動物	生殖発生毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	●	-	-	-	●	-	-
統合_3035	Lee Y.J., Lim Y.H., Shin C.H., Kim B.N., Kim J.I., Hong Y.C., Cho Y.M., and Lee Y.A	2022	Relationship between bisphenol A, bisphenol S, and bisphenol F and serum uric acid concentrations among school-aged children	Background Hyperuricemia has a suspected relationship with hypertension, metabolic syndrome, kidney disease, and cardiovascular disease. Endocrine disruptors may affect uric acid metabolism; however, few epidemiologic studies have been performed in children regarding newly developed bisphenol A (BPA) substitutes. We evaluated the associations between BPA, bisphenol S (BPS), and bisphenol F (BPF) exposure and serum uric acid concentrations in 6-year-old Korean children. Methods From the Environment and Development of Children cohort study, six-year-old children (N = 189, 261 boys) who underwent an examination during 2019–2022 were included. Anthropometry, questionnaires, and biological samples were evaluated. BPA, BPS, and BPF levels were measured from spot urine samples, and log-transformed or categorized into groups for analysis. We conducted linear regression models adjusting for age, sex, urinary creatinine levels, body mass index z-score, and estimated glomerular filtration rates. Results Mean serum uric level was 4.2 mg/dL ± 0.8 SD) without sex differences. Among the three bisphenols, higher BPS exposure was associated with increased serum uric acid concentrations (P value for trend = 0.007). When BPS levels were categorized into three groups, low-detection (<0.07 μg/L), medium (0.07–0.19 μg/L), or high (BPS > 0.19 μg/L), the high BPS group showed higher serum uric acid concentrations (by 0.26 mg/dL; 4.1–7 = 0.003) than the non-detection group after adjusting for covariates, which was significant in boys but not girls. Discussions Urinary BPS levels was positively associated with serum uric acid concentrations in 6-year-old children, and the association was more pronounced in boys. Considering the increasing use of BPS and concerning effects of hyperuricemia on health outcomes, interventive relationship should be investigated further.	PLoS ONE 17 (6), e0268503	10.1371/journal.pone.0268503	35709251	ヒト	-	-	-	-	-	-	-	-	-	-	横断研究	1	1	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3036	Li L., Wang M.Y., Jiang H.B., Guo C.R., Zhu X.D., Yao X.Q., Zeng W.W., Zhao Y., and Chi L.K	2022	Bisphenol A induces testicular oxidative stress in mice leading to ferroptosis	Bisphenol A is a common environmental factor and endocrine disruptor that exerts a negative impact on male reproductive ability. By exploring bisphenol A-induced testicular cell death using the Institute of Cancer Research (ICR) mouse model and GC-1 spermatogonia cell line, we found that bisphenol A induced ferroptosis in testicular cells. Bisphenol A exposure for 28 days in male mice was used in this study. Serum was then collected to determine the levels of superoxide dismutase and malondialdehyde. Epididymal sperm was also collected for semen analysis, and testicular tissue was collected for hematoxylin-eosin staining, determination, electron microscopic observation of mitochondrial morphology, immunohistochemistry, real-time quantitative polymerase chain reaction, and western blot analysis. Exposure to bisphenol A was found to decrease sperm quality and cause oxidative damage, iron accumulation, and mitochondrial damage in the testes of mice. In addition, bisphenol A was confirmed to affect the expression of ferroptosis-related genes, glutathione peroxidase 4 (GPX4), ferritin heavy chain 1 (FTH1), cyclooxygenase 2 (COX2), and acyl-CoA synthetase 4 (ACSL4) in mouse testicular tissues. Accordingly, our examples that bisphenol A induces oxidative stress, which leads to the ferroptosis of testicular cells. Overall, the inhibition of ferroptosis may be a potential strategy to reduce male reproductive toxicity caused by bisphenol A.	Asian J Androl. 2023 May-Jun;25(3):375-381.	10.4103/aja202266	36153926	動物	簡単	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	-	●	-	-	-	-	-	-
統合_3037	Lin M., Hua R., Ma J., Zhou Y., Li P., Xu X., Yu Z., and Quan S	2021	Bisphenol A promotes autophagy in ovarian granulosa cells by inducing AMPK/mTOR/ULK1 signalling pathway	Bisphenol A (BPA) is a widespread endocrine-disrupting chemical with monospecific effects, which could interfere with the human reproductive systems by disrupting the normal function of granulosa cells (GCs) leading to abnormal ovarian function. However, the mechanism of its toxicity on human GCs has not been clearly described thus far. Methods 106 normogonadotropic infertile women undergoing their first in vitro fertilization embryo transfer (IVF-ET) cycle were recruited. Urinary BPA level and the early outcomes of IVF-ET were analyzed. Patients were divided into high-BPA and low-BPA groups according to the median urinary BPA concentration. Human GCs were isolated from follicular fluid during oocyte retrieval. Cells were treated with BPA (10 nM, 100 nM, and 1000 nM) for 24 h in vitro supplemented by 0.9 weeks of age were poisoned with BPA at different dosages (1, 10 or 100 μg/kg) for seven days once daily for 3 weeks, while ICR rats were exposed to BPA (10 μg/kg) for 3 weeks. The concentration of 1, 10 or 100 for 24 h. BPA induced ovarian morphologic changes were analyzed by histopathology investigation. Cell viability and apoptosis were evaluated using CCK-8, TUNEL, and flowcytometric, respectively. Autophagosomes levels were determined using RLGS and the molecular mechanism studies were conducted using immunofluorescence, RT-PCR, and western blots. Results The oocyte retrieval rate, metaphase-I rate and embryo implantation rate significantly decreased with the higher level of urinary BPA concentration. Peak E2 level was lower in high-BPA group, but no statistical significance could be observed. In BPA-treated mice, cystic dilation of the follicles with a decreased number of GCs could be observed histopathologically. Decreased E2, P4, and AMH level and GCs autophagy could be observed both in vivo and in vitro with the activation of AMPK/mTOR/ULK1 signalling pathway. As being confirmed in KGN cells, phosphorylated AMPK and ULK1 increased while phosphorylated mTOR decreased, and by inhibition of autophagy using knockdown of AMPK or ULK1, adverse effects of BPA exposure in vitro could be reversed. Conclusions BPA exposure might abnormally influence human ovarian functions leading to abnormal follicle genesis, by activation of autophagy in GCs, through AMPK/mTOR/ULK1 pathway.	Environ Int. 2021 Feb;147:106298.	10.1016/j.envint.2020.106298	33387880	ヒト、動物、in vitro	卵巣/卵巣機能	1	1	1	1: 昇野マウス	1	1	コホート	1	1	1	0	1、10、100 nM	1	1	1	1	1	-	-	-	-	●	-	-	-	-	-	-
統合_3038	Lile C., Ahmed S.S.S.J., Santosh W., and Sesikeeran B	2019	Prenatal exposure to bisphenol-A altered miRNA-224 and protein expression of aromatase in ovarian granulosa cells concomitant with elevated serum estradiol levels in F1 adult offspring	This study was aimed to predict bisphenol A (BPA) -responsive miRNAs using an in silico approach and to study their expression in granulosa cells of animals exposed prenatally to BPA. Pregnant Wistar rats were administered BPA (0, 0.1, 1, 10, 100 mg/kg b.wt.) from gestation day 9 to 20. Female offspring were sacrificed at 90 days of age. Ovarian granulosa cells, BPA-affected the expression of endocrine disruption-related biochemical markers such as weight of the ovary at birth and matured pregnantal distance. BPA exposed animals showed elevated serum estradiol (E2) levels, while follicle-stimulating hormone levels were reduced. The expression of miRNA-224 and aromatase protein levels were found to be increased. This preliminary finding reveals the impact of early life exposure to BPA on the long-term ovarian functions that may be mediated through miRNA-based precious cell response. Besides, it is also a compelling indicator for the subclinical response that could have important consequences on female fertility.	J Biochem Mol Toxicol. 2019 Jun;33(6):e22317.	10.1002/jbt.22317	30817060	動物、in silico	卵巣	1	1	1	1	1	1: 飲水中濃度	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_3039	Liu R., Cai D., Li X., Liu B., Chen J., Jiang X., Li H., Li Z., Tserds K., Sun J., Bai W., and Jin Y	2022	Effects of Bisphenol A on reproductive toxicity and gut microbiota dysbiosis in male rats	Bisphenol A (BPA) is an environmental endocrine disruptor. Recent studies have shown an association between decreased spermatogenesis and gut microbiota alteration. However, the potential associations and mechanisms of BPA exposure on spermatogenesis, hormone production, and gut microbiota remain unknown. This study aims to investigate BPA-induced male reproductive toxicity and the potential link with gut microbiota dysbiosis. Male rats were exposed to BPA (0, 0.05, 5, and 50 mg/kg/day) for 35 days. Sperm quality, testicular histopathology, and serum hormone levels were evaluated. Body weight and hematopoietic stem cell (HSC) activity, liver, sex-determined the mRNA levels, and protein levels of apoptosis, fibrosis-related factors, and mammalian target of rapamycin (mTOR) pathway in testes. Finally, 16 S rDNA sequencing was used to analyze gut microbiota composition after BPA exposure. BPA exposure damaged testicular histology, significantly decreased sperm count, and increased sperm abnormalities. In addition, BPA exposure caused oxidative stress and cell apoptosis in testes. The levels of fibrosis (HSS, FC) were significantly increased, while ubiquitin-histone H2A Lys-119 (H2Aub) and ubiquitin-histone H2B Lys-120 (H2Bub) were markedly reduced. Furthermore, BPA activated the PI3K and AKT expression, but the protein expressions of mTOR and BCAT1 in testes were inhibited significantly. Additionally, the relative abundance of class Bacteroidia, Bacteroidales, and Prevotellaceae_UCG-001 were significantly increased, while Clostridia_UCG-014 was significantly decreased in the BPA exposure group compared to the control. This study highlights the relationship between BPA-induced reproductive toxicity and gut microbiota disorder and provides new insights into the prevention and treatment of BPA-induced reproductive damage.	Ecotoxicol Environ Saf. 2022 Jul 1:239:113623.	10.1016/j.ecoenv.2022.113623	35567931	動物	簡単	1	1	1	1	1	0	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_3040	Loffredo L.F. and Berdnikovs M.E.C.S	2020	Endocrine disruptor bisphenol a (BPA) triggers systemic para - inflammation and is sufficient to induce airway allergic sensitization in mice	Allergic airway diseases are accompanied by increased permeability and an inflammatory state of epithelial barriers, which are thought to be susceptible to allergen sensitization. Although exogenous chemo (proteases, allergens) of epithelial barrier disruption and sensitization are well studied, endogenous contributors (diet, metabolites, hormones, and metabolites) to allergic sensitization are much less understood. Xenoestrogens are synthetic or natural chemical compounds that have the ability to mimic endogenous estrogens and can ubiquitous in the human and water supply of developed countries. By interfering with the estrogen produced by the endocrine system, these compounds have the systemic potential to disrupt the homeostasis of multiple tissues. Our study examined the potential of prototypical xenoestrogen bisphenol A (BPA) to disrupt epithelial homeostasis in vitro and in vivo. Exposure to BPA at concentrations found in human blood (nanomolar) induced epithelial barrier dysfunction in primary human bronchial epithelial cells grown in air-liquid interface culture. Oral BPA in a time and dose-dependent manner. In vivo, the exposure to BPA through water supply or inhalation induced a systemic pool inflammatory response by promoting the expansion of innate inflammatory mediators in the skin, gut, and airway. In a murine ratiogenic antigen challenge model, chronic systemic exposure to BPA was sufficient to induce airway sensitization to innocuous chicken egg ovalbumin in the complete absence of adjuvants. Mechanistic studies are needed to test conclusively whether endocrine disruptors may play an upstream role in allergic sensitization via their ability to promote a para-inflammatory state. Keywords: bisphenol A; estrogen; xenoestrogens; para-inflammation; endocrine disruptors; allergy; asthma	Nutrients. 2020 Jan 28;12(2):343.	10.3390/nu12020343	32012983	動物、in vitro	-	1	1	1	BALB/cJ	0	25 mg/L	-	-	-	1	0	100, 500 nM	1	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_3041	Lupinek C., Hochwallner H., Johansson C., Mie A., Rigler E., Scheynius A., Alm J., and Valenta R	2019	Maternal allergen-specific IgG might protect the child against allergic sensitization	Background Analysis of allergen-specific IgE responses in birth cohorts with microarrayed allergens has provided detailed information regarding the evolution of specific IgE responses in children. High-resolution data regarding early maternal allergen-specific IgG are needed. Objective We sought to analyze IgG reactivity to microarrayed allergens in mothers during pregnancy, in cord blood samples, in breast milk, and in infants in the first years of life with the aim to investigate whether maternal allergen-specific IgG can protect against IgE sensitization in the offspring. Methods Plasma samples from mothers during the third trimester, cord blood, breast milk collected 2 months after delivery, and plasma samples from children at 6, 12, and 60 months of age were analyzed for IgG reactivity to 282 microarrayed allergens (ImmunoCAP-ISAC technology) in 99 families of the Swedish birth cohort Assessment of Lifestyle and Allergy Disease During Infancy (ALADDIN). IgE sensitizations to microarrayed allergens were determined at 5 years of age in the children. Results Allergen-specific IgG reactivity profiles in mothers, cord blood, and breast milk were highly correlated. Maternal allergen-specific IgG persisted in cord blood and 2 months. Children's allergen-specific IgG production declined from 6 to 12 months and increased thereafter. Maternal IgG reactivity to allergens in cord blood and breast milk was associated with a lower risk for IgE sensitization in children. For all 282 tested allergens, children from mothers with microarrayed (>200 ISAC standardized units) specific plasma IgG levels against an allergen had no IgE sensitization against that allergen at 5 years of age. Conclusion This is the first detailed analysis of the molecular IgG recognition profile in mothers and their children in early life. High allergen-specific IgG reactivity in the mother's plasma and breast milk and in cord blood seemed to protect against allergic sensitization at 5 years of age.	J Allergy Clin Immunol. 2019 Aug;144(2):536-548.	10.1016/j.jaci.2018.11.051	30685457	ヒト	免疫	-	-	-	-	-	-	-	-	-	-	-	コホート	1	1	1	-	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_3042	Lv Y., Li L., Fang Y., Chen P., Wu S., Chen X., Ni C., Zhu Q., Huang T., Liao Q., and Ge R.S	2019	In utero exposure to bisphenol A disrupts fetal testis development in rats	Bisphenol A (BPA) is widely used in consumer products and is a potential endocrine disruptor linked with abnormal development of male reproductive tract. However, its action and its effects on the pathways in the development of male gonad are still unclear. Here our report that effects of BPA during gestation on male gonadal development. Sprague–Dawley rats were gavaged orally with BPA (0, 5, 50, and 500 mg/kg body weight) from gestational day 13 to day 21. BPA dose-dependently decreased serum testosterone levels (0.65 ± 0.08 ng/ml and 0.37 ± 0.06 ng/ml for 50 and 500 mg/kg BPA, respectively) versus the control level (1.11 ± 0.07 ng/ml). Testicular histological examination revealed that BPA at 50 and 500 mg/kg induced Sertoli cell vacuolization and germ cell loss. BPA at 500 mg/kg also induced Leydig cell hyperplasia and their ectopic tracks, at 500 mg/kg, BPA decreased fetal Leydig cell number via inhibiting their proliferation, but not it did not affect fetal Sertoli cell number. In conclusion, the current study shows that in utero exposure to BPA inhibits fetal Leydig and Sertoli cell differentiation, possibly disrupting the development of male reproductive tract.	Environ Pollut. 2019 Mar;246:217-224.	10.1016/j.envpol.2018.12.006	30557795	動物	簡単	1	1	1	1	1	1	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	-	●	-	-	-	-	-	-
統合_3043	Matalová Y., Le Maréchal K., Sparfel L., and Gazyjack-Pilou L	2020	Differential influences of the BPA, BPS and BPF on in vitro IL-17 secretion by mouse and human T cells	The endocrine disruptor and food contaminant bisphenol A (BPA) is frequently present in consumer plastics and can produce several adverse health effects participating in the development of inflammatory and autoimmune diseases. Regulatory restrictions have been established to prevent risks for human health, leading to the substitution of BPA by structural analogues, such as bisphenol S (BPS) and F (BPF). In this study, we aimed at comparing the in vitro impact of these bisphenols, from 0.05 to 50,000 nM on Th17 differentiation, frequency and function in mouse systemic and intestinal immune T cells and in human blood T cells. This study tested the ability of these BPs, at low and environmentally relevant concentrations, i.e. 0.05 nM, to increase significantly IL-17 production in mouse T cells but not in human T cells. The use of an aryl hydrocarbon receptor (AHR) inhibitor demonstrated its involvement in this bisphenol-induced IL-17 production. We also observed an increased IL-17 secretion by BPS and BPF, and not by BPA. Increase naive T cell differentiation into pathogenic in vitro Th17 differentiation. In total, this study emphasizes the link between bisphenol exposure and the susceptibility to develop immune diseases, questioning then the value of their use to replace BPA.	Toxicology in Vitro 69	10.1016/j.tiv.2020.104993	32911021	in vitro	-	-	-	-	-	-	1	0	0.05–50,000 mg/kg	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3044	Matalová Y., Lancina C., Cartier C., Oller M., Menard S., and Gazyjack-Pilou L	2020	Perinatal oral exposure to low doses of bisphenol A, S or F impairs immune functions at intestinal and systemic levels in female offspring mice	Bisphenol A (BPA), one of the highest-volume chemicals produced worldwide, has been identified as an endocrine disruptor. Many peer-reviewing studies have reported adverse effects of low dose BPA exposure, particularly during perinatal period (gestation and/or lactation). We previously demonstrated that perinatal oral exposure to BPA (via gavage of mothers during gestation and lactation) has long-term consequences on intestinal and systemic immune homeostasis in male offspring mice. Because BPA is rapidly metabolized and eliminated, it is suspected that its substitutes, bisphenol S (BPS) and F (BPF), could be more harmful than BPA. Here, we thus assessed comparatively in BPS, BPF, and BPA, that are structurally similar and not well studied compare to BPA. Here, we aimed to compare perinatal and exposure to these bisphenols. BPA, at two doses, 0 and 50 μg/kg of body weight (BW)/day (d) on immune response at intestinal and systemic levels in female offspring mice at adulthood (Post Natal Day PND70). Methods Pregnant female mice were orally exposed to BPA, BPS or BPF at 0 or 50 μg/kg BW/d from 15th day of gestation to weaning of pups at Post Natal Day (PND) 21. Humoral and cellular immune responses of adult offspring (PND70) were analyzed at intestinal and systemic levels. Results In female offspring, perinatal oral BP exposure led to adverse effects on intestinal and systemic immune response that were dependent of the BP nature (A, S or F) and dose of exposure. Stronger impacts were observed with BPA at the dose of 50 μg/kg BW/d on inflammatory markers in feces associated with an increase of anti-E. coli IgA in plasma. BPA and BPF exposure induced prominent changes at low dose in offspring mice, in term of intestinal and systemic immune responses, providing an intestinal and systemic Th17/Treg inflammation. Conclusion These findings provide, for the first time, results of long-time consequences of BPA, S and F perinatal exposure by oral route on immune response in offspring mice. This work warns that it is mandatory to consider immune markers and dose exposure in risk assessment associated to new BPA's alternatives.	Environ Health 19 (1), 93	10.1186/s12940-020-00614-w	32867778	動物	-	1	1	1	不明	0	5 および 50 μg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-	-

毒性性評価（動物）1：該当、0：該当しない　毒性性評価（疫学）1：該当、0：該当しない　毒性性評価（in vitro）1：該当、0：該当しない　毒性性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性性基準不適合と判断されるものは作成段階評価への進め、当該性評価段階で排除に基づき排除。　利用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	毒性性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報) ※1 報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_3045	Mateiel Y., Lencina C., Placide F., Bacquie V., Carbo C., Olier M., Buettner M., Wellbrecht M., Menard S., and Guzylack-Piriou L	2020	Oral exposure to bisphenols induced food intolerance and colitis in vivo by modulating immune response in adult mice	Bisphenol (BP) A, a known food contaminant, is a possible risk factor in the epidemic of non-communicable diseases (NCD) including food intolerance and inflammatory bowel diseases (IBD). Regulatory restrictions have been taken for BPA but its substitutes, BPS and BPF, are increasingly used in food packaging. Here, we investigated the effects of orally administered BPA and BPS (0.5, 5 or 50 µg/kg bw/d) on immune system, microbiota and barrier functions. Here, we studied the effect of oral BPA at levels reported in human exposure to understand the mechanisms of immunological, physiological and microbial action on food antigens. In a murine model of allergy, we evaluated the effect of direct oral exposure to BPA at 5 µg/kg bw/d compounding to tolerable daily intake (TDI). We studied symptoms, intestinal physiology and humoral and cellular immune responses during food allergy. We explored the relationship between oral exposure to BPA and changes in the gut microenvironment. Markers of food allergy and intestinal permeability were increased following exposure to BPA. We also observed a modulated humoral and T cell response with aggravation of food allergy inflammation. Moreover, BPA exposure induced gut dysbiosis and decreased microbial diversity induced by food allergy. Altogether, these results suggest that the 2016 European Food Safety Authority (EFSA) TDI should be reviewed to consider the immunotoxicity of BPA.	Food Chem Toxicol. 2020 Dec;146:111773.	10.1016/j.fct.2020.111773	33011352	動物	免疫	1	1	0	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	●	-	-	-	-	-
統合_3046	Mitche-Ayoubi-kie B., De Carvalho M., Delage E., Dijoux E., Klein M., Brosseau C., Bodinier M., Guzylack-Piriou L., and Bouchaud G	2022	Oral exposure to bisphenol A exacerbates allergic inflammation in a mouse model of food allergy	Allergic diseases are increasing worldwide, and their precise causes are not fully understood. However, this observation can be correlated with growing chemical pollution of the environment. Bisphenol A (BPA) alters the immune system, microbiota and barrier functions. Here, we studied the effect of oral BPA at levels reported in human exposure to understand the mechanisms of immunological, physiological and microbial action on food antigens. In a murine model of allergy, we evaluated the effect of direct oral exposure to BPA at 5 µg/kg bw/d corresponding to tolerable daily intake (TDI). We studied symptoms, intestinal physiology and humoral and cellular immune responses during food allergy. We explored the relationship between oral exposure to BPA and changes in the gut microenvironment. Markers of food allergy and intestinal permeability were increased following exposure to BPA. We also observed a modulated humoral and T cell response with aggravation of food allergy inflammation. Moreover, BPA exposure induced gut dysbiosis and decreased microbial diversity induced by food allergy. Altogether, these results suggest that the 2016 European Food Safety Authority (EFSA) TDI should be reviewed to consider the immunotoxicity of BPA.	Toxicology 472	10.1016/j.tox.2022.153188	35430321	動物	-	1	1	1	不明	0	4µg/kg bw/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3047	Molenghi A., Varma S., M S., Kanbhan S., Dubasy A.K., and Basak S	2022	Prenatal exposure to bisphenol S and bisphenol A differentially affects male reproductive system in the adult offspring	Early exposure to bisphenol may result in adverse reproductive health in later life. The use of bisphenol S (BPS) has increased considerably after bisphenol A (BPA) is regulated worldwide. However, little is known about the fetal exposure to BPS compared with BPA and its effects on the reproductive system in the adult male offspring. Here, we investigated the effects of orally administered BPS and BPA (0.5, 5.0, 50.0 µg/kg bw/d) during gestation (gd0-20) on testicular development by evaluating the same DNA damage & methylation and testicular functions in the 90 d/litter rats. Male offspring prenatally exposed to BPS (0.5 µg/kg) had higher plasma testosterone than BPA and control. The male's histology results illustrated seminiferous tubule degeneration, necrosis, and vacuolization, increased testicular oxidative stress, TUNEL expression, and decreased VCAM-1 expression. BPS promotes apoptosis by up-regulating IL-6, cleaved caspase, and α-cyclin to sperm DNA fragmentation. Prenatal BPS exposure reduces sperm motility mediated via impaired PI3K-AKT signaling and increases testicular TET3/8 expression in the offspring. Exposure of the fetus to BPS interferes developmental programming of the male reproductive system in the offspring. BPS could be an equally potent endocrine disruptor affecting male reproductive functions.	Food Chem Toxicol. 2022 Sep;167:113292.	10.1016/j.fct.2022.113292	35842007	動物	免疫	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3048	Osman M.A., Mahmoud G.I., Elgammal M.H., and Hassan R.S	2021	Bisphenol a hormonal disrupture and preventive effect of rose water and clove oil	Bisphenol A (BPA) which considered synthetic estrogen that is an essential component of many plastic industries. This research was done to see the impacts of exposure of BPA on reproductive organs and hormonal levels in male and female albino Sprague Dawley rats. The protective effect of rose water and clove oil on BPA was investigated. Ninety rats were divided into 18 groups. 9 groups of males and they are like for females. The first group was considered as control group. Second group (G2) was treated with BPA (50 mg/kg/day). The third group (G3) was treated with rose water (1 ml/kg/day). The fourth group (G4) was treated with clove oil (1 ml/kg/day). The fifth group (G5) was treated with BPA (50 mg/kg/day) + rose water (1 ml/kg/day). The sixth group (G6) was treated with BPA (50 mg/kg/day) + clove oil (1 ml/kg/day). Testosterone in male rats, as estrogen in a significant increase in female estradiol hormone (T2DE), progesterone, luteinizing hormone (LH), and prolactin (PRL), while a decrease in follicular stimulating hormone (FSH) compared to control groups. Histopathological examination revealed that vacuolar and clear cell reduced testes and ovary damages induced by BPA. Fluorescein and clove oil components were scanned using GC/MS, which revealed that vacuolar and clear cell contains phenols, flavonoids, and linkers chemically confirmed that a prominent role in preventing the damage during treatment. Results indicated that the oral doses of BPA disrupted the sex hormone levels in both male and female rats caused reproduction impaired. The chemical and histopathological analysis results indicated that clove oil and rose water improved the adverse effect of BPA. Rosewater and clove oil improved the changes which were stimulated by BPA. Keywords: Bisphenol A; Clove oil; Rose water; Dairy; Testes; Sex hormones; TRH;	Biointerface Research in Applied Chemistry 11 (2), 8780 -8803	10.33263/BRIAC112.8780803	-	動物	ホルモンレベル	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3050	Ruiz-Pino F., Micali D., Franssen D., Vazquez M.J., Farinetti A., Castellano J.M., Pereira G., and Tena-Sempere M	2019	Environmentally relevant perinatal exposures to bisphenol a disrupt postnatal Kiss1/NKB neuronal maturation and puberty onset in female mice	Background: The timing of puberty is highly sensitive to environmental factors, including endocrine disruptors. Among them, bisphenol A (BPA) has been previously analyzed as potential modifier of puberty. Yet, disparate results have been reported with BPA influencing, delaying, or being neutral in its effects on puberty onset. Likewise, mechanistic analyses addressing the central and peripheral actions/targets of BPA on pubertal maturation remain incomplete and unefficient. Objectives: We aimed to provide a comprehensive characterization of the impact of early BPA exposures, especially at low, real-life doses, on the pubertal development of hypothalamic Kiss1/NKB neurons, and its functional consequences on female pubertal maturation. Methods: Pregnant CD1 female mice were orally administered BPA at 0, 10, or 50 µg/kg body weight (BW)/d from gestational day 11 to postnatal day 8 (PND8). Vaginal opening, as an external marker of puberty onset, was monitored daily from PND28 to PND60 in the female offspring. Blood and brain samples were collected at PND22, 35, 55, 21, and 30 for measuring circulating levels of gonadotropins and analyzing the hypothalamic expression of Kiss1/kisspeptin and NKB. Results: Perinatal exposure to BPA, in a range of doses largely below the no observed adverse effect level (NOAEL; 5mg/kg BW/d, according to the FDA), was associated with pubertal differences in the female progeny compared with those exposed to vehicle alone, with an earlier age of vaginal opening but unchanged body mass or circulating/pituitary hormone. Mice treated with BPA exhibited a persistent, but divergent, impairment of Kiss1 neuronal maturation, with more kisspeptin cells in the rostral (RP3V) hypothalamus but conclusively fewer kisspeptin neurons in the arcuate nucleus (ARC). Detailed quantitative analysis of the ARC population, essential for pubertal competence, revealed that the association with BPA had persistently lower Kiss1 expression during developmental maturation, which was associated with lower Tac2-(encoding NKB) levels, even at low doses (5 µg/kg BW/d) in the range of the tolerable daily intake (TDI), recently updated by the European Food Safety Authority. Conclusions: Our data attest to the consistent, but divergent, effects of gestational exposures to low concentrations of BPA, via the oral route, on phenotypic and neuroendocrine markers of puberty in female mice, with an unambiguous impact on the developmental maturation not only of Kiss1, but also of the NKB system, both essential regulators of puberty onset.	Environ Health Perspect. 2019 Oct;127(10):107011.	10.1289/EHP5570	31652106	動物	発達神経毒性	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3052	Shi M., Sekulowski N., MacLusan J.A., Wharton A., and Hayashi K	2019	Prenatal Exposure to Bisphenol A Analogues on Female Reproductive Functions in Mice	This study was performed to examine whether prenatal exposure to bisphenol (BP) A analogues, BPS and BPF, negatively impacts female reproductive functions and follicular development using mice as a model. CD-1 mice were orally exposed to control treatment (corn oil), BPA, BPS, or BPF (0.2, 20, or 50 µg/kg/day) from gestational day 11 (the presence of vaginal plug = 1) to birth. Exposure to BPS, BPF, and BPA accelerated the timing of vaginal opening in female offspring. Estrous cyclicity was disrupted by BPS and BPF, but not BPA, at 4 weeks of age. Exposure to BPS and BPF, but not BPA, caused persistent estrus and reduced fertility problems including reduced pregnancy rate, parturition issues, and increased dystocia at 6 weeks. Furthermore, the levels of serum testosterone were elevated by BPS or BPF exposure at the age of 9 months, whereas estrogen levels were not affected. On the other hand, the dysregulated expression of steroidogenic enzymes was observed in the ovary at 3, 6, or 9 months of age by BPS or BPF exposure. When we examined neonatal ovary on postnatal day 5, BPS, BPF, and BPA exposure inhibited germ cell nest breakdown and reduced number of primary and secondary follicles. These results suggest that prenatal exposure to BPA analogues, BPS and BPF, have effects on fertility in later reproductive life probably due to the disruption of early follicle genesis. bisphenol A; bisphenol S; ovary; reproduction; mice Topic: mitochondrial biogenesis cellular cell biomedicine methods/equipment cell/organism cell/organism/cells/gynecologic physiological processes environment/ecology patient/pathology/diagnosis/female reproductive function/development/perinatal exposure Issue Section: PRENATAL BPA AND REPRODUCTION	Toxicol Sci. 2019 Apr 1;168(2):561-571.	10.1093/toxsci/kfz014	30629253	動物	卵巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3053	Ullah A., Pirzada M., Jahan S., Ullah H., Razak S., Rauf N., Khan M.I., and Mahboob S.Z	2019	Prenatal BPA and its analogs BPB, BPF, and BPS exposure and reproductive axis function in the male offspring of Sprague Dawley rats	Research in the past has indicated associated long-term and low levels of exposure of bisphenol A (BPA) in early life and neuroendocrine disorders, such as obesity, precocious puberty, diabetes, and hypertension. BPA and its analogs bisphenol B (BPB), bisphenol F (BPF), and bisphenol S (BPS) have been reported to have similar or even more toxic effect as compared to BPA. Exposure of rats to BPA and its analogs BPB, BPF, and BPS resulted in decreased sperm production, testosterone secretion, and histological changes in the reproductive tissues of male rats. In the present study, BPA, BPB, BPF, and BPS were administered to drinking water at concentrations of 15, 75, and 90 µg/L) from pregnancy day (PD) 1 to PD 21. Body weight (BW), hormonal concentrations, antioxidant enzymes, and histological changes were determined in the reproductive tissues. BPA exposure significantly reduced the testosterone concentration and antioxidant enzymes activities and induced histological differences in the antioxidant enzymes, testosterone, and estradiol concentrations in the testes of male offspring. Histological examination of both testis and epididymis revealed prominent changes in the reproductive tissues. The present study suggests that BPA and its analogs BPA, BPF, and BPS affected concentrations of sex hormones and antioxidant enzymes in the development of the male reproductive system.	Hum Exp Toxicol. 2019 Dec;38(12):1344-1365.	10.1177/0960327119862335	31514588	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	●	-	-
統合_3054	Wang G., Li Y., Li Y., Zhang J., Zhou C., Wu C., Zhu Q., and Shen T	2020	Maternal vitamin D supplementation inhibits bisphenol A-induced proliferation of Th17 cells in adult offspring	Bisphenol A (BPA) exposure can increase the risk of immune-related diseases. In late life, Vitamin D3 (VA D3) has been shown to have multiple immunomodulatory actions and has been used to treat immune diseases. However, the potential beneficial effects of VA D3 on BPA-induced adverse effects have rarely been reported. We hypothesized that VA D3 may counteract the BPA-induced side effects in the immune system. Dams in offspring of VA D3 supplemented mothers. Here, we established our experimental model by exposing pregnant dams with 1000 nM BPA with or without VA D3 (0.25 µg/kg, 1 µg/kg and 4 µg/kg) treatment. We found that maternal VA D3 supplementation significantly inhibited the BPA-induced proliferation of Th17 cells in the adult offspring. Moreover, we found that there were no significant differences in the antioxidant enzymes, testosterone, and estradiol concentrations in the testes of male offspring. Our study corroborated these BPA -induced side effects on the immune system in the offspring as evidenced by attenuated upregulation of Th17 proliferation and ROR γt, IL-17 A, IL-6, and IL-23 expressions in the offspring. Our study provides the first evidence that maternal VitD3 supplementation offers benefits to the offspring by attenuating BPA -induced side effects on the immune system through vitamin D receptor (VDR) dependent regulation of transcription factors and cytokines, suggesting its translational potential.	Food and Chemical Toxicology 144	10.1016/j.fct.2020.111604	32702508	動物	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3056	Wang Y., Wu Y., and Zhang S	2022	Impact of bisphenol-A on the spliceosome and meiosis of sperm in the testis of adolescent mice	Background: Bisphenol A (BPA) has estrogenic activity and adversely affects human and animals' reproductive systems and functions. There has been a disagreement with the safety of BPA exposure at Tolerable daily intake (TDI) (5.00 mg/kg/d) value and non-observed adverse effect level (50 mg/kg/d). The current study investigated the effects of BPA exposure at various doses starting from Tolerable daily intake (5.00 mg/kg/d) to the lowest observed adverse effect level (50 mg/kg/d) on the testis development in male mice offspring. The BPA exposure lasted for 63 days from pregnancy day 0 of the dams to post-natal day (PND) 35 of the offspring. Results: The results showed that BPA exposure significantly increased testis (BPA ≥ 25 mg/kg/d) and serum (BPA ≥ 50 mg/kg/d) BPA contents of PND 35 mice. The spermatogenetic cells became loose, and the tunica of seminiferous tubules enlarged after BPA exposure at a low dose (5.00 mg/kg/d TDI). BPA exposure at a low dose (5.00 mg/kg/d) significantly reduced the expression of Sun2 protein and showed severe abnormality. The significant decrease in Sun2 suggested that BPA inhibits the transformation of spermatogenetic into spermatozoa in the testis. The RNA-seq proved that the spliceosome was significantly inhibited in the testes of mice exposed to BPA. According to the RT-qPCR, BPA exposure significantly reduced the expression of Snrpe (BPA ≥ 50 mg/kg/d) and Hnrnpu (BPA ≥ 5.0 mg/kg/d). Conclusions: This study indicated that long-term BPA exposure at Tolerable daily intake (5.00 mg/kg/d) is not safe because low-dose long-term exposure to BPA inhibits spermatogenetic meiosis in mice testis. Impairs reproductive function in male offspring.	BMC Vet Res. 2022 Jul 15;18(1):278.	10.1186/s12917-022-03336-y	35841026	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3057	Wei Y., Han C., Geng Y., Cui Y., Bao Y., Shi W., and Zhang K	2019	Maternal exposure to bisphenol A during pregnancy interferes testis development of F1 male mice	This study was conducted to investigate the effects of maternal exposure to bisphenol A (BPA) on testis development of F1 male mice. The BPA exposure model of pregnant mice was prepared by intragastric administration of BPA at the doses of 0, 5, 10, 20, and 30 mg/kg/day at gestation day (GD) 0.5–17.5. The testis index of the offspring mice was calculated at postnatal day (PND) 21 and PND 56. The results showed that BPA exposure significantly increased the testis index of PND 21 male mice ($F_{4,25} = 3.011$, $P = 0.037$). Besides, there was a non-monotonic dose–response relationship between serum hormone, ovarian receptor levels, and BPA ($F_{4,25} = 3.011$, $P = 0.037$). BPA exposure significantly increased the serum testosterone level and the testis index in F1 female mice at PND 21 and PND 56. BPA exposure also upregulated the expression of testicular Dnmt3 and inhibited the transcription of testicular Dnmt3A and Dnmt3B in F1 mice at PND 21. BPA reduced the transcriptional level of testicular DNA methyltransferase (Dnmt), increased the expression of testicular cytochrome P, caspase-9, and bax, and decreased the expression of bcl-2 in F1 mice at PND 56. Conclusion: in this study, BPA improved the apoptosis rate in the testis at PND 56 ($F = 5.01$, $P = 0.05$). Our study indicates that BPA disrupts the secretion of testosterone, estradiol, and estrogen receptors by interfering with the transcription of testicular DNA methyltransferase (Dnmt) in offspring males, which damages testicular tissues and affects the potential reproductive function.	Environ Sci Pollut Res Int. 2019 Aug;26(23):23491-23504.	10.1007/s11356-019-05579-z	31201698	動物	精巣	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-
統合_3058	Wei Y., Han C., Li S., Cui Y., Bao Y., and Shi W	2020	Maternal exposure to bisphenol A during pregnancy interferes ovaries development of F1 female mice	This study was conducted to investigated the effects of maternal exposure bisphenol A (BPA) on ovaries development of F1 female mice. The BPA exposure model of pregnant mice was prepared by intragastric administration of BPA at the doses of 0, 5, 10, 20, and 30 mg/kg/day at gestation day (GD) 0.5–17.5. The ovaries index of the offspring mice was calculated at postnatal day (PND) 21 and PND 56. The results showed that BPA at 5 mg/kg, 10 mg/kg, 20 mg/kg, 30 mg/kg and 50 mg/kg significantly increased the ovaries index of PND 21 female mice ($F_{4,25} = 3.011$, $P = 0.037$). Besides, there was a non-monotonic dose–response relationship between serum hormone, ovarian receptor levels, and BPA ($F_{4,25} = 3.011$, $P = 0.037$). BPA exposure significantly increased the serum testosterone level and the ovaries index in F1 females at PND 21 and PND 56. BPA increased the ovarian/uterine index in F1 females at PND 21 and PND 56. BPA exposure also upregulated the expression of ovarian Dnmt3 and inhibited the transcription of ovarian Dnmt3A and Dnmt3B in F1 mice at PND 21. BPA reduced the transcriptional level of ovarian DNA methyltransferase (Dnmt), increased the expression of ovarian cytochrome P, caspase-9, and bax, and decreased the expression of bcl-2 in F1 mice at PND 56. Conclusion: in this study, BPA improved the apoptosis rate in the ovaries at PND 56 ($F = 5.01$, $P = 0.05$). Our study indicates that BPA disrupts the secretion of testosterone, estradiol, and estrogen receptors by interfering with the transcription of ovarian DNA methyltransferase (Dnmt) in offspring females, which damages ovarian tissues and affects the potential reproductive function.	Environ Sci Pollut Res Int. 2019 Aug;26(23):23491-23504.	10.1016/j.theriogenology.2019.09.045	31593881	動物	卵巣発達	1	1	1	1: 昇明マウス	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	●	-	-
統合_3059	Wu S., Huang D., Su X., Yan H., Ma A., Li L., Wu L., and Sun Z	2020	The prostaglandin synthases, COX-2 and L-PGDS, mediate prostate hyperplasia induced by low-dose bisphenol A	This study aimed to identify prostaglandin synthases (PGS) that mediate bisphenol A (BPA)-induced prostatic hyperplasia and explore their underlying mechanisms. In an in vivo study, male adult Sprague-Dawley rats were treated with different concentrations of BPA (12, 50, 90, or 270 µg/kg/d, i.g., daily), or with vehicle for 5 weeks. Results revealed that low-dose BPA-induced prostatic hyperplasia with increased PCNA(+)/CD81-cells. BPA significantly upregulated the expression of cyclooxygenase-2 (COX-2) and NF-κB in the dorsolateral prostate (P < 0.05) and the expression of lipocalin-type prostaglandin D synthase (L-PGDS) in ventral prostate (P < 0.05). The level of estradiol (E2) testosterone (T) and expression of androgen receptor (AR) and estrogen receptor α (ERα) were also altered. In in vitro studies, elevated low-dose BPA (0.1–10 nM) promoted the proliferation of human prostate fibroblasts and epithelial cells, and significantly upregulated the expression of COX-2 and L-PGDS in the cells. The two types of cell proliferation induced by BPA were inhibited by COX-2 inhibitor NS-398 and L-PGDS inhibitor AT-56, respectively. Our findings indicate that COX-2 and L-PGDS mediate BPA-induced prostatic hyperplasia through pathways involving cell proliferation and apoptosis, which might be related to the functions of ERα and AR. The role of COX-2/NF-κB pathway in dorsolateral prostate requires further research.	Sci Rep. 2020 Aug 4;10(1):13108.	10.1038/s41598-020-69809-y	32753632	動物	前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	1	1	-	1	-	-	1	-	-	●	-	-	-	-	-

別添-2　統合文献リスト

毒性評価（動物）1：該当、0：該当しない　毒性評価（疫学）1：該当、0：該当しない　毒性評価（in vitro）1：該当、0：該当しない　毒性評価はタイトル及び要旨の情報に基づき可能な範囲で実施。明らかに毒性発現率不適合と判断されるものは作成段階評価へ進め、当該物質評価段階で排除に基づき排除。　引用評価機関 ●：該当

統合No.	著者名	発行年	タイトル	アブストラクト	書誌情報	doi	PMID	ヒト/動物/in vitro/ex vivo/in silico	分野（疫学/動物）	哺乳動物	経口投与	BPA単独ばく露	一般的な動物種及び系統の無処置動物	対照群と3用量以上のBPA投与群	10 mg/kg/日以下の用量設定	コホート研究/症例対照研究/メタアナリシス	全ての集団	全てのばく露経路	BPA単独ばく露	遺伝毒性試験	遺伝毒性試験以外については100mM以下の濃度設定の試験	適格性評価基準適合（1534報）	依頼性評価対象文献（1012報）	疫学納品文献(716報)	動物納品文献(299報)※1報取得不可を含む	疫学情報抽出文献（170報）	動物情報抽出文献（123報）	EFSA 2023	EFSA 2016	EFSA 2015	BIR	KEMI	ANSES	FDA	NIFDS	CLARITY-BPA
統合_3060	Wu S., Huang D., Su X., Yan H., Wu J., and Sui Z.	2019	Oral exposure to low-dose bisphenol A induces hyperplasia of dorsolateral prostate and upregulates EGFR expression in adult Sprague-Dawley rats	Prostate is sensitive to endocrine hormone level, and the synergistic effect of estrogen and androgen is critical in prostate growth. The change of signal pathways caused by the imbalance of estrogen and androgen might function in the occurrence of prostate diseases. As a well-known endocrine disruptor compound, bisphenol A (BPA) can disturb the normal function of endocrine hormone and affect prostate development. This study aims to investigate the effects of low-dose BPA, comparable to actual human exposure, on the prostate development of adult male rats and explore the underlying mechanisms. Forty-eight male rats were randomly divided into four groups (n = 12 each) and were treated with BPA (10, 100, or 400 μg/kg bw/day) or 1 % gavage in corn oil by gavage for 4 weeks. BPA significantly increased the DLP weight, the DLP organ coefficient, and the prostate epithelial height (p < 0.01) of rats (age-dependently). Microarray analysis and quantitative real-time polymerase chain reaction showed that BPA significantly upregulated the transcriptional levels of some genes, including platelet/endothelial cell adhesion molecule 1 (pecam1), cadherin 5 type 2 (cdh5), and Fos. Furthermore, the expression of PCNA (p < 0.01), androgen receptor (p < 0.01), and EGF receptor (EGFR) (p < 0.01) in DLP was increased significantly by BPA treatment, and the expression of estrogen receptor alpha was also upregulated. The findings evidenced that low-dose BPA could induce DLP hyperplasia in adult rats, and the upregulated EGF-EGFR pathway that was responsive to estrogen and androgen might play an essential role in the DLP hyperplasia induced by low-dose BPA.	Toxicol Ind Health. 2019 Oct;35(10):647-659.	10.1177/0748233719885565	31771501	動物	前立腺	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	-	-	-	●	-	-	-	-	-
統合_3061	Yanagisawa R., Koike E., Win-Shwe T.T., and Takano H	2019	Oral exposure to low dose bisphenol A aggravates allergic airway inflammation in mice	Bisphenol A (BPA) is widely used in many consumer products and has adverse effects on human health including allergic diseases. We investigated the effects of low dose BPA, comparable to actual human oral exposure, on allergic asthma in vivo. C3H/HeJ male mice were fed a chow diet containing BPA (equivalent to 0.08, 0.80, or 8.00 μg/day/kg bw) and were sensitized by intratracheal instillation (ITI) of ovalbumin (OVA). Two weeks later, mice were challenged with OVA (10 μg/50 μL/mouse) by ITI every two weeks from 5–12 weeks of age. All doses of BPA plus OVA enhanced pulmonary inflammation and airway hyperresponsiveness, and increased key mRNA levels of Th2 cytokine/chemokine, and serum OVA-specific IgE and IgG1 levels. Furthermore, BPA enhanced OVA-induced activation of pulmonary and hepatic NF-κB and serum amyloid A (SAA) levels. Next, we investigated the effects of BPA on OVA-induced DC-T cell interaction. Furthermore, BPA enhanced OVA-incorporated cell proliferation and protein levels of IL-4 and IL-5 in mediastinal lymph node (ML) cells in OVA-sensitized mice. In bone marrow-derived DCs (BMDCs), middle dose BPA with OVA increased DC-T cell interaction. In conclusion, oral exposure to low dose BPA at levels equivalent to human exposure can aggravate allergic asthmatic responses through enhancement of Th2-skewed responses, lung hormone receptor downregulation, and NF-κB and SAA-mediated systemic change.	Toxicology Reports 6, 1253-1262	10.1016/j.toxrep.2019.11.012	31788436	動物	-	1	0	1	C3H/HeJSlc	1	0.08, 0.8, 8.0 mg/kg/day/BPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3062	Zou H., Wang S., Liu Y., Mu J., Yang L., Zhou Y., Yi P., Niu Y., Huang Y., and Lu Y	2020	The effect of hormonal levels and oxidative stress on bisphenol A and soy isoflavone reproductive toxicity in murine offspring	Previous studies have suggested that human exposure to bisphenol A (BPA) and soy isoflavones (SIFs) can occur during pregnancy. The combination of these chemicals is hypothesized to have a toxic impact on the fetus. This study investigated the reproductive toxicity of BPA and SIFs in mice and explored the underlying mechanisms. Pregnant mice were exposed to BPA (50 mg/kg/day), SIFs (500 mg/kg/day), or a combination of BPA and SIFs via food during gestation. Exposure to BPA and SIFs as fetal development, including weight, organ weight, anogenital distance and histopathological changes in the testes of F1 offspring mice exposed in vitro. Hormonal effects were determined by measuring serum levels of estrogen receptor (ESR), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (T). Additionally, mitochondrial DNA copy numbers, and the serum levels of malondialdehyde and superoxide dismutase, were determined to evaluate alterations in oxidative stress and potential toxicity. Exposure to BPA and SIFs increased the body weight of the pups and reduced the testicular organ coefficient. Exposure to BPA as well as testes weight. Moreover, BPA exposure also induced testicular lesions. The seminiferous tubules of testis were denatured in varying degrees and the lumen wall structure was disordered. The levels of ESR in all offspring and the T levels in male offspring significantly increased, compared with controls. Co-exposure to BPA and SIFs exacerbated these changes. In body weight, testicular lesions and hormonal levels, relative to BPA exposure alone. Additionally, oxidative damage was only induced by high dose BPA. Collectively, these findings suggested that BPA and SIFs could have synergistic effect on the reproductive system, which could be mediated by the regulation of ESR expression and testosterone release.	Mol Med Rep. 2020 Dec;22(6):4938-4946.	10.3892/mmr.2020.11544	33173981	動物	ホルモンレベル	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	●	-	-	-	-	-
統合_3063	Gayrard, V., Lacroix, M. Z., Grandin, F. C., Collet, S. H., Mila, H., Vigui, C. Gély, C. A., Rabozzi, B., Bouchard, M. L. and-I, R., Toutain, P. L., & Picard-Hagen, N.	2019	Oral Systemic Bioavailability of Bisphenol A and Bisphenol S in Pigs.	Background: Given its hormonal activity, bisphenol S (BPS) as a substitute for bisphenol A (BPA) could actually increase the risk of endocrine disruption if its toxicokinetics (TK) properties, namely its oral availability and systemic persistency, were higher than those of BPA. Objectives: The TK behavior of BPA and BPS was investigated by administering the two compounds by intravenous and oral routes in piglet, a known valid model for investigating oral TK. Methods: Experiments were conducted in piglets to evaluate the kinetics of BPA, BPS, and their glucuro-conjugated metabolites in plasma and urine after intravenous administration of BPA, BPS, and BPS glucuronide (BPS-GLUC) and oral administration of BPA, BPS, or isopropanol with BPS, and to have plasma clearance (CL) values. A physiologically based TK model describing the kinetics of BPA and BPS and their glucuronides in blood was then developed to estimate the oral fraction absorbed (Fabs) of the two compounds. Results: The data indicated that almost all the BPS oral dose was absorbed and transported into the liver where only 41% of BPS was glucuronidated, leading to a systemic bioavailability of 57.5%. In contrast, only 7.7% of the oral dose of BPA was absorbed and underwent an extensive first-pass glucuronidation either in the gut (18%) or in the liver (53%), thus accounting for the low systemic bioavailability of BPA (0.6%). Due to the higher oral absorption of BPS, its coexposure with BPA, in comparison with BPA and its known plasma clearance (3.5 l/min/kcorr), the oral BPS systemic exposure was on average about 290 times higher than for BPA for an equal oral intake dose of the two compounds. Conclusion: Given the similar digestive tracts of pigs and humans, our results suggest that replacing BPA with BPS will likely lead to increased internal exposure to an endocrine active compound that could be of concern for human health. https://doi.org/10.1289/EHP4599	Environ Health Perspect. 2019 Jul;127(7):77005.	10.1289/EHP4599	31313948	動物	ADME	1	1	1	0	0	0	-	-	-	-	-	-	-	-	1	1	-	1	-	-	-	-	-	●	-	-	-	-	-
統合_3064	Goodrich, J. M., Ingle, M. E., Domino, S. E., Treadwell, M. C., Dolinoy, D. C., Burant, C., Meeker, J. D., & Padmanabhan, V.	2019	First trimester maternal exposures to endocrine disrupting chemicals and metals and fetal size in the Michigan Mother Infant Pairs study.	Exposures to endocrine disrupting chemicals and metals are near ubiquitous worldwide, and their potential impact on children's is a major public health concern. This pilot study was designed to characterize exposures to phthalates, phenols and metals among pregnant women in the first trimester, and to examine associations with fetal biometrics and birth weight. A total of 31 chemicals and elements were analyzed in urine from 56 mothers with full-term newborns from the Michigan Mother Infant Pairs study. Bivariate analyses identified predictors of exposure biomarkers. Associations between birth weight, Fenton z-scores and second trimester fetal biometrics were examined using multivariable linear regression models. Mixtures of chemicals were analyzed using Bayesian kernel machine regression (BKMR). Maternal urinary concentrations of phenols were widely detected and had comparable median concentrations to those reported in other populations of pregnant women. Phthalate metabolites were detected in 50–100% of samples. Mono-2-ethylhexyl phthalate was significantly associated with higher birth weight and Fenton z-score. Other first trimester associations observed for bisphenol S. Estimated femur length from ultrasonography was significantly inversely associated with arsenic, barium and lead. While limited by sample size, this study is one of the first to evaluate birth outcomes with respect to emerging endocrine disrupting chemicals and to examine associations between toxicants and fetal biometrics. Exposure assessment was provided by the National Institute of Environmental Health Sciences' Children's Health Exposure Analysis Resource (NIEHS CHEAR), a resource available to children's studies with the goal of combining data across cohorts in an effort to characterize the impact of toxicants on child health from birth and beyond. Keywords: birth outcomes; metals; phenols; phthalates; prenatal exposures.	J Dev Orig Health Dis. 2019 Aug;10(4):447-458.	10.1017/S2040174418001065X	30696509	ヒト	生殖発生	-	-	-	-	-	-	-	-	-	-	コホート	1	1	-	-	-	1	1	1	-	-	-	-	-	●	-	-	-	-	-
統合_3065	Uzi, S., Ullah, A., Shaheen, G., & Jahan, S.	2020	Exposure of BPA and itsalternatives like BPB, BPF, and BPS impair subsequent reproductive potentialsin adult female Sprague Dawley rats.	Bisphenol A (BPA) and its alternatives are extensively used in household and industrial products. BPA and its alternatives have affinity for estrogen receptors and mimic its actions. The present study aims to examine the comparative effects of BPA and its alternatives bisphenol B (BPB), bisphenol F (BPF), and bisphenol S (BPS) on the reproductive health in adult female rats. One hundred and seventy-poor rewaring female rats (90 ± 35 g) were divided into 17 groups and assigned to different treatments. Control animals received gavages were injected with the corresponding concentrations of 50 000 μg/kg/d in 0.5 mg/kg/d of BPA, BPB, BPF, and BPS for 28 days. The results showed adverse morphological and histopathological alterations in rat ovaries in all treated groups. A remarkable decrease was observed in antral and corpus luteum follicles while the oral treatment and cystic follicles in the BPA-treated group. Similarly, BPB, BPF, and BPS also induced cystic follicles in the ovaries. Moreover, BPA and its alternatives significantly increased the levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) while decreased the values of thiobarbituric acid reactive substances (TBARS) and reactive oxygen species (ROS) was observed when BPA and its alternatives groups were compared with the control. Moreover, serum and ovarian also observed with alterations in their concentrations when treated groups were compared with the control. The current data suggest that BPA and its alternatives exposure during the per-pubertal stage have the potential to induce oxidative stress and histopathological changes during follicular development in female rats. Keywords: Bisphenol A, B, F and S; ROS; antioxidant enzymes; histopathology; oxidative stress markers.	Toxicology mechanisms and methods, 30(1),60-72.	10.1080/15376516.2019.1652873	31424294	動物	-	1	0	1	不明	不明	50 000 μg/kg/d in 0.5 mg/kg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3066	Shi, M., Whorter, A. E., Sakuloski, N., Maclean, J. A., & Hayashi, K.	2019	Prenatal exposure to bisphenol A, E, and S induces transgenerational effects on male reproductive functions in mice.	This study was performed to examine the transgenerational effects of bisphenol (BP) A analogs, BPE and BPS on male reproductive functions using mice as a model. CD-1 mice (F0) were orally treated to control (vehicle) or BPA, BPE, or BPS (0.5 or 50 μg/kg/day) from gestational day 7 the cesarean of vaginal plug = 1) to birth. Male (n=6 and 7) and F2 offspring were used to generate F3 males. Prenatal exposure to BPA, BPE, and BPS decreased sperm counts and/or motility and disrupted the progression of germ cell development as morphometric analyses exhibited an abnormal distribution of the stages of spermatogenesis in F3 males. Dysregulated serum levels of estradiol (E2) and testosterone, as well as expression of steroidogenic enzymes in F3 adult testis were also observed. In the seminal fluids, although sperm count and DNA damage were not affected, mRNA levels of DNA methyltransferases, histone methyltransferases, and their associated factors were increased by BP exposure. Furthermore, BP exposure induced transcriptome expression of DNMT3A in the F3 testis. Genome-wide DNA methylation analyses revealed that the number of differentially methylated regions (DMRs) in sperm was significantly affected in male testis, target exposure DNMT3A was altered by BP exposure, although DNMT3A, H3K9me2, and H3K9me3 expression remained stable. These results suggest that prenatal exposure to BPA, BPE, and BPS induces transgenerational effects on male reproductive functions, probably due to altered epigenetic modification following disruption of DNMT3 and histone marks in the neonatal and/or adult testis.	Toxicological Sciences, 172(2), 303-315.	10.1093/toxsci/kfz207	31532523	動物	-	1	1	1	不明	0	0.5 または 50 μg/kg/d	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	●	-	-	-	-	-
統合_3067	Gear R, Kendziorski JA, Belcher SM.	2017	Effects of bisphenol A on incidence and severity of cardiac lesions in the NCTR-Sprague-Dawley rat: A CLARITY-BPA study.	The goal of this study was to determine whether bisphenol A (BPA) had adverse effects indicative of cardiac toxicity. As part of the 'Consortium Linking Academic and Regulatory Insights on BPA Toxicity' (CLARITY-BPA), study dams and offspring were exposed by daily gavage to five doses of BPA ranging from 2.5 to 25000 μg/kg/day. 0.05 or 0.5 μg/kg/day (7 or either) estradiol (EE) or 0.3% carboxymethylcellulose vehicle. Developmental exposures were from gestational day 6 through postnatal day 21 (weaning). Hearts from 1 year old male and female offspring were examined for histopathology. Compared to controls, body weight of continuously dosed females was reduced and exposure to synthetic estrogen (EE) increased body weight in males exposed to EE, and consistent with this, cardiomyocyte hypertrophy was observed. Exposure-related changes in collagen accumulation were minor and limited to highest EE exposure groups with increased collagen accumulation in PND21 males. Decreased collagen was observed in hearts of 1 year old exposed females at PND90 and PND180. In BPA- or EE-treated females cardiomyopathy incidence and severity was significantly increased compared to control females at PND21 with equivalent degeneration observed in both males and females at PND21 and PND90. Keywords: BPA; Cardiomyopathy; Clarity-BPA; Endocrine; Estrogen; Heart.	Toxicol Lett. 2017 Jun 5;275:123-135.	10.1016/j.toxlet.2017.05.011	28499613	動物	心臓	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	●
統合_3068	Cheong A., Johnson SA, Howald EC, Ellersieck MR, Camacho L, Lewis SM, Vanlandingham MM, Ying J, Ho SM, Rosenfeld CS.	2018	Gene expression and DNA methylation changes in the hypothalamus and hippocampus of adult rats developmentally exposed to bisphenol A or ethinyl estradiol: a CLARITY-BPA consortium study.	Bisphenol A (BPA), an endocrine disrupting chemical (EDC), is a ubiquitous pollutant. As part of the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA), we sought to determine whether exposure of Sprague-Dawley rats to 2,500 μg/kg/day BPA (BPA) or 0.1 μg/kg/day ethinyl estradiol (EE) through postnatal day 21 through postnatal day 21 induces behavior-relevant gene expression and DNA methylation changes in hippocampus and hypothalamus at adulthood. PND and DNA were isolated from both regions. Expression of ten genes (Esrrb, Esrrg, Dnmt3a, Dnmt3b, Esr1, Esr2, Kcna, Gnb, Ide, and Bdnf) presumably altered by early life BPA/EE exposure was examined. Three genes (Bdnf, Esrrb, and Esr1) were studied for DNA methylation changes in their putative 5' promoter regions. Molecular changes in hippocampus were correlated to behavioral changes in female offspring. Hippocampal Bdnf expression was significantly increased in BPA, EE, and BPA/EE exposure groups. Hypothalamic Bdnf expression was increased in BPA/EE exposure groups. Hippocampal Esrrb expression was increased in BPA, EE, and BPA/EE exposure groups. Hypothalamic Esrrb expression was increased in EE exposure group. Hippocampal and hypothalamic Esr1 expression was increased in BPA/EE exposure groups. Hippocampal Esrrb expression in females showed a weak negative association with sniffing current hole in thermo-maze. Hippocampal expression of Kcna, Esr2, Ide, and Dnt was strongly associated with olfactory of control rats in thermo-maze. Findings suggest BPA exposure induced non-EE-like gene expression and epigenetic changes in adult-not-hippocampi, a region involved in spatial navigation.	Epigenetics. 2018;13(7):704-720.	10.1080/15592294.2018.1497388	30001178	動物	発達神経	1	1	1	1	1	1	-	-	-	-	-	-	-	-	1	1	-	1	-	1	●	-	-	-	-	-	-	-	●