

## カドミウムに関する新規知見 (2008年10月～)

番号	分類	タイトル	著者	雑誌	要約	原著
1	尿中Cdと骨粗鬆症	Urinary cadmium and osteoporosis in U.S. Women $\geq$ 50 years of age: NHANES 1988-1994 and 1999-2004.	Gallagher CM, Kovach JS, Meliker JR.	Environ Health Perspect. 2008 Oct;116(10):1338-43. Epub 2008 Jun 13.	BACKGROUND: Urinary cadmium (U-Cd) has been associated with decreased peripheral bone mineral density (BMD) and osteoporosis. This association, however, has not been confirmed using femoral BMD, the international standard for diagnosing osteoporosis, at levels $<$ 1.0 microg Cd/g creatinine. OBJECTIVES: Our goal was to investigate the statistical association between U-Cd, at levels $\leq$ 1 microg/g creatinine, and osteoporosis, as indicated by hip BMD and self-report in a population-based sample of U.S. women $\geq$ 50 years of age. METHODS: We drew data from the National Health and Nutrition Examination Surveys for 1988-1994 (n = 3,207) and 1999-2004 (n = 1,051). Osteoporosis was indicated by hip BMD cutoffs based on the international standard and self-report of physician diagnosis. We analyzed U-Cd levels for association with osteoporosis using multiple logistic regression. RESULTS: Women $\geq$ 50 years of age with U-Cd levels between 0.50 and 1.00 microg/g creatinine were at 43% greater risk for hip-BMD-defined osteoporosis, relative to those with levels $\leq$ 0.50 microg/g (odds ratio = 1.43; 95% confidence interval, 1.02-2.00; p = 0.04). We observed similar effect estimates using self-report of physician-diagnosed osteoporosis. Smokers did not show a statistically increased risk. CONCLUSIONS: Results suggest that U.S. women are at risk for osteoporosis at U-Cd levels below the U.S. Occupational Safety and Health Administration's 3-microg/g safety standard. Given null findings among smokers, dietary Cd, rather than tobacco, is the likely source of Cd-related osteoporosis risk for the U.S. female population $\geq$ 50 years of age.	有
2	カドミウム曝露と死亡率	Cadmium-related mortality and long-term secular trends in the cadmium body burden of an environmentally exposed population.	Nawrot TS, Van Hecke E, Thijs L, Richart T, Kuznetsova T, Jin Y, Vangronsveld J, Roels HA, Staessen JA.	Environ Health Perspect. 2008 Dec;116(12):1620-8. Epub 2008 Jul 24. Click here to read	BACKGROUND: Few population studies have reported on the long-term changes in the internal cadmium dose and simultaneously occurring mortality. OBJECTIVE: We monitored blood cadmium (BCd), 24-hr urinary cadmium (UCd), and mortality in an environmentally exposed population. METHODS: Starting from 1985, we followed BCd (until 2003), UCd (until 1996), and mortality (until 2007) among 476 and 480 subjects, randomly recruited from low-exposure areas (LEA) and high-exposure areas (HEA). The last cadmium-producing plant in the HEA closed in 2002. RESULTS: From 1985-1989 to 1991-1996, BCd decreased by 40.3% and 18.9% in the LEA and HEA, respectively (p $<$ 0.0001 for between-area difference). From 1991-1996 until 2001-2003, BCd remained unchanged in the HEA (+ 1.8%) and increased by 19.7% in the LEA (p $<$ 0.0001). Over the entire follow-up period, the annual decrease in BCd averaged 2.7% in the LEA (n = 258) and 1.8% in the HEA (n = 203). From 1985-1989 to 1991-1996, UCd fell by 12.9% in the LEA and by 16.6% in the HEA (p = 0.22), with mean annual decreases of 2.7% (n = 366) and 3.4% (n = 364). Over 20.3 years (median), 206 deaths (21.5%) occurred. At baseline, BCd (14.6 vs. 10.2 nmol/L) and UCd (14.1 vs. 8.6 nmol/24-hr) were higher in deaths than in survivors. The risks (p $\leq$ 0.04) associated with a doubling of baseline UCd were 20% and 44% for total and noncardiovascular mortality, and 25% and 33% for a doubling of BCd. CONCLUSIONS: Even if zinc-cadmium smelters close, historical environmental contamination remains a persistent source of exposure. Environmental exposure to cadmium increases total and noncardiovascular mortality in a continuous fashion without threshold.	有

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3	Cd 摂取量と腎尿細管機能障害	Association of lifetime cadmium intake or drinking Jinzu River water with the occurrence of renal tubular dysfunction.	Kobayashi E, Suwazono Y, Dochi M, Honda R, Kido T.	Environ Toxicol. 2008 Oct 20. [Epub ahead of print]	This study was performed to clarify whether lifetime cadmium (Cd) intake (LCd) calculated from consumption of Cd-polluted rice and other foods, or drinking and/or cooking with Jinzu River water is associated with the occurrence of renal tubular dysfunction and to estimate the threshold level of LCd using a benchmark dose procedure. From participants in the 1967 and 1968 health examinations, the 2607 subjects (1430 men and 1177 women) who were aged 50 years or more, and who had either resided in the current hamlet since birth or moved there from a nonpolluted area and resided for a total of 30 years or longer were chosen as the target population. Based on a multiple logistic regression analysis performed for abnormal urinary findings (proteinuria, glucosuria, or proteinuria with glucosuria) using LCd as the explanatory variable with or without consideration of use of the river water for drinking and/or cooking, it was inferred that both factors of LCd and use of the river water influenced the occurrence of renal tubular dysfunction, with LCd appearing to exert a greater impact compared to drinking/cooking with the river water. Moreover, the threshold values of LCd for proteinuria with glucosuria were estimated to be 2.91 g in men and 1.79 g in women, without adjustment for use of the river water. After adjustment for its use, the values of proteinuria were calculated to be 0.93 g in women. When assuming user/nonuser status of the river water, the threshold level was calculated as 0.75/0.93 g in women. The difference of 0.18 g was interpreted as representing the influence of drinking/cooking with the river water. (c) 2008 Wiley Periodicals, Inc. Environ Toxicol, 2008.	有
4	Cd 摂取量と腎尿細管機能障害	Influence of consumption of cadmium-polluted rice or Jinzu River water on occurrence of renal tubular dysfunction and/or Itai-itai disease.	Kobayashi E, Suwazono Y, Dochi M, Honda R, Kido T.	Biol Trace Elem Res. 2009 Mar;127(3):257-68. Epub 2008 Nov 1.	The aim of this study was to clarify whether consumption of cadmium (Cd)-polluted rice or Jinzu River water exerted any influence on the occurrence of renal tubular dysfunction and/or Itai-itai disease. From the participants of health examinations conducted in 1967 and 1968, 3,078 subjects who had resided for >30 years in the present hamlet and were aged >50 years were selected as the target population and were divided according to their residence in 55 hamlets. In a multiple regression analysis, the regression coefficients between rice-Cd concentration and prevalence of abnormal urinary findings (proteinuria, glucosuria, or proteinuria with glucosuria) or patients with Itai-itai disease were statistically significant between both sexes. The correlation between the prevalence of users of Jinzu River water and the occurrence of glucosuria in men as well as abnormal urinary findings in women was not statistically significant. We surmise that eating Cd-polluted rice and drinking and/or cooking with Jinzu River water influenced the occurrence of Itai-itai disease. The occurrence of renal tubular dysfunction is likely to have also been influenced by both factors, with eating Cd-polluted rice having a greater impact on the occurrence of renal tubular dysfunction as compared to drinking and/or cooking with Jinzu River water.	有

番号	分類	タイトル	著者	雑誌	要約	原著
5	透析患者の尿・血中Cd濃度	Evaluation of toxic metals in blood and urine samples of chronic renal failure patients, before and after dialysis.	Kazi TG, Jalbani N, Kazi N, Jamali MK, Arain MB, Afridi HI, Kandhro A, Pirzado Z.	Ren Fail. 2008;30(7):737-45.	The determination of toxic elements in the biological samples of human beings is an important clinical screening procedure. The aim of this work was to determine total content of toxic elements-aluminum (Al), cadmium (Cd), and lead (Pb)-in whole blood and urine samples of male chronic renal failure patients (CRFPs) on maintenance hemodialysis from 2006 to 2007. The study included 100 CRFPs, plus 150 healthy volunteers in the control group. The concentration of toxic elements (TEs) were determined in blood sample before and after hemodialysis, while urine sample was determined once, before dialysis. Toxic elements were analyzed by electrothermal atomic absorption spectrometer, prior to microwave-induced acid digestion. The accuracy of the total Al, Cd, and Pb measurements was tested by simultaneously analyzing certified reference materials. No significant differences were established between the analytical results and the certified values (paired t-test at $p > 0.05$ ). The levels of TEs in blood samples of patients before dialysis were found to be higher than blood samples after dialysis session. In the control group, the blood levels of Al, Cd, and Pb were significantly lower than the chronic renal failure patients. Moreover, the study shows that analyzing levels of Al, Cd, and Pb may be useful in hemodialysis patients in evaluating TEs status.	有
6	Cd汚染と慢性腎不全	Chronic renal failure among farm families in cascade irrigation systems in Sri Lanka associated with elevated dietary cadmium levels in rice and freshwater fish (Tilapia).	Bandara JM, Senevirathna DM, Dasanayake DM, Herath V, Bandara JM, Abeysekara T, Rajapaksha KH.	Environ Geochem Health. 2008Oct;30(5):465-78. Epub 2008 Jan 17.	Chronic renal failure (CRF), in the main agricultural region under reservoir based cascade irrigation in Sri Lanka has reached crisis proportion. Over 5,000 patients in the region are under treatment for CRF. The objective of this study is to establish the etiology of the CRF. Concentrations of nine heavy metals were determined in sediments, soils of reservoir peripheries, water and Nelumbo nucifera (lotus) grown in five major reservoirs that supply irrigation water. All five reservoirs carried higher levels of dissolved cadmium (Cd), iron (Fe) and lead (Pb). Dissolved Cd in reservoir water ranged from 0.03 to 0.06 mg/l. Sediment Cd concentration was 1.78-2.45 mg/kg. No arsenic (As) was detected. Cd content in lotus rhizomes was 253.82 mg/kg. The Provisional Tolerable Weekly Intake (PTWI) of Cd based on extreme exposure of rice is 8.702-15.927 microg/kg body weight (BW) for different age groups, 5-50 years. The PTWI of Cd due to extreme exposure of fish is 6.773-12.469 microg/kg BW. The PTWI on a rice staple with fish is 15.475-28.396 microg/kg BW. The mean urinary cadmium (UCd) concentration in CRF patients of age group 40-60 years was 7.58 microg Cd/g creatinine and in asymptomatic persons UCd was 11.62 microg Cd/g creatinine, indicating a chronic exposure to Cd. The possible source of Cd in reservoir sediments and water is Cd-contaminated agrochemicals. The CRF prevalent in north central Sri Lanka is a result of chronic dietary intake of Cd, supported by high natural levels of fluoride in drinking water, coupled with neglecting of routine de-silting of reservoirs for the past 20 years.	有

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7	腎毒性	Nephrotoxicity of cadmium & lead.	Gonick HC.	Indian J Med Res. 2008 Oct;128(4):335-52. Click here to read	Cadmium and lead are divalent cations with a propensity to settle in the proximal tubule of the nephron, leading to nephrotoxicity. The pathophysiological results, however, tend to diverge. Cadmium in sufficient cumulative dosage leads to the production of the Fanconi syndrome, a generalized proximal tubular reabsorptive defect thought to be related to inhibition of both ATP production and Na-K-ATPase activity. On the other hand, lead accumulation in the proximal tubule leads to hyperuricaemia and gout, presumably by inhibiting uric acid secretion, and diminished glomerular filtration rate (GFR). Fanconi syndrome is seen unusually only in children and experimental animals. Cadmium nephrotoxicity is heralded by increased excretion of beta2-microglobulin, retinol binding protein and alpha1-microglobulin, indicative of decreased proximal tubule function. Beta2-microglobulinuria is not found in lead nephropathy. In lead nephropathy albuminuria is absent or minimal whereas in cadmium nephropathy albuminuria is variable. From the standpoint of pathology, both entities are characterized by tubulointerstitial disease and fibrosis, but only early lead nephropathy is characterized by the presence of proximal tubule nuclear inclusion bodies, due to the combination of lead with a lead binding-protein.	有
8	腎臓への影響	Renal effects evolution in a Chinese population after reduction of cadmium exposure in rice.	Wu X, Liang Y, Jin T, Ye T, Kong Q, Wang Z, Lei L, Bergdahl IA, Nordberg GF.	Environ Res. 2008 Oct;108(2):233-8. Epub 2008 Aug 8.	Cadmium is a well-known nephrotoxic agent with extremely long biological half-time of 10-30 years in human. To investigate the evolution of cadmium-induced renal effects in the population, a number of 148 residents who lived in cadmium-polluted area were followed-up for 3 years after the reduction of cadmium exposure in rice. Urinary cadmium (UCd), beta(2)-microglobulin (B2M) and albumin (ALB) were analyzed in 1995 and 1998, respectively. The results demonstrated that the changes of renal effects of residents depended on the levels of UCd before inflow of cadmium to human body declined. In cases where UCd were less than 10 microg/g creatinine in 1995, evidence was found indicating significant decreases in proteinuria (i.e., B2M and ALB) 3 years later, whereas, in cases where the excretion of UCd exceeded 10 microg/g creatinine in 1995, progression was observed. The study of dose-response relationships between UCd and B2M or ALB also showed that the cadmium-induced renal dysfunction might be reversible if UCd concentration was low-level before exposure decreasing, otherwise it might be irreversible or aggravated.	有

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9	カルシウム・リン代謝	Serial Follow-Up Study on Renal Handling of Calcium and Phosphorus After Soil Replacement in Cd-Polluted Rice Paddies Estimated Using a General Linear Mixed Model.	Kobayashi E, Suwazono Y, Honda R, Dochi M, Nishijo M, Kido T, Nakagawa H.	Biol Trace Elem Res. 2008 Dec 13. [Epub ahead of print]	A 10-year follow-up study was conducted to investigate the effects of renal handling of calcium (Ca) and phosphorus (P) after the removal of cadmium-polluted soil in rice paddies and replacing it with nonpolluted soil. Using a general linear mixed model, serial changes of Ca and P concentrations in urine and serum (Ca-U/S, P-U/S), fractional excretion of Ca (FECa), and percent tubular reabsorption of P (%TRP) were determined in 37 persons requiring observation in the Cd-polluted Kakehashi River Basin, Japan. Ca-U and Ca-S remained within the normal range in both sexes. FECa in men returned to the normal level within 3.3 years from the completion of soil replacement. Overall, it is suggested that the renal handling of Ca showed no or only a slight change throughout the observation period in both sexes. P-U decreased gradually. P-S showed lower than normal values in the men and values at the lower end of the normal range in women, although the values recovered gradually to normal. %TRP values remained low throughout the observation period and the values did not recover in either sex. However, the results of P-U and P-S suggested that the renal handling of P may recover after the completion of soil replacement.	無
10	骨への影響	Cadmium-induced bone effect is not mediated via low serum 1,25-dihydroxy vitamin D.	Engström A, Skerving S, Lidfeldt J, Burgaz A, Lundh T, Samsioe G, Vahter M, Akesson A.	Environ Res. 2009 Feb;109(2):188-92. Epub 2008 Dec 6.	Cadmium is a widespread environmental pollutant, which is associated with increased risk of osteoporosis. It has been proposed that cadmium's toxic effect on bone is exerted via impaired activation of vitamin D, secondary to the kidney effects. To test this, we assessed the association of cadmium-induced bone and kidney effects with serum 1,25-dihydroxyvitamin D (1,25(OH)(2)D); measured by enzyme immunoassay. For the assessment, we selected 85 postmenopausal women, based on low (0.14-0.39 microg/L) or high (0.66-2.1 microg/L) urinary cadmium, within a cross-sectional population-based women's health survey in Southern Sweden. We also measured 25-hydroxy vitamin D, cadmium in blood, bone mineral density and several markers of bone remodeling and kidney effects. Although there were clear differences in both kidney and bone effect markers between women with low and high cadmium exposure, the 1,25(OH)(2)D concentrations were not significantly different (median, 111 pmol/L (5-95th percentile, 67-170 pmol/L) in low- and 125 pmol/L (66-200 pmol/L) in high-cadmium groups; p=0.08). Also, there was no association between 1,25(OH)(2)D and markers of bone or kidney effects. It is concluded that the low levels of cadmium exposure present in the studied women, although high enough to be associated with lower bone mineral density and increased bone resorption, were not associated with lower serum concentrations of 1,25(OH)(2)D. Hence, decreased circulating levels of 1,25(OH)(2)D are unlikely to be the proposed link between cadmium-induced effects on kidney and bone.	有

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11	生殖への影響	Concentration of trace elements in human semen and relation to spermatozoa quality.	Slivkova J, Popelkova M, Massanyi P, Toporcerova S, Stawarz R, Formicki G, Lukac N, Putala A, Guzik M.	J Environ Sci Health A Tox Hazard Subst Environ Eng. 2009 Mar;44(4):370-5. Click here to read	In this study the concentrations of trace elements such as lead, cadmium, iron, nickel, copper and zinc in the human semen (n = 47), occurrence of pathological spermatozoa, and correlations of these elements to pathological forms were investigated. For each sample of human spermatozoa at least 500 spermatozoa were evaluated. Metal contents were determined by the voltametric method and flame absorption spectrophotometry method. The concentrations of trace elements in human semen were: lead 1.49 +/- 0.40 mg.kg(-1), cadmium 0.13 +/- 0.15 mg.kg(-1), iron 2.59 +/- 0.21 mg.kg(-1), nickel 0.40 +/- 0.07 mg.kg(-1), copper 0.28 +/- 0.06 mg.kg(-1), and zinc 153.93 +/- 67.08 mg.kg(-1), respectively. The total percentage of pathological spermatozoa was 41.61 +/- 9.80% with predominancy of broken flagellum, flagellum torso and separated flagellum. In relation to trace elements the analysis showed correlation between copper and lead (r = -0.47), nickel and iron (r = 0.36), lead and flagellum ball (r = -0.39), cadmium and large heads (r = 0.37) and between iron and other forms of pathological spermatozoa (r = -0.32). Results of this study describe possible effects of trace elements on the spermatozoa quality in normal human sperm.	有
12	汚染地域のCd摂取量の推定	Influence of Drinking and/or Cooking with Jinzu River Water on the Development of Itai-Itai Disease.	Kobayashi E, Suwazono Y, Dochi M, Honda R, Kido T, Nakagawa H.	Biol Trace Elem Res. 2008 Dec 18. [Epub ahead of print] Click here to read	This study was undertaken to estimate the amount of cadmium (Cd) exposure needed for the development of Itai-itai disease and the influence of using Jinzu River water for drinking and/or cooking on its development. The subjects comprised 38 Itai-itai disease patients admitted both for questionnaire survey and medical testing. The period when the patients started to perceive leg/back pain was defined as 'mild disease onset' and that when they experienced the most severe manifestations such as ambulatory disturbance as 'severe disease onset'. In a comparison of non-users/users of river water, mean age and lifetime Cd intake (LCd) estimated from the daily consumption of rice and other foods at the onset of mild or severe disease showed smaller values in the users than non-users. LCd in non-users/users of river water for drinking and/or cooking were estimated as 3.46-3.60 g/2.58-2.63 g at mild disease onset and 4.24-4.44 g/3.50-3.54 g at severe disease onset. A portion of the differences in LCd in non-users/users is attributable to the influence of Cd consumption from the use of river water, although it was suggested that LCd estimated from eating Cd-polluted rice exerted a greater influence on the development of Itai-itai disease than drinking and/or cooking with Cd-polluted river water.	無

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13	汚染地域の健康リスク評価	Regional assessment of cadmium pollution in agricultural lands and the potential health risk related to intensive mining activities: a case study in Chenzhou City, China.	Zhai L, Liao X, Chen T, Yan X, Xie H, Wu B, Wang L.	J Environ Sci (China). 2008;20(6): 696-703.	The purpose of this study was to assess the extent of cadmium (Cd) contamination in agricultural soil and its potential risk for people. Soils, rice, and vegetables from Chenzhou City, Southern China were sampled and analyzed. In the surface soils, the 95% confidence interval for the mean concentration of Cd varied between 2.72 and 4.83 mg/kg (P < 0.05) in the survey, with a geometric mean concentration of 1.45 mg/kg. Based on the GIS map, two hot spot areas of Cd in agricultural soils with high Cd concentrations were identified to be located around the Shizhuyuan, Jinshiling, and Yaogangxian mines, and the Baoshan and Huangshaping mines, in the center of the city. About 60% of the total investigated area, where the agricultural soil Cd concentration is above 1 mg/kg, is distributed in a central belt across the region. The critical distances, at which the soil Cd concentration were increased by the mining activities, from the mines of the soils were 23 km for the Baoshan mine, 46 km for the Huangshaping mine, and 63 km for the Shizhuyuan mine, respectively. These are distances calculated from models. The Cd concentrations in rice samples ranged from 0.01 to 4.43 mg/kg and the mean dietary Cd intake from rice for an adult was 191 microg/d. Results of risk indexes showed that soil Cd concentrations possessed risks to local residents whose intake of Cd from rice and vegetables grown in soils in the vicinity of the mine was 596 microg/d.	無
14	尿中Cdと死亡率	Cadmium Levels in Urine and Mortality among U.S. Adults	Andy Menke, Paul Muntner, Ellen K. Silbergeld, Elizabeth A. Platz, Eliseo Guallar	Environmental Health Perspectives Volume 117, Number 2, February 2009	Background: Cadmium exposure has been associated with increased all-cause, cancer, and cardiovascular disease mortality. However, studies investigating this association have included participants with considerably higher levels of cadmium than those found in the general population. Objective: We aimed to evaluate the association of creatinine-corrected urinary cadmium levels with all-cause and cause-specific mortality in the U.S. general population. Methods: We analyzed the relationship between cadmium measured in 13,958 adults who participated in the Third National Health and Nutrition Examination Survey in 1988-1994 and were followed through 31 December 2000, and all-cause, cancer, cardiovascular disease, and coronary heart disease mortality. Results: The geometric mean levels of urinary cadmium per gram of urinary creatinine in study participants were 0.28 and 0.40 µg/g for men and women, respectively (p < 0.001). After multivariable adjustment, including smoking, a major source of cadmium exposure in nonoccupationally exposed populations, the hazard ratios [95% confidence interval (CI)] for all-cause, cancer, cardiovascular disease, and coronary heart disease mortality associated with a 2-fold higher creatinine-corrected urinary cadmium were, respectively, 1.28 (95% CI, 1.15-1.43), 1.55 (95% CI, 1.21-1.98), 1.21 (95% CI, 1.07-1.36), and 1.36 (95% CI, 1.11-1.66) for men and 1.06 (95% CI, 0.96-1.16), 1.07 (95% CI, 0.85-1.35), 0.93 (95% CI, 0.84-1.04), and 0.82 (95% CI, 0.76-0.89) for women. Conclusions: Environmental cadmium exposure was associated with an increased risk of all-cause, cancer, and cardiovascular disease mortality among men, but not among women. Additional efforts are warranted to fully explain gender differences on the impact of environmental cadmium exposure.	有