Annexes

Annex 1

Identification of food-borne parasites for consideration

An online questionnaire was utilized to prioritize 93 listed parasites at a regional and global level with respect to their public health significance and trade implications. The questionnaire also provided a valuable resource for the experts in developing criteria to be used for the ranking process (Table A1.1). The results were grouped into four tiers related to the global relevance of the listed parasites. Tier 1 and Tier 2 parasites were classified as "important" ('very' or 'somewhat') from a global perspective by at least 50% (n=25) and 40% (n=12) of experts, respectively.

TABLE A1.1 Tiered list of parasites under consideration

Tier 1 parasites (identified by more than 50% of the experts as being globally important)		
Anisakis simplex	*Echinococcus granulosus*	*Toxocara canis*
Anisakis spp.	*Echinococcus multilocularis*	*Toxocara cati*
Ascaris lumbricoides	*Entamoeba histolytica*	*Toxoplasma gondii*
Clonorchis sinensis	*Fasciola gigantica*	*Trichinella britovi*
Cryptosporidium hominis.	*Fasciola hepatica*	*Trichinella pseudospiralis*
Cryptosporidium parvum	*Giardia lamblia*	*Trichinella spiralis*
Cryptosporidium spp.	*Taenia saginata*	*Trichuris trichiura*
Diphyllobothrium latum	*Taenia solium*	*Trypanosoma cruzi*
Diphyllobothrium spp.		
Tier 2 parasites (scored by more than 40% of experts as being globally important)		
Ancylostoma duodenale	*Gnathostoma spinigerum*	*Opisthorchis felineus*
Balantidium coli	*Hymenolepis nana*	*Sarcocystis* spp.
Cyclospora cayetanensis	*Metagonimus* spp.	*Taenia asiatica*
Enterobius vermicularis	*Necator americanus*	*Trichinella nativa*

Tier 3 parasites (those with the greatest number of "very important" global scores or regional scores and those with the highest cumulative importance scores, i.e. sum of number of experts indicating a parasite is global and regionally important)		
Angiostrongylus cantonensis	*Opisthorchis viverrini*	*Sarcocystis hominis*
Blastocystis spp.	*Paragonimus heterotremus*	*Strongyloides stercolaris*
Capillaria philippinensis	*Paragonimus* spp.	*Trichinella murelli*
Fasciolopsis buski	*Paragonimus westermani*	
Tier 4 – Remaining parasites		
Alaria alata	*Echinostoma revolutum*	*Nanophyetus salmincola*
Alaria americana	*Echinostoma* spp.	*Paragonimus kellicoti*
Alaria spp.	*Gastrodiscoides hominis*	*Pseudoterranova decipiens*
Ancylostoma ceylanicum	*Gnathostoma binucleatum*	*Sarcocystis fayeri*
Angiostrongylus costaricensis	*Gnathostoma hispidu*	*Sarcocystis suihominis*
Baylisascaris	*Haplorchis pumilo*	*Spirometra erinacei*
Blastocystis hominis	*Haplorchis* spp.	*Spirometra mansoni*
Capillaria hepatica	*Haplorchis taichui*	*Spirometra mansonoides*
Centrocestus spp.	*Heterophyes* spp.	*Spirometra ranarum*
Contracaecum/Phocascaris	*Hymenolepis diminuta*	*Spirometra* spp.
Cystoisospora belli	*Kudoa septempunctata*	*Taenia multiceps*
Dicrocoelium dendriticum	*Lecithodendriid flukes*	*Taenia serialis*
Dientamoeba fragilis	*Linguatula serrata*	*Trichinella papuae*
Dioctophyme renale	*Mesocestoides lineatus*	*Trichinella zimbabwensis*
Diplogonoporus grandis	*Mesocestoides variabilis*	*Trichostrongylus* spp.

The Tier 3 list comprised those with the greatest number of "very important" global scores or regional scores, and those with the highest cumulative importance scores (sum of number of experts indicating a parasite is global or regionally important), while Tier 4 contained the remaining parasites. The experts decided to further screen this 4-tiered list through grouping of parasites by genus or family (Table A1.2), and where applicable, based on common routes of transmission, clinical manifestations, and food-borne sources of infection. This resulted in a list of 24 parasites for the ranking exercise (Table 2 in Section 2.2 in the main report). Table A1.3 lists parasites that were considered important by the experts at the regional or national level but were excluded at the global level for the stated reasons.

TABLE A1.2. Parasite groupings

Parasites	Grouping	Parasite	Grouping
Anisakis simplex *Anisakis* spp. *Pseudoterranova decipiens*	Anisakidae	*Paragonimus heterotremus* *Paragonimus* spp. *Paragonimus westermani* *Paragonimus kellicoti*	*Paragonimus* spp.
Cryptosporidium hominis *Cryptosporidium parvum* *Cryptosporidium* spp.	*Cryptosporidium* spp.	*Sarcocystis* spp. *Sarcocystis hominis* *Sarcocystis fayeri* *Sarcocystis suihominis*	*Sarcocystis* spp.
Diphyllobothrium latum *Diphyllobothrium* spp. *Diplogonoporus grandis*	Diphyllobothriidae	*Spirometra erinacei* *Spirometra mansoni* *Spirometra mansonoides* *Spirometra ranarum* *Spirometra* spp.	*Spirometra* spp.
Fasciola gigantica *Fasciola hepatica*	*Fasciola* spp.	*Toxocara canis*	*Toxocara* spp.
Metagonimus spp. *Centrocestus* spp. *Heterophyes* spp. *Haplorchis pumilo* *Haplorchis* spp. *Haplorchis taichui*	Heterophyidae	*Trichinella britovi* *Trichinella pseudospiralis* *Trichinella native* *Trichinella murelli* *Trichinella papuae* *Trichinella zimbabwensis*	*Trichinella* spp.
Opisthorchis felineus *Opisthorchis viverrini*	Opisthorchiidae		

TABLE A1.3. Parasites excluded from original list

Broad Category	Parasites EXCLUDED	Criteria for exclusion
Meat-borne	*Taenia asiatica*	Regional
	Taenia serialis	Unlikely / rare zoonosis
Fish- and shellfish-borne	*Capillaria philippinensis*	Regional – Philippines
	Contracaecum/ Phocascaris	Proportion of cases attributable to food-borne infection negligible
	Echinostoma spp.	Regional – SE Asia
	Gnathostoma spp.	Regional – SE Asia
	Kudoa septempunctata	Regional – SE Asia
	Lecithodendrid flukes	Regional – SE Asia
Plant (fruit- and vegetable-borne, including berries, fruit juice)	*Blastocystis* spp.	Proportion of cases attributable to food-borne infection negligible
	Strongyloides stercoralis	Proportion of cases attributable to food-borne infection negligible
	Ancylostoma spp.	Proportion of cases attributable to food-borne infection negligible
	Necator americanus	Proportion of cases attributable to food-borne infection negligible
"Other"	*Angiostrongylus cantonensis*	Regional – Asia Pacific
	Hymenolepis spp.	Proportion of cases attributable to food-borne infection negligible

Annex 2

Food-borne parasite ranking exercise: summary card

Group:		Parasite/food:				
Criterion	**Bin 0**	**Bin 1**	**Bin 2**	**Bin 3**	**Bin 4**	**Score**
Number of global food-borne illnesses (manifesting disease)	<10 000	10 000 – 100 000	100 000 – 1 000 000	1 000 000 – 10 000 000	$>10^7$	
Global distribution (number of regions)	N/A	1	2	3-4	>4	
Acute morbidity severity (disability weight)	0 (none)	<0.03 (very mild)	0.03–0.1 (mild)	0.1–0.30 (moderate)	>0.30 (severe)	
Chronic morbidity severity (disability weight)	0 (none)	<0.03 (very mild)	0.03-0.1 (mild)	0.1–0.30 (moderate)	>0.30 (severe)	
Fraction of illness that is chronic (%)	0%chronic	<25% chronic	25–50% chronic	50–75% chronic	>75% chronic	
Case-fatality ratio (%)	0%	0–0.1%	0.1–1%	1–10%	>10%	
Likelihood of increased human burden (%)	None	0–25% (low)	25–50% (moderate)	75–100% (high)	100% (still increasing)	
How relevant is this parasite-food pathway for international trade?	Not at all	Some relevance	High relevance			
Scope of impact to economically vulnerable communities?	None	Low	Moderate	High		
What is the quality of available evidence for this parasite?	Very Poor	Poor	Adequate	Good	Very Good	

Further comments relevant for the discussion on risk management

Annex 3

Food-borne parasite ranking exercise form: explanation of criteria

The summary card used to conduct this exercise should be considered an expert elicitation. We are asking for your expert judgment on 9 scored parameters, each of which is intended to capture some aspect of the global importance of each parasite. We realize that data may not be available to support your scores, but we ask you to use your knowledge of the literature and your considered opinion to answer these questions.

Please indicate group and parasite/food pathway on the sheet.

We ask that for each parasite you estimate each criterion, using the levels marked in the bins to indicate your group score. You may circle multiple bins as marked in the example below to indicate a broader range of values, but it is CRITICAL that you come to a SINGLE CONSENSUS BEST GUESS SCORE for the criterion and mark it numerically in the rightmost column.

Please take notes on a separate piece of paper to indicate important assumptions or data sources that you would like to record. Please mark on that paper the group and parasite/food pathway so we can associate it with your scores.

Please remark additional comments relevant to risk management below and on the back.

Example:

	Bin 0	Bin 1	Bin 2	Bin 3	Bin 4	Score
Mortality rate (case-fatality ratio) (%)	0%	0–0.1%	0.1–1%	1–10%	>10%	**2**

Criterion No. 1. Number of global food-borne illnesses

Criterion: Number of individuals worldwide that manifest clinical illness

Explanation: This criterion measures the magnitude of global food-borne disease as the number of people worldwide who have clinical

symptoms of illness and who were infected by food. If you do not feel that you can estimate this number directly, you can calculate it based on numbers you may feel more comfortable with. Namely, it can be considered a function of the global prevalence of infection multiplied by the percent of infections that are result from food consumption multiplied by the percent of infections that are symptomatic multiplied by the global population of (7 billion people). For parasites that are generally regarded as acute infections (e.g. *Trichinella*), it is incidence times percent symptomatic times percent food-borne times global population.

For example: Your best estimate is that Parasite A has a global prevalence of about 20%, of which about 50% you believe to be food-borne. Of these infections, the literature suggests that 10% of infections are symptomatic. This equates to a global illness rate of 1% (20% × 50% × 10%). Thus, you would estimate about 70 000 000 cases (1% of 7×109).

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
<10 000 illnesses	10 000 – 100 000 illnesses	100 000 – 1 000 000 illnesses	1 000 000 – 10 000 000 illnesses	>10 000 000 illnesses

Criterion No. 2. Geographical distribution (endemic regions)

Criterion: Number of regions in which this parasite is geographically distributed (in which it shows a natural cycle)

Explanation: This criterion reflects the global distribution of the parasite across world regions as a simple count of the number of major regions (Africa, Asia, Europe, Near East, North America, Latin America and the Carribbean, Pacific) in which the disease is regularly found.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
Not applicable	1 region	2 regions	3-4 regions	> 4 regions

Criterion No. 3. Acute Morbidity Severity

Criterion: Loss of health-related quality of life due to acute infection

Explanation: This criterion reflects the degree to which an acute manifestation of illness reduces health-related quality of life. The value of the criterion is anchored between 0 (full health, asymptomatic, no illness) to 1 (worst possible health state or death). It depends on both the severity and duration of illness. For a large number of health conditions, including many infectious diseases and some parasitic diseases, disability weights have already been published.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
0 (none)	< 0.03 (very mild)	0.03 –0.01 (mild)	0.01–0.30 (moderate)	>0.30 (severe)

Decision rules: If a pathogen causes more than one acute disease, a population weighted average is applied. Calculate your best guess point estimates for identified acute conditions and weight by likelihood. Then assign a bin using the ranges above.

Refer to the table of disability weights below (from Havelaar *et al.,* 2010; Annex 1) or see WHO publications. The *Global Burden of Disease 2004 Update* includes a summary table on page 33 (WHO, 2008).

This annex to the 2004 report includes more detailed disability weights (WHO, 2004; see http://www.who.int/healthinfo/global_burden_disease/GBD2004_DisabilityWeights.pdf)

Table of disability weights for acute and chronic conditions

Very mild (disability weight <0.03)	Duration (in days)	Moderate (0.1<disability weight <0.3)	Duration (in days)
Otitis media	14	Inflammatory bowel disorder	183
Hepatitis	30	Reactive arthritis	183
Folliculitis	7	Tuberculosis	365
Cystitis	14	Chronic pulmonary disease (bronchitis, asthma, emphysema)	365
Gastroenteritis, severe	10–15		

Conjunctivitis	7	Diabetes mellitus	365
Tonsillitis	7		
Bronchitis	14		
Mild (0.03<disability weight <0.1)		**High (disability weight >0.3)**	
Allergic rhinitis	119	Renal failure	365
Reactive arthritis	42	Guillain-Barré syndrome	365
Tinea pedis	183	Visual disorder, severe	365
Eczema	35	Paraplegia	365
Otitis externa	35	AIDS	365
Gastroenteritis, hospitalized	7–14	Meningitis	
Laryngitis	7	Dementia	365
Sinusitis	183		
Irritable bowel syndrome	183		
Haemolytic uremic syndrome	30		
Visual disorder, mild	365		
Hepatitis	92		
Gastroenteritis, chronic	183		
Influenza	14		

Criterion No. 4. Chronic Morbidity Severity

Criterion: Loss of health-related quality of life associated with chronic illness.

Explanation: This criterion reflects the degree to which a chronic manifestation of illness reduces health-related quality of life. The value of the criterion is anchored between 0 (full health, asymptomatic, no illness) to 1 (worst possible health state or death). It depends on both the severity and duration of illness. For a large number of health conditions, including many infectious diseases and some parasitic diseases, disability weights have already been published.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
0 (none)	<0.03 (very mild)	0.03–0.01 (mild)	0.01–0.30 (moderate)	>0.30 (severe)

Decision rules: If a pathogen causes more than one chronic disease, a population weighted average is applied. Calculate your best guess point estimates for identified chronic conditions and weight by likelihood. Then assign a bin using the ranges above.

Refer to Criterion 3 for additional guidance on disability weights.

Criterion No. 5. Fraction chronic

Criterion: Percent of global food-borne illnesses (estimated in Criterion 1) that are considered chronic (see note below; this is a weighting criterion only)

Explanation: This criterion is used to partition the illnesses estimated in Criterion 1 into those with acute manifestations and those with chronic manifestations (scored in Criteria 3 & 4). It is assumed that 100% of illnesses estimated in Criterion 1 manifest in either acute or chronic illness. Note that this fraction will not be directly scored as a criterion in the scoring model; rather, it will be used to weight acute and chronic disease severities (Criteria 3 & 4). Therefore, the bin numbers do not go from "less important" to "more important" as do categories for other parasites.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
0%	<25% chronic	25–50% chronic	50–75% chronic	>75% chronic

Decision rule: We recognize that some portion of chronic illness may be preceded by acute infection and therefore the actual percentages may not add up to 100%. However, for this exercise, we ask you to ignore this overlap and simply focus on providing a best estimate for the fraction that is chronic.

Criterion No. 6. Mortality rate

Criterion: Case-fatality ratio

Explanation: This criterion estimates the likelihood that a given cases of illness will result in death. Mortality rate is dependent on disease symptoms and severity, as well as underlying health of the infected person.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
0%	0 –0.1%	0.1–1%	1–10%	>10%

Criterion No. 7. Increasing trend in disease

Criterion: Likelihood of a significant increase in human illness.

Explanation: This criterion reflects the potential for the human health burden associated with this particular parasite to increase in the near term, for example through changes in food production, processing and consumption.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
None	0–25% (low)	25–50% (moderate, or unsure)	75–100% (high)	100% (still increasing)

Criterion No. 8. International trade

Criterion: Relevance of the parasite and its PRIMARY food sources or vehicles to affect international trade.

Explanation: This qualitative criterion estimates the degree to which this particular parasite and its main food sources or vehicles may affect international trade. While the characteristics of the parasite or disease severity relate to trade, it is largely a function of the food source or vehicle; if the primary food-borne pathway is not widely traded, or not currently traded from a region in which the parasite is currently endemic, it may not be likely to have an impact on trade. At the same time, if the parasite is in a food product that is widely traded or if there are current issues associated with the parasite-food pathway, it is of greater relevance.

Ranges:

Bin 0	Bin 1	Bin 2
No relevance	Some relevance	High relevance

Criterion No. 9. Distributional impacts (socio-economic impact)

Criterion: Scope of impact to economically vulnerable populations

Explanation: This criterion reflects the degree to which this disease affects economically vulnerable communities, namely the extent to which this parasite causes reductions in household or community productivity, or the ability of a household or community to have access food (i.e. can produce and/or purchase food). Vulnerable communities include pastoral communities, small fishing communities, small rural communities in developing countries, migrant populations in developed countries, minority indigenous populations (Inuit in Canada, aboriginals in Australia), or other similar communities.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3
None	Low	Moderate	High
	Primarily affects individual households; affected households have reduced productive capacity or have reduced access to food	Primarily impacts individual households but also affects communities; households have reduced productive capacity or access to food; communities also have some reduced productive capacity or access to food	Affects entire communities; communities bear major losses to productive capacity and/or have seriously diminished access to food.

Criterion No. 10. Quality of evidence

Criterion: Quality of available evidence to support judgments (Not a scored criterion)

Explanation: This question reflects the extent to which you feel you were able to assess criterion-based data or information for a specific parasite.

Ranges:

Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
Very Poor	Poor	Adequate	Good	Very Good

Comments

Lastly, please indicate comments, if any, that should be considered in the discussion of risk management for this parasite food pathway

References

Havelaar, A.H., van Rosse, F., Bucura, C., Toetenel, M.A., Haagsma, J.A., Kurowicka, D., Heesterbeek, J.H., Speybroeck, N., Langelaar, M.F., van der Giessen, J.W., Cooke, R.M. & Braks, M.A. 2010. Prioritizing emerging zoonoses in the Netherlands. PLoS One, 5(11): e13965. [Online doi: 10.1371/journal.pone.0013965.]

WHO. 2004. Global burden of disease 2004 update: Disability weights for diseases and conditions. Available at http://www.who.int/healthinfo/global_burden_disease/GBD2004_DisabilityWeights.pdf Accessed 2013-07-05.

WHO. 2008. Global Burden of Disease 2004 Update. See http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_part3.pdf Accessed 2013-07-05.

Annex 4

Criteria weights worksheet

The overall parasite score is given by two equations:

$$C1*W1 + C2*W2 + C345*W345 + C6*W6 + C7*W7 + C8*W8 + C9*W9 \quad \textit{Eq. 1}$$

$$C345=\{C3*(1-C5) + C4*C5\} \quad \textit{Eq. 2}$$

where C are criteria scores normalized to a 0–1 scale and W are the criteria weights, which sum to 100%. Eq. 2 calculates the average severity weight for the parasite, an average of chronic disability weight and acute disability weight using the fraction of illnesses that are chronic. Thus, criteria 3, 4 and 5 have one associated weight, denoted as W345. Otherwise the calculation is straightforward: normalized parasite criteria scores are multiplied by fractional weights.

Criteria weights are simply the fraction of the total score reflected by the criteria in question. Therefore, if you think 25% of the overall score should be driven by C1, W1 should be marked with a 25. For comparison purposes, equal weighting of all criteria would result in a value of 14.285%.

Make sure that all numbers sum to 100%, and that no criterion weight is less than 5%. Please use integers only (no decimal points).

Criterion	Weighting Code	Criterion Weight (Fraction of Total Score)
C1. Number of global food-borne illnesses	W1	
C2. Global distribution	W2	
C3. Acute morbidity severity C4. Chronic morbidity severity C5. Chronic illness fraction	W345	
C6. Case fatality rate	W6	
C7. Increasing illness potential	W7	
C8. Trade relevance	W8	
C9. Impacts to economically vulnerable communities	W9	
SUM		100%

Annex 5

Sensitivity analysis

In addition to the results presented in the main text, a number of analyses were conducted to examine elicited scores and the sensitivity of the ranking results to different model inputs.

First, variability was examined across groups in elicited scores. Figure A5.1 shows group scores for all nine criteria, averaged over all parasites scored by each group. Because each group scored a slightly different set of parasites, the average scores are not directly comparable, but they do show some interesting patterns. Criterion 2, on the global distribution of disease of each parasite, shows consis-

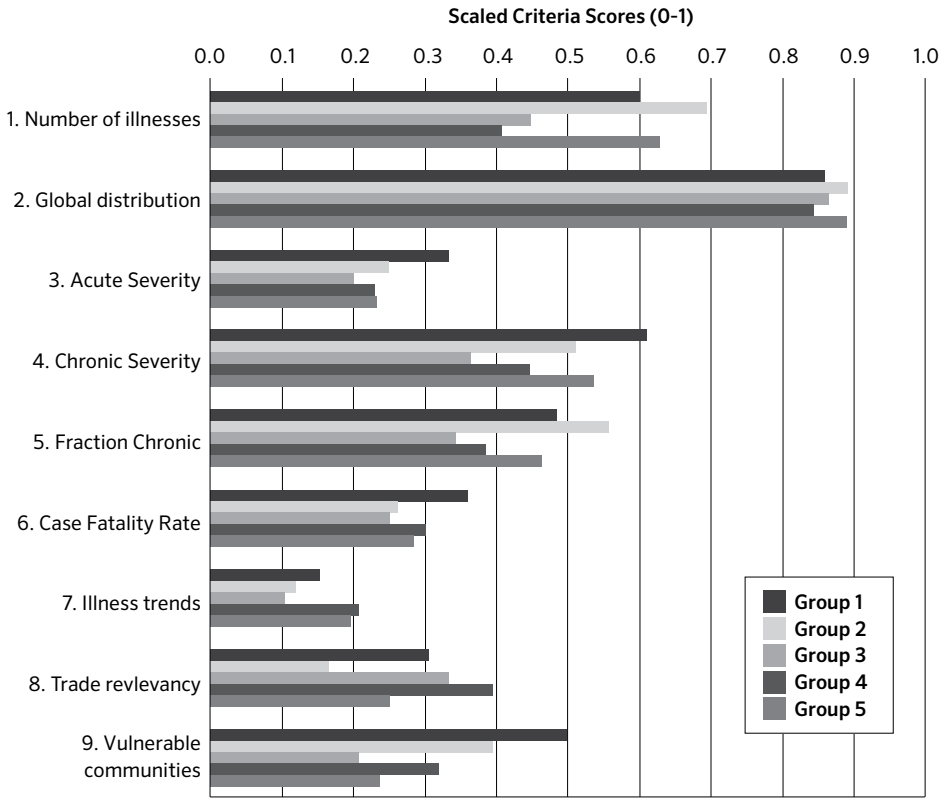


FIGURE A5.1. Group scores by criteria, averaged across parasites

tently high average scores, which suggests that experts generally agreed that the set of screened pathogens reflects parasites of global relevancy. The severity of chronic disease consistently scored higher than the severity of acute disease for this set of parasites. Overall, scores for illness trends were low, suggesting that current, endemic disease may be more of a concern than disease movement or emergence.

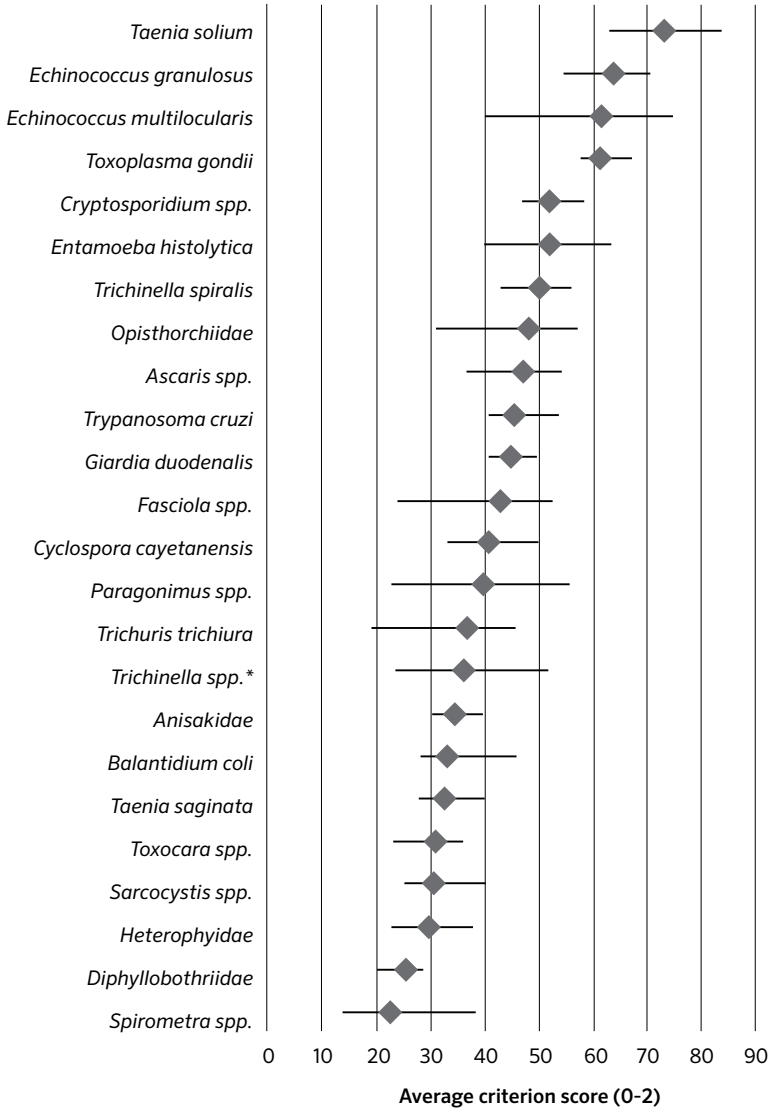


FIGURE A5.2. Means and ranges of normalized risk scores across expert groups under baseline model conditions

Just as there is variability across expert groups in average criteria scores across parasites, there is variability across groups for specific parasites. This is shown in Figure A5.2, which shows the mean normalized risk scores presented in the main text of the report, as well as the ranges of estimates across groups. Some parasites, such as *Toxoplasma gondii*, have relatively little variability across experts, while parasites such as *Echinococcus multilocularis* and *Paragonimus*, have notably larger variability. This variance can be interpreted as a signal of the strength of scientific knowledge about a given parasite: the greater the variance, the greater the uncertainty in information available to experts.

In examining sensitivity of the model itself, alternative weighting schemes were of particular interest.

In some multi-criteria decision analyses, different groups of experts are used to score the individual criteria and to develop the weights that define how criteria scores will be combined into a final risk score. That is, subject matter experts are elicited for criteria scores, while risk managers are elicited for criteria weights. In part due to time and resource constraints, weights were elicited from expert groups, as well as from the FAO/WHO Secretariat, acting as risk managers. The mean of elicited weights across all participants was used for the baseline model and ranking.

Criterion weights were roughly similar across experts and risk managers, as shown in the rounded values presented in Table A5.1. Risk managers tended to put greater weight on potential for increased illness, trade relevance and impacts to economically vulnerable communities than did experts, but all participants tended to put greater weight on public health criteria. These are compared with an equal weighting scheme, in which each criterion is treated as of equal importance in the overall risk score.

Sensitivity analyses of rankings were conducted around three alternative weighting schemes: mean of expert weights, mean of risk manager weights, and equal criteria weighting. Table A5.2 and Figure A5.3 show multicriteria risk scores (normalized to 0–100) for global foodborne parasites for the baseline and the three alternative schemes mentioned above. Although different schemes result in slightly different scores, the ranking is fairly robust among the alternative schemes.

Sensitivity analyses of rankings were conducted around three alternative weighting schemes: mean of expert weights, mean of risk manager weights, and equal criteria weighting. Table A5.2 and Figure A5.3 show multicriteria risk scores (normalized to 0–100) for global foodborne parasites for the baseline and the three alternative schemes mentioned above. Although different schemes result in slightly different scores, the ranking is fairly robust among the alternative schemes.

TABLE A5.1. Mean of elicited criteria weights used in multicriteria ranking

Scoring criterion		Weighting			
		Baseline	Expert	Secretariat	Equal
W1.	Number of global foodborne illnesses	0.22	0.24	0.20	0.14
W2.	Global distribution	0.14	0.15	0.12	0.14
W345.	Morbidity severity	0.22	0.23	0.21	0.14
W6.	Case-fatality ratio	0.15	0.16	0.15	0.14
W7.	Increasing illness potential	0.07	0.06	0.09	0.14
W8.	Trade relevance	0.10	0.06	0.13	0.14
W9.	Impacts on economically vulnerable communities	0.10	0.09	0.11	0.14

Given the similarities in expert and Secretariat scores, the biggest differences can be seen in the equal weighting scheme, though even under that scheme the ranks of the first four parasites are identical. Figure A5.4 shows how these alternativee schemes affect the rank order of parasites in the overall ranking. The dots show the baseline rank, while the vertical lines display the range of ranks across the three alternative scenarios. This figure shows that ranks are quite stable, with some parasite-specific deviation. Those with the greatest deviation in scores are *Taenia saginata* and *Cyclospora cayetanensis*, followed by *Trichinella spiralis*, *Ascaris* spp., *Paragonimus* spp., *Anisakidae* and *Toxocara* spp. Most of these are parasites with higher scores in trade relevancy or impacts on socio-economically vulnerable populations, as the equal weighting scheme increases the importance of these criteria.

TABLE A5.2. Normalized multicriteria risk scores for global foodborne parasites under alternative criteria weighting schemes

	Weighting scheme			
	Baseline	Expert	Secretariat	Equal
Taenia solium	72.9	73.1	72.7	70.7
Echinococcus granulosus	63.6	65.9	61.8	60.5
Echinococcus multilocularis	61.6	65.0	58.8	56.8
Toxoplasma gondii	61.0	64.9	57.7	53.0

Cryptosporidium spp.	51.8	54.7	49.4	46.9
Entamoeba histolytica	51.8	55.5	48.7	46.0
Trichinella spiralis	49.9	48.8	50.8	50.1
Opisthorchiidae	47.9	49.3	46.7	43.8
Ascaris spp.	47.1	50.9	43.9	40.1
Trypanosoma cruzi	45.4	46.6	44.4	40.1
Giardia duodenalis	44.7	48.0	41.9	38.5
Fasciola spp.	42.7	44.5	41.3	39.8
Cyclospora cayetanensis	40.6	40.4	40.8	41.6
Paragonimus spp.	39.5	41.9	37.5	34.2
Trichuris trichiura	36.6	39.6	34.0	32.1
Trichinella spp.*	36.0	36.6	35.5	36.4
Anisakidae	34.1	33.1	35.0	36.1
Balantidium coli	33.0	35.6	30.8	29.7
Taenia saginata	32.3	30.7	33.7	35.6
Toxocara spp.	30.8	33.7	28.4	26.2
Sarcocystis spp.	30.3	31.1	29.7	29.4
Heterophyidae	29.3	30.2	28.5	27.8
Diphyllobothriidae	25.2	25.9	24.7	24.3
Spirometra spp.	22.5	23.5	21.6	19.8

In addition to examining alternative criterion weights, alternative sets of criteria were explored. In particular, rankings were generated based on public health criteria alone. Figure A5.3 shows the result of an alternative ranking model utilizing only criteria 1–6, with equal criteria weighting (W1=W2=W345=W6=0.25). These results show greater differences than with prior exploration of weighting schemes alone, though the order is largely preserved. The removal of the other criteria resulted in a notable downward shift in rankings of parasites with trade importance, such as *Taenia solium*, *Trichinella spiralis*, *Taenia saginata*, *Cyclospora* spp. and Anisakidae. This sensitivity analysis suggests that while trade relevancy is not the primary driver underlying overall risk scores in the baseline scenario, it did exert an important influence on the final rankings.

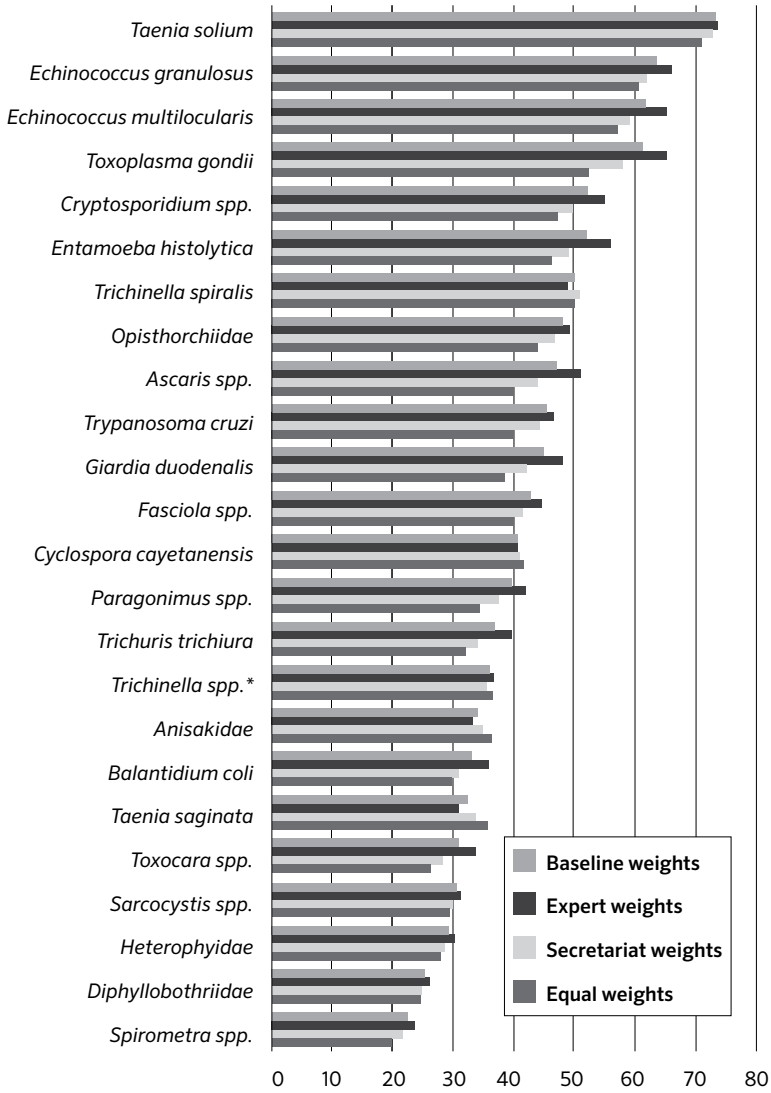


FIGURE A5.3. Comparison of multicriteria risk scores of global foodborne parasites across alternative criterion weighting schemes

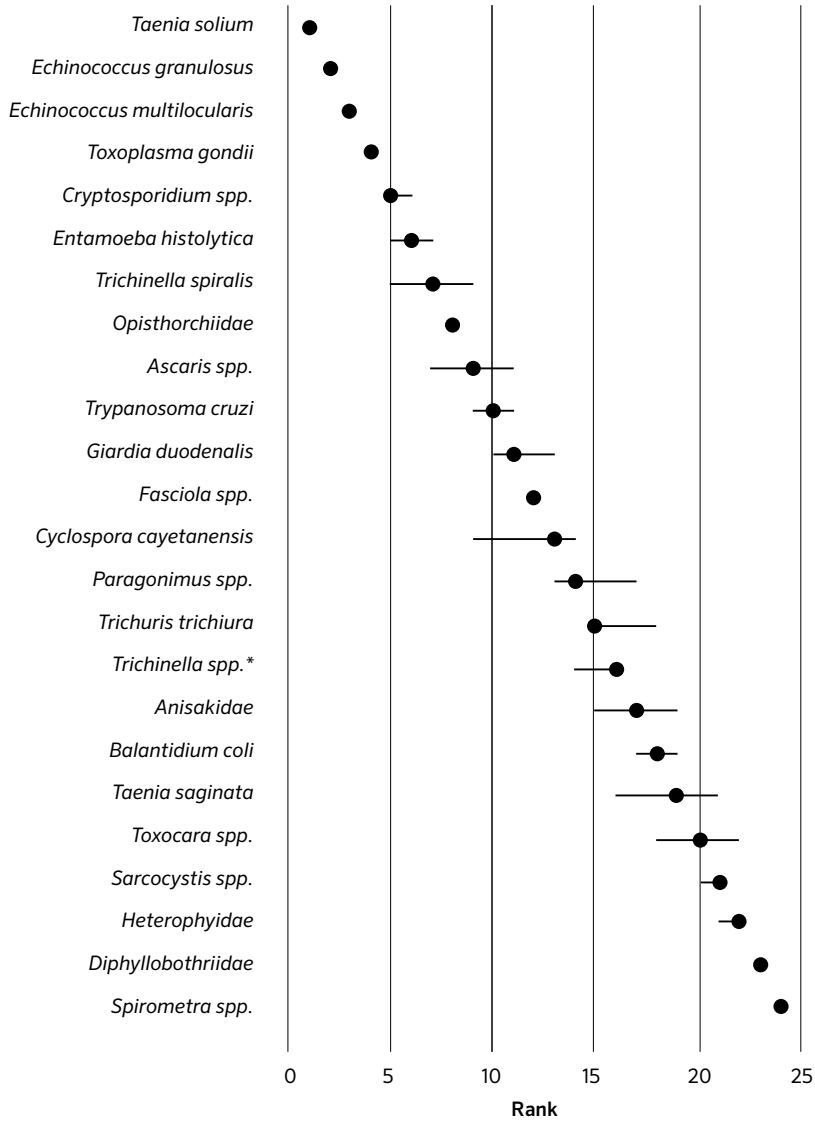


FIGURE A5.4. Rank scores of global foodborne parasites across alternative criterion weighting schemes, presented as ranges around baseline ranks

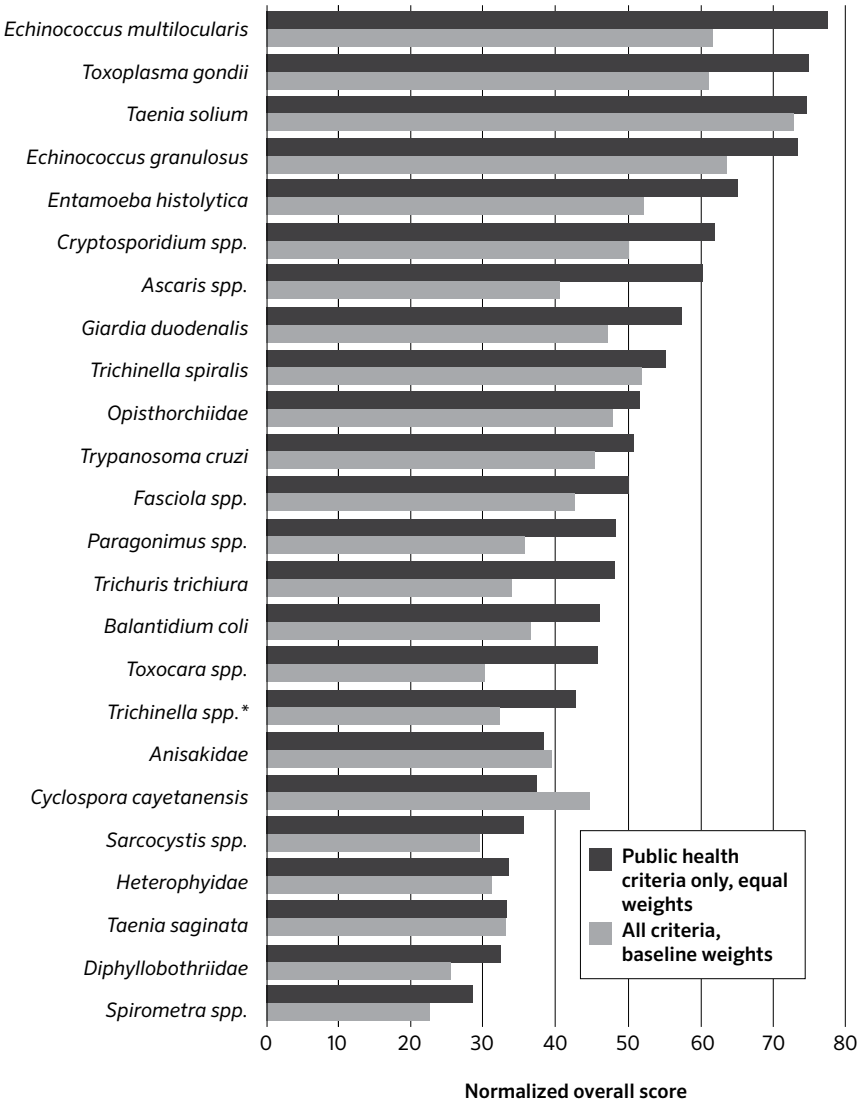


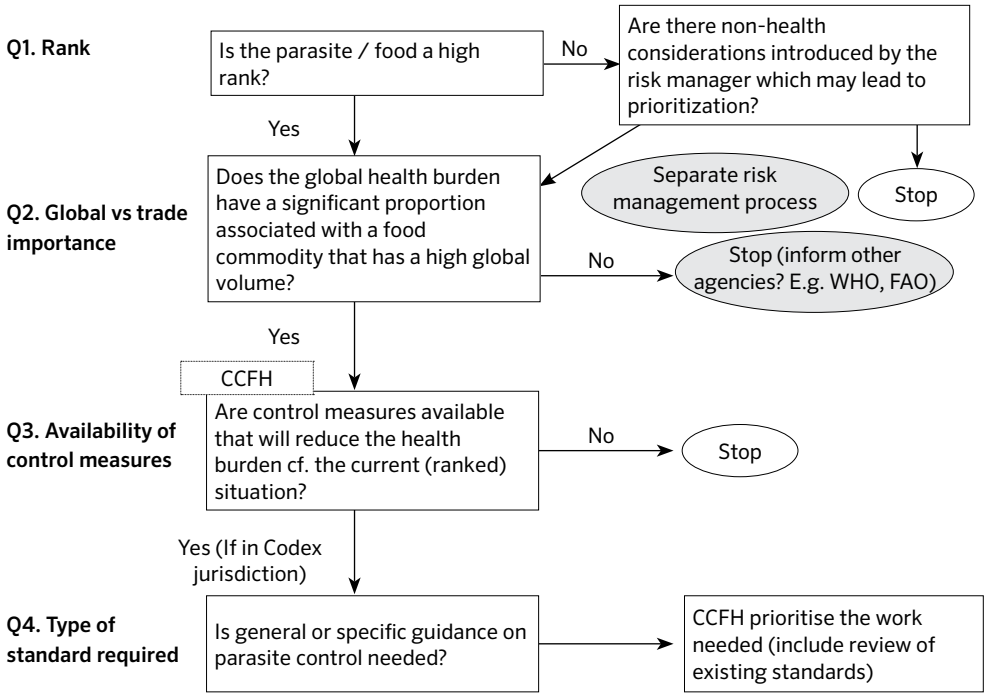
FIGURE A5.5. Multicriteria ranking of global foodborne parasites based on public health criteria only, weighted equally, compared with baseline ranking based on all criteria and elicited weightingsc

Annex 6

Risk management actions

The Codex Alimentarius Commission recognizes the requirement for a multidisciplinary inter-sectoral approach for the control of food-borne parasites, given their unique life-cycles and epidemiology as demonstrated by their efforts to work closely with OIE as well as FAO and WHO in the development of risk management guidance related to specific parasites. However, as Codex is aiming to address food-borne parasites in a more generic manner, as well as to develop specific guidance for priority hazards, following the trend towards risk-based standards and adopting a food-chain approach, Codex requested additional information from FAO and WHO to assist it in that endeavour. This report aims to provide at least some of the information required by CCFH in prioritizing its work on food-borne parasites. An example of a decision-tree approach that CCFH or other risk managers could use in the prioritization of ranked parasites and their primary vehicle of concern is presented below.

FIGURE A6.1. Decision tree for the risk management process



Annex 7

Specific information for the ranked parasites

For a Glossary of Parasitological Terms, see Annex section A7.25

After the meeting, the experts developed informative summaries for the resulting 24 ranked parasites, for use by risk managers or any interested stakeholder. A glossary was also provided by the expert group to help the reader with the terminology.

A7.1 ANISAKIDAE AND ANISAKIASIS

General information

Anisakiasis refers to infection of people with nematode larvae belonging to the nematode Family Anisakidae, and it is a serious zoonotic disease. Although there are several zoonotic species in this family, the two species most often associated with anisakiasis are *Anisakis simplex* the 'herring worm' and *Pseudoterranova decipiens*, the 'cod worm' (Chai, Murrell and Lymbery, 2005). The complex life history of *A. simplex* involves a marine intermediate host (euphasid crustacean), a paratenic host (marine fish or squid) and a definitive host (marine mammal).

Anisakiasis occurs when people ingest third-stage larvae that occur in the viscera or muscle of a wide range of marine fish and squids. Humans are accidental intermediate hosts in which the parasites rarely develop further; this invasion can cause gastrointestinal abscesses.

Geographical distribution

Anisakiasis occurs throughout the world, but is reported most frequently from Asia (especially Japan) and Western Europe, where risky food behaviour customs (i.e., eating raw, lightly cooked, or marinated fish in dishes such as sushi, salted or smoked herring, gravlax, and ceviche) are common (Lymbery and Cheah, 2007). Recent molecular genetic studies have shown that these species, *A. simplex* and *P. decipiens*, actually comprise a number of sibling species, often with distinct geographical and host ranges, or both (Mattiucci *et al.*, 2005). Within the Anisakis simplex complex are: *A. simplex* (*sensu stricto*), found in the northern Atlantic; *A. simplex* C, found in the northern Pacific and southern waters below 30°N; and

A. pegreffi, found in the Mediterranean Sea. Three species have also been described for the *Pseudoterranova decipiens* complex: *P. decipiens* A in the northeast Atlantic and Norwegian Sea, *P. decipiens* C in the northwest Atlantic and Barents Sea, and *P. decipiens* B throughout northern waters. Where the ranges of these species overlap, they appear to preferentially utilize different definitive host species.

Historically, most authors estimate there have been 15 000 to 20 000 total human cases. There has been an increase in reported prevalence throughout the world in the last two decades, probably due to better diagnostic tools, increased demand for seafood, and a growing demand for raw or lightly cooked food, although none of these factors has been rigorously evaluated. The areas of highest prevalence are Japan (after eating sushi and sashimi), and along the Pacific coast of South America (from eating ceviche, seviche or cebiche).

Disease

When humans eat infected fish harbouring live third-stage larvae, the larvae migrate to the gastrointestinal mucosa, where they die, but induce the formation of abscesses. Presumptive diagnosis in humans may be made on the basis of the patient's recent food habits (Gutierrez, 2011). Definitive diagnosis requires demonstration of worms by gastroscopy or surgery. No treatment is recommended for transient infection. In the gastrointestinal form (embedded larvae), surgery or gastroscopic procedure is also curative.

There is little information on chronic morbidity. However, the development of allergy to the parasite's allergens (even when the fish is thoroughly cooked) is now recognized. Gastroallergic anisakiasis is an acute IgE-mediated generalized reaction, manifested by urticaria and anaphylaxis, with or without accompanying gastrointestinal symptoms (Audicana and Kennedy, 2008). Occupational allergy, including asthma, conjunctivitis and contact dermatitis, has also been observed in fish-processing workers.

There is little information available on illness fraction or case fatality rates, probably because most cases are acute and treated.

Trade relevance

Anisakid infections are a trade issue because of regulations imposed by countries on imports. Many countries have regulations requiring inspection of fish for zoonotic parasites, and for inactivating any nematode larvae, etc., that may be present. Regulations and inactivation methods may differ in specifics between countries. (See EU, no date; and Chapter 5 in FDA, no date).

Impact on economically vulnerable populations

Developing countries can be affected by the necessity of taking steps to ensure fish exports are free of live anisakids. The inactivation methods described above can be expensive, and when not completely successful lead to rejection of exports by importing countries, especially fresh fish products.

References

Audicana, M.T. & Kennedy, M. 2008. *Anisakis simplex*: from obscure infectious worm to inducer of immune hypersensitivity. *Clinical Microbiology Reviews,* 21(2): 360–379.

Chai, J.Y., Murrell, K.D. & Lymbery, A.J. 2005. Fish-borne parasitic zoonoses: status and issues. *International Journal for Parasitology*, 35(11-12): 1233–1254.

EU. No date. EU import conditions for seafood and other fishery products. Web site. Available at http://ec.europa.eu/food/international/trade/im_cond_fish_en.pdf Accessed 2013-06-23.

FDA (Federal Drug Administration). No date. Chapter 5 – Parasites, in: *Fish and Fishery Products Hazards and Controls Guidance*. 4th Edition, November 2011. Available at http://www.fda.gov/downloads/Food/GuidanceRegulation/UCM252393.pdf Accessed 2013-08-24

Gutierrez, Y. 2011. Anisakidae. pp. 778–787 (Ch. 12), in: R.L. Guerrant, D.H. Walker and P.F. Weller (editors). *Tropical Infectious Diseases: Principles, Pathogens and Practice*. 3rd edition. Saunders, Philadelphia, USA.

Lymbery, A.J. & Cheah, F.Y. 2007. Anisakid nematodes and anisakiasis. pp. 185–207, in: K.D. Murrell and B. Fried (editors). *Food-borne parasitic zoonoses*. Springer, New York, USA.

Mattiucci, S., Nascetti, G., Dailey, M., Webb, S.C., Barros, N.B., Cianchi, R. & Bullini, L. 2005. Evidence for a new species of *Anisakis* Dujardin, 1845: morphological description and genetic relationships between congeners (Nematoda: Anisakidae). *Systematic Parasitology*, 61(3): 157–161.

A7.2 *ASCARIS* SPP.

General information

Ascaris lumbricoides is the large intestinal roundworm (nematode) of humans, and the infection is termed 'ascariasis' or 'ascariosis', and rarely 'ascarosis'. 'Ascariasis' is the most widely used, and will be used here. The adult worms are large (females up to 35 cm, males up to 31 cm in length), and individual worms can weigh as much as 7 or 8 g (Elkins and Haswellelkins, 1989). The adults occupy the small intestine and the female lays large numbers of eggs (estimated to be in the hundreds of thousands of eggs per day per female) (Brown and Cort, 1927; O'Lorcain and Holland, 2000). The eggs are voided in the faeces and are sticky, thick shelled and highly persistent in the environment such that they can survive for several years in soil. They contaminate water supplies following rain or flooding, vegetables either directly from soil or by irrigation, and probably the hands and clothing of agricultural workers or other people in contact with contaminated soil. The practice of using human faeces as fertilizer in subsistence farming presents a significant risk of continued transmission.

Ascaris suum is the large roundworm of pigs and is considered to be a separate species from *A. lumbricoides*. The two species are virtually indistinguishable morphologically, immunologically and biochemically, although there are some distinguishing immunological and biochemical features (e.g. Kennedy *et al.,* 1987). DNA-based surveys have indicated that *A. suum* is mostly confined to pigs, and *A. lumbricoides* to humans, but that there is evidence of cross-infections such that *A. suum* may present a significant risk to humans Peng and Criscione, 2012; Zhou *et al.,* 2012; Nejsum *et al.,* 2005). In regions endemic for both parasites it appears mostly, but not exclusively, to be the case that adult worms of *A. lumbricoides* have a host preference for humans, and adult worms of *A. suum* have a host preference for pigs (Peng and Criscione, 2012). In regions where *A. lumbricoides* does not occur in humans, there have been cases of infection with *A. suum* that have been attributed to contamination from pig farms (Nejsum *et al.,* 2005; Anderson, 1995).

In both species, infection occurs by ingestion of viable eggs, which hatch in the small intestine, releasing the infective-stage larvae of the parasite, which is in its third developmental stage (L3). The larvae then undergo a tissue migration involving the liver then the lungs. In the lungs the larvae break through to the air spaces, migrate up the trachea, are then swallowed and thereby re-introduced to the gastrointestinal tract, where they mature to adult worms in the small intestine.

The global prevalence of human ascariasis in the 1990s was estimated to be approximately 1.5 billion with 100–200 million people affected clinically, a large proportion of whom were children (reviewed in O'Lorcain and Holland (2000) and

Peng and Criscione (2012). More recent estimates are slightly lower at 1.2 billion people infected, which is largely due to China's large-scale treatment programmes (reviewed in O'Lorcain and Holland (2000) and Peng and Criscione (2012)), but some estimates remain as high as 2 billion people currently infected.

Geographical distribution

The distribution of both species of *Ascaris* is essentially global, but with low prevalences in countries with well-developed sanitation systems, and very high prevalences in regions with poor sanitation. The greater association with tropical and subtropical countries may merely be because many of these have poorer overall sanitation systems and parasite control programmes, and the viability and development to infectivity of eggs is favoured under warm, moist conditions. Exposure of humans to eggs of *A. suum* will be less likely in regions where pigs are not farmed.

Disease

Ascariasis in humans presents mainly in the gut (small intestine and ileum) and the lungs, though larval migration through the liver and peritoneum likely also cause damage (O'Lorcain and Holland, 2000). In the gut, the worms can occur in such numbers that blockage and rupture or perforation can occur in extreme cases. The parasites have also been known to cause death by migrating into and blocking the pancreatic or bile ducts. The worms in the gut can cause malabsorption and anorexia, which will contribute to malnutrition (O'Lorcain and Holland, 2000). The malabsorption may be due to a loss of brush border enzymes, erosion and flattening of the villi, and inflammation of the lamina propria, and premature cessation of lactase production has also been intimated (O'Lorcain and Holland, 2000). Migration of larvae through the lungs can cause severe immune hypersensitivity responses (Loeffler's Syndrome) that may be life-threatening. This appears to be more common in arid areas when periodic rains mobilise dormant *Ascaris* eggs from soil and other sources such as latrines, resulting in a high level of contamination of water and food supplies. It is highly likely that severe pulmonary reactions can be caused by exposure to the eggs of either *A. lumbricoides* or *A. suum* (as is known in sheep and cattle from exposure to *A. suum* eggs, and in experimentally infected animals such as rats, mice and rabbits, the larvae of either species reach the lungs). Infection with adult *Ascaris* can be detected by observation of eggs in faeces, although this requires the presence of a reproductive female. *A. suum* infections of humans in developed countries is often with single or low numbers of worms. Loeffler's Syndrome can be detected by X-ray appearance of shadows on the lungs (Loeffler, 1956), and detection of larvae and eosinophils in sputum or throat swabs. A characteristic feature of infection with parasitic worms is high levels of IgE antibody and eosinophils in blood, and eosinophils and mast cells in infected tissues; there is evidence that allergic-type immune responses may be part

of the protective response to Ascaris (McSharry *et al.,* 1999). Important allergens have been described from *Ascaris*. See O'Lorcain and Holland (2000) for further detail on ascariasis disease symptoms and other effects.

Trade relevance

Contamination of fresh produce with Ascaris eggs has not been an issue in trade up to now. The main risk here is through fresh vegetables that have been contaminated with eggs directly from the soil in which they were grown, or the water with which they were irrigated or treated and prepared post-harvest. Trade in pigs can clearly also be a source of infection to new areas. The robustness of Ascaris eggs means that they can survive for long periods during transport, and they can survive low temperatures, including freezing to some degree, desiccation and chemical attack, though not cooking. Once soil is contaminated with viable eggs, it can remain so for up to a decade.

Impact on economically vulnerable populations

The potential impact of ascariasis is chronic and insidious for communities, and can be severe and even life-threatening for individuals. In addition to the overt disease symptoms due to A. lumbricoides infection detailed above, there is evidence that chronic infection can affect the growth rate and final height, of children, and their cognitive development (reviewed in O'Lorcain and Holland, 2000, and Bundy, Walson and Watkins, 2013), which is likely to be particularly so in double or multiple infections with other species of worm parasites. In regions where pigs are kept, the risks of intestinal infection with adult A. suum may be low, but migratory larvae will still cause damage to liver and lungs, and it is likely that the risk of Loeffler's Syndrome will be similar with either species of Ascaris. Lamentably little research has been carried out on the prevalence, morbidity and mortality due to Loeffler's Syndrome or less acute but chronic, repetitive damage to the lungs, in humans infected with either parasite. This paucity of information on the pulmonary stage of infection is particularly unfortunate given the possibility that lung damage could exacerbate lung infections and consequent mortality in children (O'Lorcain and Holland, 2000).

Other relevant information

Drugs for the treatment for the intestinal stage of ascariasis are cheap, readily available and relatively free of side-effects. Treatments for the tissue migratory phases would be rare, partly because of the difficulty of diagnosis, and possibly also the risk of causing deleterious reactions to dead larvae in liver, lungs or elsewhere (O'Lorcain and Holland, 2000). There are no vaccines available against ascariasis. There continues to be a debate about whether infection with Ascaris or other helminth parasites increases or decreases the risk of allergic reactions to environmental allergens (Pinelli *et al*., 2009).

References

General sources

Holland, C.V. (Editor). 2013. *Ascaris: The Neglected Parasite.* CABI Publishing, Wallingford, Oxfordshire, UK, and Cambridge, MA, USA.

Specific sources cited

Anderson, T.J.C. 1995. Ascaris infections in humans from North America – molecular evidence for cross-infection. *Parasitology*, 110: 215–219.

Brown, H.W. & Cort, W.W. 1927. The egg production of Ascaris lumbricoides. *Journal of Parasitology*, 14: 88–90.

Bundy, D.A.P., Walson, J.L. & Watkins, K.L. 2013. Worms, wisdom, and wealth: why deworming can make economic sense. *Trends in Parasitology*, 29: 142–148.

Elkins, D.B. & Haswellelkins, M. 1989. The weight-length profiles of *Ascaris lumbricoides* within a human community before mass treatment and following re-infection. *Parasitology*, 99: 293–299.

Kennedy, M.W., Qureshi, F., Haswellelkins, M. & Elkins, D.B. 1987. Homology and heterology between the secreted antigens of the parasitic larval stages of *Ascaris lumbricoides* and *Ascaris suum*. *Clinical and Experimental Immunology,* 67: 20–30.

Loeffler, W. 1956. Transient lung infiltrations with blood eosinophilia. *International Archives of Allergy and Applied Immunology,* 8: 54–59.

McSharry, C., Xia, Y., Holland, C.V. & Kennedy, M.W. 1999. Natural immunity to *Ascaris lumbricoides* associated with immunoglobulin E antibody to ABA-1 allergen and inflammation indicators in children. *Infection and Immunity*, 67: 484–489.

Nejsum, P., Parker, E.D. Jr, Frydenberg, J., Roepstorff, A., Boes, J., Haque, R., Astrup, I., Prag, J. & Skov Sørensen, U.B. 2005. Ascariasis is a zoonosis in Denmark. *Journal of Clinical Microbiology,* 43(3): 1142–1148.

O'Lorcain, P. & Holland, C.V. 2000. The public health importance of *Acaris lumbricoides*. *Parasitology*, 121: S51–S71.

Peng, W. & Criscione, C.D. 2012. Ascariasis in people and pigs: new inferences from DNA analysis of worm populations. *Infection Genetics and Evolution,* 12: 227–235.

Pinelli, E., Willers, S.M., Hoek, D., Smit, H.A., Kortbeek, L.M., Hoekstra, M., de Jongste, J., van Knapen, F., Postma, D., Kerkhof, M., Aalberse, R., van der Giessen, J.W. & Brunekreef, B. 2009 Prevalence of antibodies against *Ascaris suum* and its association with allergic manifestations in 4-year-old children in The Netherlands: the PIAMA birth cohort study. *European Journal of Clinical Microbiology & Infectious Diseases*, 28(11): 1327–1334.

Zhou, C., Li, M., Yuan, K., Deng, S. & Peng, W. 2012. Pig *Ascaris*: an important source of human ascariasis in China. *Infection Genetics and Evolution*, 12: 1172–1177.

A7.3 *BALANTIDIUM COLI*

General information

Balantidium coli is a protozoan parasitic species that causes the disease balantidiasis (CDC, no date; Anon., 2003). It is the only member of the ciliate phylum known to be pathogenic to humans (CDC, no date; Anon., 2003a). Infection occurs when the cysts are ingested, usually through contaminated food or water. This parasite lives in the caecum and colon of humans. *B. coli* has two developmental stages, a trophozoite stage and a cyst stage. Trophozoites multiply and encyst due to the dehydration of faeces. It can thrive in the gastrointestinal tract as long as there is a balance between the protozoan and the host without causing dysenteric symptoms. Infection most likely occurs in people with malnutrition due to the low stomach acidity or people with immune compromised systems (Anon., 2003b; Schuster and Ramirez-Avila, 2008).

Geographical distribution

The disease is considered to be rare and occurs in less than 1% of the human population. Most infections occur in developing countries where faeces are more likely to get in contact with food and drinking water. In addition to humans, pigs and other animals carry the disease. People who raise pigs have a greater risk of getting infected with balantidiasis. Co-infections with other parasites are likely to aggravate the damage wrought by each individual parasite, and they probably share common sources of infection (i.e. contaminated water) (Roberts and Janovy, 2009).

Balantidiasis in humans is common in the Philippines, but it can be found anywhere in the world, especially among those that are in close contact with swine. It has been noted in Latin America, Bolivia, Southeast Asia and New Guinea.

Disease

Common symptoms of balantidiasis include chronic diarrhoea, occasional dysentery (diarrhoea with passage of blood or mucus), nausea, foul breath, colitis (inflammation of the colon), abdominal pain, weight loss, deep intestinal ulcerations, and possibly perforation of the intestine. Fulminating acute balantidiasis is when the disease comes very suddenly and with great intensity. Haemorrhaging can occur, which can lead to shock and death. Untreated fulminating acute balantidiasis is reported to have a fatality rate of 30%. In acute disease, explosive diarrhoea may occur as often as every twenty minutes. Perforation of the colon may also occur in acute infections which can lead to life-threatening situations. If balantidiasis is not treated the persistent diarrhoea leads to high fluid loss and dehydration. If abdominal bleeding occurs, it can lead to death (Schuster and Ramirez-Avila, 2008).

Trade relevance

There have not yet been significant trade issues with respect to findings of *B. coli* in foods, but with the increasing number of surveillance studies reporting positive results worldwide, and the growing number of produce-associated illness outbreaks, more trade issues resulting in import restrictions and recalls may occur in the future. *B. coli* causes reduced production performance in the animals affected, which has an impact on the economy, both locally for farmers and nationally for the country (Roberts and Janovy, 2009).

Impact on economically vulnerable populations

The disease is a problem primarily in developing countries, where water sources may be contaminated with swine or human faeces. Balantidiasis infections can be prevented by following appropriate hygiene practices (such as not using human faeces as fertilizer in agriculture; washing hands after going to the toilet and before meals; washing vegetables; and cooking meat properly). Infective *B. coli* cysts are killed by heat (Schuster and Ramirez-Avila, 2008).

References

Anon[ymous]. 2003a. The Parasite: *Balantidium coli*. The Disease: Balantidiasis. Introduction. Web site prepared by A. Ramachandran. Last updated 2003-05-23; accessed 2013-06-18. Online at http://www.stanford.edu/group/parasites/ParaSites2003/Balantidium/Balantidium_coli_ParaSite.htm.

Anon. 2003b. The Parasite: *Balantidium coli*. The Disease: Balantidiasis. Morphology. Web site prepared by A. Ramachandran. Last updated 2003-05-23; accessed 2013-06-18. Online at http://www.stanford.edu/group/parasites/ParaSites2003/Balantidium/Morphology.htm

CDC (Centres for Disease Control and Prevention). No date. Parasites and Health: Balantidiasis [Balantidium coli]. Online. See: http://www.dpd.cdc.gov/dpdx/HTML/Balantidiasis.htm Accessed 2013-06-18.

Schuster, F.L. & Ramirez-Avila, L. 2008. Current world status of *Balantidium coli*. *Clinical Microbiology Review*, 21(4): 626–638.

Roberts, L.S. & Janovy, J. Jr. 2009. *Foundations of Parasitology*. 8th Edition. McGraw-Hill, New York, USA.

A7.4 *CRYPTOSPORIDIUM* SPP.

General information

Cryptosporidium spp. are protozoan parasites reported worldwide in a large number of different hosts, including humans. The infectious stages of *Cryptosporidium* spp., known as oocysts, are shed with the faeces of the host and can survive for long periods under cool and moist conditions.

Routes of transmission include waterborne, person-to-person, zoonotic and food-borne. The waterborne route is numerically the most important means of transmission of cryptosporidiosis. Numerous waterborne outbreaks of cryptosporidiosis have occurred worldwide as a result of oocyst contamination of drinking water sources and recreational water. The largest waterborne illness outbreak of any kind in the United States of America occurred in the spring of 1993, when an estimated 403 000 people became ill with cryptosporidiosis in Milwaukee, Wisconsin. Food-borne transmission of cryptosporidiosis is thought to be much less common than waterborne or person-to-person transmission; about 8% of domestically acquired cases in the United States of America are food-borne (Scallan *et al.,* 2011). It is, however, emerging as an important public health issue.

Food-borne outbreaks of cryptosporidiosis associated with the consumption of fresh produce have been reported mainly in the United States of America and in northern Europe (Dixon *et al.,* 2011; Robertson and Chalmers, 2013). The foods implicated in these outbreaks have included green onions, sandwich-bar ingredients, parsley, carrots, red peppers, and lettuce. In some cases these outbreaks were attributed to infected food-handlers. A large outbreak affecting approximately 300 people occurred in the UK in 2012 and was associated with the consumption of pre-cut bagged salad products (HPA, 2013). There have also been four cryptosporidiosis outbreaks associated with drinking unpasteurized apple cider, all in the United States of America. Unpasteurized milk has been associated with outbreaks of cryptosporidiosis in Australia and the UK. Chicken salad was implicated in an outbreak in the United States of America and may have been contaminated by a food worker who also operated a daycare facility.

Numerous surveys performed worldwide have reported the presence of *Cryptosporidium* oocysts on a wide variety of fresh produce items (Dixon *et al.,* 2013). *Cryptosporidium* oocysts have also been reported worldwide in the gills and tissues of oysters and other molluscan shellfish, including clams, cockles and mussels (Fayer, Dubey and Lindsay, 2004).

Control measures to reduce the likelihood of contamination of produce at the pre-harvest stage with *Cryptosporidium* include the use of good quality water for irrigation, mixing of pesticides, or washing and processing; restricting access of livestock and other animals to crop lands and surface waters; monitoring the health of farm workers and encouraging good hygiene; and using only composted manure as fertilizer. Post-harvest control measures include the use of good quality water for washing and processing produce; monitoring and enforcing good personal hygiene in food handlers; prevention of cross-contamination; and the incorporation of HACCP plans. At the consumer level, good hygiene and avoidance of cross-contamination are again important control measures. Thorough washing of fresh produce is recommended, but probably will not be fully effective in removing all contaminating oocysts. Although oocysts are somewhat resistant to freezing, they can be inactivated by storing produce at -20°C for >24 hours, or at -15°C for at least a week. Alternatively, oocysts will be readily destroyed in foods that are subsequently cooked.

Geographical distribution

In recent years, human infection with *Cryptosporidium* spp. has emerged as a global public health problem. Prevalence, however, is very difficult to determine as data is not available from many countries. In one estimate, the prevalence of *Cryptosporidium* in patients with gastroenteritis was 1–4% in Europe and North America, and 3–20% in Africa, Asia, Australia, and South and Central America (Current and Garcia, 1991). Laberge and Griffiths (1996) estimated that the prevalence rates based on oocyst excretion were 1–3% in industrialized countries, and up to 10% in developing countries. Cryptosporidiosis has been reported in 106 countries worldwide (Fayer, 2008).

Approximately twelve species of *Cryptosporidium*, and several genotypes, have been reported in humans. However, 90% of reported human infections involve *C. hominis*, which is found primarily in humans, and *C. parvum*, which is an important zoonotic species. *C. hominis* is thought to account for more human cases than *C. parvum* in North America, Australia, Asia, sub-Saharan Africa and some parts of Europe. Generally speaking, *C. parvum* is more prevalent in rural or agricultural regions, probably as a result of zoonotic transmission. In recent years, *C. meleagridis* has been reported more commonly in humans. For example, Cama *et al.* (2008) reported a relatively high prevalence of infection with *C. meleagridis* in children in Peru. Similarly, *C. cuniculus* was found to be the third most commonly identified species, after *C. parvum* and *C. hominis,* in sporadic cases of cryptosporidiosis in the UK (Chalmers *et al.,* 2011). Several other *Cryptosporidium* species and genotypes are only occasionally found in humans (Xiao, 2010).

Disease

Cryptosporidiosis is an enteric disease which is self-limiting in immunocompetent individuals. The disease is characterized by watery diarrhoea and a variety of other symptoms, including, abdominal pain, weight loss, nausea, vomiting, fever and malaise (Chalmers and Davies, 2010). Symptoms in some immunocompromised patients become chronic, debilitating and potentially life-threatening. Cryptosporidiosis accounts for up to 6% of all reported diarrhoeal illnesses in immunocompetent persons (Chen *et al.,* 2002). Twenty-four percent of AIDS patients with diarrhoea are infected with *Cryptosporidium* spp. (Guerrant, 1997). In the United States of America, Scallan *et al*. (2011) reported a hospitalization rate of 25%, and a death rate of 0.3%, in laboratory-confirmed cases of cryptosporidiosis. In addition to the patients' immune status, there is some evidence that clinical manifestations of cryptosporidiosis may also be partially dependent upon the species of *Cryptosporidium* involved in the infection. With the exception of Nitazoxanide, which is approved in the United States of America for treating diarrhoea caused by *Cryptosporidium* in immunocompetent patients, drug development has been largely unsuccessful against cryptosporidiosis.

Trade relevance

There have not yet been significant trade issues with respect to the finding of *Cryptosporidium* oocysts in foods, but with the increasing number of surveillance studies reporting positive results in a wide variety of foods worldwide, and the growing number of produce-associated illness outbreaks, more trade issues resulting in import restrictions and recalls may occur in the future. As has already been seen with respect to *Cyclospora cayetanensis* in fresh berries, these actions could have significant impacts on the agricultural industry and the economy of developing countries that produce and export fresh produce. An ISO international standard for the detection and enumeration of *Cryptosporidium* and *Giardia* in fresh leafy green vegetables and berry fruits is currently being drafted and may have implications for trade in future as more standardized food testing is done.

Impact on economically vulnerable populations

Along with giardiasis, cryptosporidiosis was included in the WHO Neglected Diseases Initiative in 2004. Diseases included in this initiative "occur mainly in developing countries where climate, poverty and lack of access to services influence outcomes", and where they "impair the ability of those infected to achieve their full potential, both developmentally and socio-economically" (Savioli, Smith and Thompson, 2006). As such, cryptosporidiosis in particular may have considerable negative impacts on economically vulnerable populations.

References

Cama, V.A., Bern, C., Roberts, J., Cabrera, L., Sterling, C.R., Ortega, Y., Gilman, R.H. & Xiao, L. 2008. *Cryptosporidium* species and subtypes and clinical manifestations in children, Peru. *Emerging Infectious Diseases*, 14: 1567–1574.

Chalmers, R. M. & Davies, A.P. 2010. Minireview: clinical cryptosporidiosis. *Experimental Parasitology*, 124: 138–146.

Chalmers, R.M., Elwin, K., Hadfield, S.J. & Robinson, G. 2011. Sporadic human cryptosporidiosis caused by *Cryptosporidium cuniculus*, United Kingdom, 2007–2008. *Emerging Infectious Diseases*, 17: 536–538.

Chen, X.M., Keithly, J.S., Paya, C.V. & LaRusso, N.F. 2002. Cryptosporidiosis. *New England Journal of Medicine*, 346: 1723–1731.

Current, W.L. & Garcia, L.S. 1991. Cryptosporidiosis. *Clinical Microbiology Reviews*, 4: 325–358.

Dixon, B.R., Fayer, R., Santin, M., Hill, D.E. & Dubey, J.P. 2011. Protozoan parasites: *Cryptosporidium, Giardia, Cyclospora* and *Toxoplasma*. pp. 349–370, in: J. Hoorfar (editor). *Rapid detection, characterization and enumeration of food-borne pathogens.* ASM Press, Washington D.C., USA.

Dixon, B., Parrington, L., Cook, A., Pollari, F. & Farber, J. 2013. Detection of *Cyclospora, Cryptosporidium* and *Giardia* in ready-to-eat packaged leafy greens in Ontario. *Canada. Journal of Food Protection*, 76: 307–313.

Fayer, R. 2008. Biology. pp. 1–42, in: R. Fayer and L. Xiao (editors). *Cryptosporidium and Cryptosporidiosis.* 2nd edition. CRC Press and IWA Publishing, Boca Raton, FL, USA.

Fayer, R., Dubey, J.P. & Lindsay, D.S. 2004. Zoonotic protozoa: from land to sea. *Trends in Parasitology*, 20: 531–536.

Guerrant, R.L. 1997. Cryptosporidiosis: an emerging, highly infectious threat. *Emerging Infectious Diseases*, 3: 51–57.

HPA (Health Protection Agency). 2012. Investigation into an outbreak of *Cryptosporidium* infection in spring 2012. Online HPA Press Release 2013-03-19. See: http://www.hpa.org.uk/NewsCentre/ NationalPressReleases/2013PressReleases/130319Investigationintoanoutbreakofcryptosporidium/ Accessed 2013-06-18.

Laberge, I. & Griffiths, M.W. 1996. Prevalence, detection and control of *Cryptosporidium* in food. *International Journal of Food Microbiology*, 32: 1–26.

Robertson, L.J. & Chalmers, R.M. 2013. Food-borne cryptosporidiosis: is there really more in Nordic countries? *Trends in Parasitology*, 29: 3–9.

Savioli, L., Smith, H. & Thompson, A. 2006. *Giardia* and *Cryptosporidium* join the "Neglected Diseases Initiative". *Trends in Parasitology*, 22: 203–208.

Scallan, E., Hoekstra, R.M., Angulo, F.J., Tauxe, R.V., Widdowson, M.A., Roy, S.L., Jones, J.L. & Griffin, P.M. 2011. Food-borne illness acquired in the United States – major pathogens. *Emerging Infectious Diseases,* 17(1): 7–15.

Xiao, L. 2010. Molecular epidemiology of cryptosporidiosis: an update. *Experimental Parasitology*, 124: 80–89.

A7.5 *CYCLOSPORA CAYETANENSIS*

General information

Cyclospora cayetanensis is a coccidian parasite that can be acquired by ingestion of contaminated raw produce (vegetables, herbs and fruits) and possibly drinking water. Sporulated oocysts excyst in the gastrointestinal tract and invade the epithelial cells of the small intestine, where asexual and sexual multiplication occurs. Unsporulated oocysts are formed and excreted in the faeces of the infected individual. It takes 7–15 days under ideal environmental conditions for these oocysts to sporulate and become infectious. Oocysts measure 8–10 µm in diameter and autofluoresce when exposed to UV light. Sporulated oocysts consist of two sporocysts, each containing two sporozoites. *C. cayetanensis* seems to be specifically anthroponotic. A few reports described *Cyclospora* oocysts in the faeces of dogs, ducks and chickens, but unsuccessful experimental infections and lack of histopathological evidence of infection do not support the availability of an intermediate or definitive host other than human (Ortega and Sanchez, 2010) and these undoubtedly represented spurious passage of oocysts. In the past decade, other *Cyclospora* species have been described in non-human primates, but molecular information has confirmed that these species are not *C. cayetanensis* (Eberhard *et al.,* 1999).

In the United States of America, it is estimated that annually the mean number of episodes of gastroenteritis caused by *Cyclospora* is 11 407 (CI: 137–37 673) with a 6.5% hospitalization rate (Scallan *et al.,* 2011). To date, no deaths have been reported due to *Cyclospora* infections and there is no evidence that *Cyclospora* is endemic in the United States of America.

Waterborne transmission can occur (Rabold *et al.*, 1994). Oocysts have been identified in water used for human consumption in various studies; however, foodborne transmission has been reported more frequently and has been linked to lettuce, basil, snow peas and berries (blackberries and raspberries) (Shields and Olson, 2003) that were consumed raw, and frequently associated with social events. In 1996, 1465 cases of cyclosporiasis, associated with consumption of Guatemalan raspberries, were reported in the United States of America and Canada. In 1997, 1012 more cases were reported associated with the consumption of Guatemalan raspberries, and 342 cases implicated contaminated basil. In 1998, raspberry importations were not permitted into the United States of America whereas importation into Canada continued. That year, 315 cases of cyclosporiasis were reported in Canada, again implicating raspberries imported from Guatemala (Herwaldt, 2000). Since then, Cyclospora cases have been reported in the United States of America every year, and in most instances no specific food commodity has been associated with those outbreaks. Outbreaks of *Cyclospora* have also been reported in

Europe (Doller *et al*., 2002). In most instances, reports from Europe describe cases associated with travel to endemic areas (Cann *et al*., 2000; Clarke and McIntyre, 1996; Green *et al*., 2000). In December 2000, 34 persons acquired cyclosporiasis in Germany. The food items implicated as a result of the epidemiological investigation (butterhead lettuce (from Southern France), mixed lettuce (from Bari, Italy), and chives (from Germany)) were not available for microbiological examination (Doller *et al*., 2002).

Geographical distribution

Cyclospora has been reported to be endemic in China, Cuba, Guatemala, Haiti, India, Mexico, Nepal, Peru and Turkey. Other reports from travellers suggest that *Cyclospora* could also be endemic in other tropical regions, including Bali, Dominican Republic, Honduras, Indonesia, Papua New Guinea and Thailand (Ortega and Sanchez, 2010). The prevalence of *Cyclospora* in these regions has changed as the socio-economic conditions of the populations have changed. There are reports of infection in parts of Africa, but the absence of infection has been noted in many studies that looked specifically for it, and further study and confirmation of the distribution of the organisms in this part of the world is required.

Disease

Cyclosporiasis is characterized by watery diarrhoea, nausea, abdominal pain and anorexia. Low-grade fever, flatulence, fatigue and weight loss have also been reported. Biliary disease, Guillain-Barrè Syndrome and Reiter's Syndrome have been reported to follow *Cyclospora* infections (Ortega and Sanchez, 2010).

The severity of illness is higher in children, the elderly, and immunocompromised individuals. Symptomatic cyclosporiasis is common in naïve (non-endemic) populations. Illness usually lasts 7–15 days, but in immunocompromised and a few immunocompetent individuals it can last up to 3 months (Bern *et al.,* 2002). Recurrence has been reported in HIV patients. The drug of choice to control infection is trimethoprim sulfamethoxazole, but in patients who are allergic to sulfa, ciprofloxacin has been used as an alternative treatment. If not treated, the host's immune response should eventually control the infection (Pape *et al.,* 1994).

In endemic areas, children under 10 years frequently acquire the infection, and as they grow and have repeated exposures, infections can be less symptomatic and of shorter duration (Bern *et al.,* 2000, 2002; Hoge *et al.,* 1995; Ortega *et al.,* 1993). The environmental conditions that favour *Cyclospora* endemicity are not fully elucidated, nor are the conditions that allow for a marked seasonality characteristic in locations where *Cyclospora* is endemic (Lopez *et al.,* 2003; Madico *et al.,* 1997; Schlim *et al.,* 1999).

Trade relevance and impact on economically vulnerable populations

Cyclospora has affected international trade and susceptible populations. This was very evident during the 1995–1997 outbreaks in the United States of America. Importation of berries (Herwaldt, 2000), particularly raspberries, was affected, causing significant financial losses to the producers, exporters and importers. In 1996, United States of America strawberry growers were affected as it was assumed that cases of cyclosporiasis were linked with California strawberries. The California Strawberry Commission estimated that this false assumption led to US$ 16 million in lost revenue to the growers in California during the month of June in that year. Later it was determined that these outbreaks were associated with the consumption of imported Guatemalan raspberries (Herwaldt *et al.,* 1997). In 1996, before the *Cyclospora* outbreaks occurred, the number of raspberry growers in Guatemala was estimated to be 85. By 2002, only 3 remained. For many growers the decision to leave the industry was based on losses due to the lack of foreign demand of their berries and export markets closures (Calvin, Flores and Foster, 2003). The losses resulting from these outbreaks were significant not only financially but also for the reputation of the Guatemalan berry industry and the communities involved.

The global burden and prevalence of this parasite worldwide need to be considered. Its effect in global trade has been notorious in commodities imported from endemic areas. However, effects on the economy and health of the population in endemic countries, where exports are not an element of consideration in terms of outbreaks in developed countries, need to be further studied.

References

Bern, C., Hernandez, B., Lopez, M.B., Arrowood, M.J., De Merida, A.M. & Klein, R.E. 2000. The contrasting epidemiology of *Cyclospora* and *Cryptosporidium* among outpatients in Guatemala. *American Journal of Tropical Medicine and Hygiene*, 63: 231–235.

Bern, C., Ortega, Y., Checkley, W., Roberts, J.M., Lescano, A.G., Cabrera, L., Verastegui, M., Black, R.E., Sterling, C. & Gilman, R.H. 2002. Epidemiologic differences between cyclosporiasis and cryptosporidiosis in Peruvian children. *Emerging Infectious Diseases*, 8: 581–585.

Calvin, L., Flores, L. & Foster, W. 2003. Case Study: Guatemalan raspberries and *Cyclospora*. Food Safety in Food Security and Food Trade series, Focus 10, Brief 7. Part of the 2020 Vision For Food, Agriculture, and the Environment programme. IFPRI, Washington DC, USA. See http://www.ifpri.org/sites/default/files/publications/focus10_07.pdf Accessed 2013-06-18.

Cann, K.J., Chalmers, R.M., Nichols, G. & O'Brien, S.J. 2000. *Cyclospora* infections in England and Wales: 1993 to 1998. *Communicable Diseases and Public Health,* 3: 46–49.

Clarke, S.C. & McIntyre, M. 1996. The incidence of *Cyclospora cayetanensis* in stool samples submitted to a district general hospital. *Epidemiology & Infection*, 117: 189–193.

Doller, P.C., Dietrich, K., Filipp, N., Brockmann, S., Dreweck, C., Vonthein, R., Wagner-Wiening, C. & Wiedenmann, A. 2002. Cyclosporiasis outbreak in Germany associated with the consumption of salad. *Emerging Infectious Diseases*, 8: 992–994.

Eberhard, M.L., da Silva, A.J., Lilley, B.G. & Pieniazek, N.J. 1999. Morphologic and molecular characterization of new *Cyclospora* species from Ethiopian monkeys: *C. cercopitheci* sp.n., *C. colobi* sp.n., and *C. papionis* sp.n. *Emerging Infectious Diseases*, 5: 651–658.

Green, S. T., McKendrick, M.W., Mohsen, A.H., Schmid, M.L. & Prakasam, S.F. 2000. Two simultaneous cases of *Cyclospora cayatensis* enteritis returning from the Dominican Republic. *Journal of Travel Medicine,* 7(1): 41–42.

Herwaldt, B.L. 2000. *Cyclospora cayetanensis*: a review, focusing on the outbreaks of cyclosporiasis in the 1990s. *Clinical Infectious Diseases*, 31(4): 1040–1057.

Herwaldt, B.L., Ackers, M.L. and 52 others [The Cyclospora Working Group]. 1997. An outbreak in 1996 of cyclosporiasis associated with imported raspberries. *New England Journal of Medicine*, 336(22): 1548–1556.

Hoge, C.W., Echeverria, P., Rajah, R., Jacobs, J., Malthouse, S., Chapman, E., Jimenez, L.M. & Shlim, D.R. 1995. Prevalence of *Cyclospora* species and other enteric pathogens among children less than 5 years of age in Nepal. *Journal of Clinical Microbiology*, 33: 3058–3060.

Lopez, A.S., Bendik, J.M., Alliance, J.Y., Roberts, J.M., da Silva, A.J., Moura, I.N., Arrowood, M.J. Eberhard, M.L. & Herwaldt, B.L. 2003. Epidemiology of *Cyclospora cayetanensis* and other intestinal parasites in a community in Haiti. *Journal of Clinical Microbiology*, 41: 2047–2054.

Madico, G., McDonald, J., Gilman, R.H., Cabrera, L. & Sterling, C.R. 1997. Epidemiology and treatment of *Cyclospora cayetanensis* infection in Peruvian children. *Clinical Infectious Diseases,* 24(5): 977–981.

Ortega, Y.R. & Sanchez, R. 2010. Update on *Cyclospora cayetanensis,* a food-borne and waterborne parasite. *Clinical Microbiology Reviews*, 23: 218–234.

Ortega, Y.R., Sterling, C.R., Gilman, R.H., Cama, V.A. & Diaz, F. 1993. *Cyclospora* species – a new protozoan pathogen of humans. *New England Journal of Medicine*, 328(18): 1308–1312.

Pape, J.W., Verdier, R.I., Boncy, M., Boncy, J. & Johnson, W.D. Jr. 1994. *Cyclospora* infection in adults infected with HIV. Clinical manifestations, treatment, and prophylaxis. *Annals of Internal Medicine*, 121: 654–657.

Rabold, J.G., Hoge, C.W., Shlim, D.R., Kefford, C., Rajah, R. & Echeverria, P. 1994. *Cyclospora* outbreak associated with chlorinated drinking water. *Lancet*, 344: 1360–1361.

Scallan, E., Hoekstra, R.M., Angulo, F.J., Tauxe, R.V., Widdowson, M.A., Roy, S.L., Jones, J.L. & Griffin, P.M. 2011. Food-borne illness acquired in the United States – major pathogens. *Emerging Infectious Diseases*, 17:7-15.

Shields, J.M. & Olson, B.H. 2003. *Cyclospora cayetanensis*: a review of an emerging parasitic coccidian. *International Journal of Parasitology*, 33: 371–391.

Shlim, D.R., Hoge, C.W., Rajah, R., Scott, R.M., Pandy, P. & Echeverria, P. 1999. Persistent high risk of diarrhea among foreigners in Nepal during the first 2 years of residence. *Clinical Infectious Diseases*, 29: 613–616.

A7.6 *DIPHYLLOBOTHRIUM* SPP.

General information

Human diphyllobothriasis is a fish-borne zoonosis distributed worldwide and it is transmitted by cestodes belonging to the genus *Diphyllobothrium*. The life cycle of these tapeworms involves two intermediate hosts (zooplankton and some marine and freshwater fish species, especially those anadromous species that migrate from salt to fresh water to spawn), and piscivorous mammals and birds as definitive hosts. Fourteen of the 50 known species of *Diphyllobothrium* so far described are known to infect humans (Scholz *et al.,* 2009). The occurrence of the disease is closely linked to the consumption of raw or undercooked freshwater or marine fishes.

Diphyllobothriasis is considered a mild illness and is not reportable, therefore the estimates of global illnesses attributed to this fish-borne zoonosis are based on limited human surveys and clinical case reports. Chai, Murrell and Lymbery (2005) estimated global infection at 20 million. Dorny and co-workers (2009) estimated that in about 20% of the infections, clinical manifestations occur.

Geographical distribution

Americas

Until 1982, diphyllobothriasis was a reportable disease in the United States of America, with 125–200 cases reported during the period 1977–1981 (Ruttenber *et al.,* 1984). In North America, most cases occur in the Great Lakes region and Alaska, although cases have been reported elsewhere (Cushing and Bacal, 1934; Margolis, Rausch and Robertson, 1973; Turgeon, 1974). The following species of *Diphyllobothrium* were documented as infecting humans in North America: *D latum, D dendriticum, D. dalliae, D. lanceolatum, D. ursi, D. alascense* and, just recently, *D. nihonkaiense* (reviewed by Scholz *et al.,* 2009).

Human infections are commonly reported within the Southern Cone of South America, most commonly with *D. latum* and *D. pacificum* (Mercado *et al*., 2010), which includes Chile (Mercado *et al*., 2010; Torres *et al*., 1993), Argentina (Semenas, Kreiter and Urbanski, 2001) and Peru (Lumbreras *et al*., 1982) on the Pacific coast. In Chile, 0.4–1.4% of the population shed *Diphyllobothrium* eggs in high-risk zones (Torres *et al*., 1993; Navarrete and Torres, 1994).

Asia

In Japan, it is estimated that, on average, about 100 cases per year of diphyllobothriasis occur (Oshima and Kliks, 1987), and in the Republic of Korea, at least 47 cases have been reported since 1971 (Lee *et al.,* 2007; Jeon *et al.,* 2009), most commonly with *D. nihonkaiense*. In China, 12 cases (Guo *et al.,* 2012) of infection

with *D. latum* were reported in 2009–2011; however, these figures are likely to be a gross underestimate of true incidence. Sporadic reports of clinical illness have also been reported in Malaysia (Rohela *et al.,* 2002, 2006), India (Devi *et al.,* 2007; Duggal *et al.,* 2011; Ramana *et al.,* 2011) and Taiwan (Chou *et al.,* 2006; Lou *et al.,* 2007). In easternmost Russia, where *D. klebanovskii* is considered the important zoonotic species, human prevalence usually ranges from 1.0 to 3.3%. Since the completion of the Krasnoyaek Reservoir on the Enisel River the prevalence of *D. klebanovskii* has risen as high as 7.7% in people living along the reservoir shore (Scholz *et al.,* 2009; Chai, Murrell and Lymbery, 2005).

Europe

D. latum has been considered to be the principal species infecting humans in Europe, with *D. dendriticum* present in northern Europe. The incidence appears to be on the decline overall. In Scandinavian countries it persists in several regions. Currently Switzerland, Sweden, Finland and Estonia report more than 10 cases per year (440 in Estonia in 1997), while Lithuania, Poland, Hungary, Italy and France average 2–10 cases annually. Only sporadic cases occur in Norway, Austria and Spain. Over 30 cases have been identified on the Swiss shores of Lake Maggiore since 1990, and 70 cases on the Swiss and French shores of Lake Leman between 1993 and 2002 (Dupouy-Camet and Peduzzi, 2004).

Disease

Severity of acute morbidity

Acutely, patients may experience vomiting, abdominal discomfort, cramps, diarrhoea and shed ribbon-like proglottids in their faeces (Lumbreras *et al.,* 1982; Ramana *et al.,* 2011; Wicht *et al.,* 2008).

Severity of chronic morbidity

This was reviewed by Scholtz *et al.* (2009). In addition to chronic relapsing diarrhoea and abdominal discomfort (Wicht *et al.,* 2008; Choi, Lee and Yang, 2012), prolonged or heavy infection may cause megaloblastic anaemia due to a parasite-mediated dissociation of the vitamin B12-intrinsic factor complex within the gut lumen, making B12 unavailable to the host. Approximately 80% of the B12 intake is absorbed by the worm, with a differential absorption rate of 100:1 in relation to absorption by the host (Scholz *et al.,* 2009).

Chronic illness fraction

About 40% of infected individuals may show low B12 levels, but only 2% or less develop clinical anaemia, which is hyperchromic and macrocytic and may be associated with low platelets or low white blood cell counts (Scholz *et al.,* 2009). This deficiency may produce damage to the nervous system, including peripheral neuropathy or central nervous system degenerative lesions (Scholz *et al.,* 2009).

Case fatality rates
No reports.

Increase in human illness potential
Increased human illness is unlikely with regards to severity, but is potentially an emerging zoonosis due to increased globalization associated with travel and trade, as well as increases in global popularity of eating dishes such as sushi and sashimi. Risks are mostly associated with wild-caught fish given the primarily sylvatic nature of the parasite's life cycle.

Trade relevance
As the demands for 'premium' quality fish and fishery products increase, harvesting and export of wild-caught fish from diphyllobothriid-endemic areas that are transported chilled (not frozen) pose the greatest risk to trade (Chetrick, 2007). Inactivation of larvae (plerocercoids) requires cooking fish at 55°C for at least 5 minutes, or freezing it at -18°C for at least 24 h before consumption. An increasing number of human cases of diphyllobothriasis due to 'exotically' located *Diphyllobothrium* species are being reported (de Marval *et al.,* 2013). To date, *D. nihonkaiense* infection has been reported in three Swiss (Wicht, de Marval and Peduzzi, 2007; Shimizu *et al.,* 2008) and two French locals (Paugam *et al.,* 2009; Yera *et al.,* 2006) and a case of *D. dendriticum* (de Marval *et al.,* 2013) in a Swiss local that had most likely consumed salmon imported from Finland (Wicht *et al.,* 2008).

Impact on economically vulnerable populations
True incidence and contribution to morbidity remain unascertained. The zoonosis is likely to have impacts, especially within developing communities, due to the neglected nature of parasitism.

Other relevant information
In those areas where mass drug administration programmes are carried out and known to be endemic for diphyllobothriasis, it may be important to consider the inclusion of praziquantel and educational measures aimed at discouraging the practice of eating insufficiently cooked fish.

References

Chai, J.Y., Murrell, K.D. & Lymbery, A.J. 2005. Fish-borne parasitic zoonoses: status and issues. *International Journal for Parasitology*, 35(11-12): 1233–1254.

Chetrick, J. 2007. Sales of premium products to EU drive record U.S. seafood exports. FAS Worldwide, March 2007: 1–3. Online. Available at https://www.fas.usda.gov/info/fasworldwide/2007/03-2007/EUSeafood.pdf Accessed 2013-06-20.

Choi, H.J., Lee, J. &Yang, H.J. 2012. Four human cases of *Diphyllobothrium latum* infection. *Korean Journal of Parasitology*, 50(2): 143–146.

Chou, H.F., Yen, C.M., Liang, W.C. & Jong, Y.J. 2006. *Diphyllobothriasis latum*: the first child case report in Taiwan. *Kaohsiung Journal of Medical Science*, 22(7): 346–351.

Cushing, H.B. & Bacal, H.L. 1934. *Diphyllobothrium latum* (Fish Tapeworm) infestation in eastern Canada with particular reference to its increasing prevalence. *Canadian Medical Association Journal*, 30(4): 377–384.

de Marval, F., Gottstein, B., Weber, M. & Wicht, B. 2010 Imported diphyllobothriasis in Switzerland: molecular methods to define a clinical case of *Diphyllobothrium* infection as *Diphyllobothrium dendriticum*, August 2010. *EuroSurveillance*, 18(3): ii, 20355.

Devi, C.S., Shashikala, Srinivasan, S., Murmu, U.C., Barman, P. & Kanungo, R. 2007. A rare case of diphyllobothriasis from Pondicherry, South India. *Indian Journal of Medical Microbiology,* 25(2): 152–154.

Dorny, P., Praet, N., Deckers, N. & Gabriel, S. 2009. Emerging food-borne parasites. *Veterinary Parasitology*, 163(3): 196–206.

Duggal, S., Mahajan, R.K., Duggal, N. & Hans, C. 2011. Case of sparganosis: a diagnostic dilemma. *Indian Journal of Medical Microbiology,* 29(2): 183–186.

Dupouy-Camet, J. & Peduzzi, R. 2004. Current situation of human diphyllobothriasis in Europe. *EuroSurveillance*, 9(5): 31–35.

Guo, A.J., Liu, K., Gong, W., Luo, X.N., Yan, H.B., Zhao, S.B., Hu, S.N. & Jia, W.Z. 2012. Molecular identification of *Diphyllobothrium latum* and a brief review of diphyllobothriosis in China. *Acta Parasitologica*, 57(3): 293–296.

Jeon, H.K., Kim, K.H., Huh, S., Chai, J.Y., Min, D.Y., Rim, H.J. & Eom, K.S. 2009. Morphologic and genetic identification of *Diphyllobothrium nihonkaiense* in Korea. *Korean Journal of Parasitology*, 47(4): 369–375.

Lee, E.B., Song, J.H., Park, N.S., Kang, B.K., Lee, H.S., Han, Y.J., Kim, H.J., Shin, E.H. & Chai, J.Y. 2007. A case of *Diphyllobothrium latum* infection with a brief review of diphyllobothriasis in the Republic of Korea. *Korean Journal of Parasitology*, 45(3): 219–223.

Lou, H.Y., Tsai, P.C., Chang, C.C., Lin, Y.H., Liao, C.W., Kao, T.C., Lin, H.C., Lee, W.C. & Fan, C.K. 2007. A case of human diphyllobothriasis in northern Taiwan after eating raw fish fillets. *Journal of Microbiology, Immunology and Infection*, 40(5): 452–456.

Lumbreras, H., Terashima, A., Alvarez, H., Tello, R. & Guerra, H. 1982. Single dose treatment with praziquantel (Cesol R, EmBay 8440) of human cestodiasis caused by *Diphyllobothrium pacificum*. *Tropenmedizin und Parasitologie*, 33(12): 5–7.

Margolis, L., Rausch, R.L. & Robertson, E. 1973. *Diphyllobothrium ursi* from man in British Columbia – first report of this tapeworm in Canada. *Canadian Journal of Public Health*, 64(6): 588–589.

Mercado, R., Yamasaki, H., Kato, M., Munoz, V., Sagua, H., Torres, P. & Castillo, D. 2010. Molecular identification of the *Diphyllobothrium* species causing diphyllobothriasis in Chilean patients. *Parasitology Research*, 106(4): 995–1000.

Navarrete, N. & Torres, P. 1994. [Prevalence of infection by intestinal helminths and protozoa in school children from a coastal locality in the province of Valdivia, Chile] [Article in Spanish]. *Boletín Chileno de Parasitología*, 49(3-4): 79–80.

Oshima, T. & Kliks, M. 1987. Effects of marine mammal parasites on human health. *International Journal of Parasitology*, 17(2): 415–421.

Paugam, A., Yera, H., Poirier, P., Lebuisson, A. & Dupouy-Camet, J. 2009. [*Diphyllobothrium nihonkaiense* infection: a new risk in relation with the consumption of salmon] [Article in French]. *Presse Med [La Presse Médicale]*, 38(4): 675–657.

Ramana, K., Rao, S., Vinaykumar, M., Krishnappa, M., Reddy, R., Sarfaraz, M., Kondle, V., Ratnamani, M. & Rao, R. 2011. Diphyllobothriasis in a nine-year-old child in India: a case report. *Journal of Medical Case Reports*, 5: 332.

Rohela, M., Jamaiah, I., Chan, K.W. & Yusoff, W.S. 2002. Diphyllobothriasis: the first case report from Malaysia. *Southeast Asian Journal of Tropical Medicine and Public Health,* 33(2): 229–230.

Rohela, M., Jamaiah, I., Goh, K.L. & Nissapatorn, V. 2006. A second case of diphyllobothriasis in Malaysia. *Southeast Asian Journal of Tropical Medicine and Public Health*, 37(5): 896–898.

Ruttenber, A.J., Weniger, B.G., Sorvillo, F., Murray, R.A. & Ford, S.L. 1984. Diphyllobothriasis associated with salmon consumption in Pacific coast states. *American Journal of Tropical Medicine and Hygiene*, 33(3): 455–459.

Scholz, T., Garcia, H.H., Kuchta, R. & Wicht, B. 2009. Update on the human broad tapeworm (genus *Diphyllobothrium*), including clinical relevance. *Clinical Microbiology Reviews*, 22(1): 146–160.

Semenas, L., Kreiter, A. & Urbanski, J. 2001. New cases of human diphyllobothriasis in Patagonia, Argentina. *Revista de Saude Publica,* 35(2): 214–216.

Shimizu, H., Kawakatsu, H., Shimizu, T., Yamada, M., Tegoshi, T., Uchikawa, R. & Arizono, N. 2008. *Diphyllobothriasis nihonkaiense*: possibly acquired in Switzerland from imported Pacific salmon. *Internal Medicine*, 47(14): 1359–1362.

Torres P., Franjola, R., Weitz, J.C., Peña, G. & Morales, E. 1993. [New records of human diphyllobothriasis in Chile (1981–1992), with a case of multiple *Diphyllobothrium latum* infection] [Article in Spanish]. *Boletín Chileno de Parasitología*, 48(3-4): 39–43.

Turgeon, E.W. 1974. Letter: *Diphyllobothrium latum* (fish tapeworm) in the Sioux Lookout zone. *Canadian Medical Association Journal*, 111(6): 507, 509.

Wicht, B., de Marval, F. & Peduzzi, R. 2007. *Diphyllobothrium nihonkaiense* (Yamane *et al*., 1986) in Switzerland: first molecular evidence and case reports. *Parasitology International*, 56(3): 195–199.

Wicht, B., de Marval, F., Gottstein, B. & Peduzzi, R. 2008. Imported diphyllobothriasis in Switzerland: molecular evidence of *Diphyllobothrium dendriticum* (Nitsch, 1824). *Parasitology Research*, 102(2): 201–204.

Yera, H., Estran, C., Delaunay, P., Gari-Toussaint, M., Dupouy-Camet, J. & Marty, P. 2006. Putative *Diphyllobothrium nihonkaiense* acquired from a Pacific salmon (*Oncorhynchus keta*) eaten in France; genomic identification and case report. *Parasitology International*, 55(1): 45–49.

A7.7 *ECHINOCOCCUS GRANULOSUS*

General information

Echinococcus granulosus is a small (3–7 mm) cestode (tapeworm) belonging to the Taeniidae family. It belongs to the *Echinococcus* genus, which includes six species. The most important species of the genus in terms of public health importance and geographical distribution are *E. granulosus*, which causes cystic echinococcosis (CE) and *E. multilocularis*, which causes alveolar echinococcosis (AE).

Echinococcus species require two mammalian hosts for completion of their life-cycles (end and intermediate hosts). Tapeworm segments containing eggs (gravid proglottids) or free eggs are passed in the faeces of the definitive host, a carnivore. The eggs are ingested by intermediate hosts (many mammalian species), in which the larval stage (metacestodes) and infectious elements (protoscoleces) develop and cause CE. The cycle is completed if an infected intermediate host is eaten by a suitable carnivore. A common source of infection for carnivores is offal from infected livestock.

Infection of humans is due to accidental ingestion of *E. granulosus* eggs passed into the environment with faeces from definitive hosts (dogs are the main sources). *E. granulosus* is maintained in domestic and wildlife reservoirs, and its transmission is influenced by human activities, behaviour, hygiene, environmental factors and the lack of cooperation among public health, agriculture and local authorities. Eggs of *E. granulosus* are highly resistant to environmental conditions and can remain infective for many months (up to about 1 year in a moist environment at lower ranges of temperatures of about +4°C to +15°C). Eggs are sensitive to desiccation, and are killed within 4 days at a relative humidity of 25%, and within 1 day at 0%. Heating to 60–80°C will kill these eggs in less than 5 minutes. Most importantly, *E. granulosus* eggs can survive freezing temperatures (Eckert *et al.,* 1992; Gemmell and Lawson, 1986)

There are at least ten genetic variants (G1 to G10) of *E. granulosus,* of which seven (sheep strain G1, Tasmanian sheep strain G2, buffalo strain G3, cattle strain G5 (*E. ortleppi*), camel strain G6, pig strain G7/G9 and cervid strain G8) have been shown to be infectious for humans. The strain most often associated with human CE appears to be the common sheep strain (G1).

CE is not considered to be 'strictly' a food-borne disease because the infection occurs by ingestion of the *Echinococcus* eggs via contact with contaminated soil, infected dogs, or by consumption of food (mainly vegetables) or water contaminated with infected dog faeces. Food may be an important vehicle of transmission, but it may not be the primary vehicle for transmission for these parasites.

However, given the wide distribution and relatively high incidence and severity of CE, and since CE is one of the major contributors to the global burden of parasitic zoonoses (Torgerson and Macpherson, 2011), it is necessary to consider its food-borne route.

There are continuing challenges in diagnosing CE in different host species, including humans (Barnes *et al.,* 2012). In addition, no global estimates exist to date of CE burden in humans, and the incidence data is gathered from published literature that is generally based on surgical cases. Consequently, human cases of CE are systematically underreported by healthcare systems. Serra *et al.* (1999) and Nazirov, Ilkhamov and Ambekov (2002) reported that up to 75% of clinic- or hospital-diagnosed cases are never recorded in local or national databases or published reports.

One of the major factors influencing the prevalence of CE is close contact with untreated dogs, the habit and popular tradition of eating raw or inadequately cooked foods, and drinking water contaminated with *Echinococcus* eggs.

Geographical distribution

E. granulosus has a worldwide geographical distribution, with endemic foci present in every continent. Its distribution and prevalence depends on the presence of large numbers of sheep, cattle, goat and camel flocks that are the intermediate hosts of the parasite, and their close contact with dogs, the main final host, which transmit the infection to humans. At the same time, the highest prevalence of CE in human and animal hosts is found in countries of the temperate zones, including several parts of Eurasia (the Mediterranean regions, southern and central parts of Russia, central Asia, China), Australia, some parts of America (especially South America) and north and east Africa (Dakkak, 2010; Eckert *et al.,* 2001; Grosso *et al.,* 2012; Thompson and McManus, 2002). Due to the wide geographical distribution and extent greater than previously believed, CE is currently considered an emerging or re-emerging disease (Grosso *et al.,* 2012; Thompson and MacManus, 2002; Torgerson *et al.,* 2003).

Human CE, which is the most common *Echinococcus* spp. infection, probably accounts for more than 95% of the estimated 3 million global cases, with human AE causing only 0.3–0.5 million cases (Zhang, Ross and McManus, 2008). The annual incidence of CE can range from less than 1 to >200 per 100 000 inhabitants in various endemic areas (Pawlowski, Eckert and Vuitton, 2001; Dakkak, 2010).

Disease

The oncospheres released from ingested *E. granulosus* eggs enter the blood stream after penetration of the intestinal mucosa, and are distributed to the liver and other

sites, where development of cysts begins. The liver is the most common site of the echinococcal cyst (>65%), followed by the lungs (25%); the cyst is seen less frequently in the spleen, kidneys, heart, bone or central nervous system (Moro and Schantz, 2009). The cysts vary greatly in size and shape, and may be present in large numbers in one organ. The location of cysts and cyst morphology depends on host factors and on the *E. granulosus* strain.

The incubation period ranges between 2 and 15 years in general, and clinical manifestations of CE are variable and determined by the site, size and condition of the cysts. It has been shown that rates of growth of cysts are variable, ranging from 1 to 5 cm in diameter per year (Moro and Schantz, 2009), and that the cysts of *E. granulosus* can grow to more than 20 cm in diameter in humans, but the clinical manifestations are generally mild and the disease remains asymptomatic for a considerable period. Thus, CE is a chronic cyst-forming disease characterized by long-term growth of the cysts in internal organs for several years (Spruance, 1974). The slowly growing hydatid cysts can attain a volume of several litres and contain many thousands of infectious elements (protoscoleces). Due to the slow-growing nature of the cyst, even if the infection is frequently acquired in childhood, most cases with localization of cysts in the liver and lung become symptomatic and are diagnosed in adult patients. At the same time, cysts located in the brain or eye can cause severe clinical symptoms even when small; thus, most cases of intracerebral echinococcosis are diagnosed in children (Moro and Schantz, 2009).

The signs and symptoms of hepatic echinococcosis can include hepatic enlargement (with or without a palpable mass in the right upper quadrant), right epigastric pain, nausea, biliary duct obstruction and vomiting. Pulmonary involvement can produce chest pain, cough and haemoptysis. CE is rarely fatal, but occasionally death occurs because of anaphylactic shock, or cardiac tamponade (Bouraoui, Trimeche and Mahdhaoui, 2005). Rupture of the cysts and sudden release of the contents can precipitate allergic reactions and produce fever, urticaria, eosinophilia and mild to fatal anaphylactic shock, as well as cyst dissemination that results in multiple secondary echinococcosis disease. Larval growth in bones is atypical; when it occurs, invasion of marrow cavities and spongiosa is common and causes extensive erosion of the bone.

The mortality rate, among surgical cases, is about 2 to 4%, and it increases considerably if surgical and medical treatment and care are inadequate (Zhang, Ross and McManus, 2008; Dakkak, 2010).

Trade relevance of cystic echinococcosis

A number of scientific publications have reported that *E. granulosus* might be imported either with intermediate or definitive hosts (Boubaker *et al.,* 2013).

This could represent a threat for those countries currently free from the parasite. Therefore, consideration may need to be given to the development of tools for pre-mortem diagnosis of hydatidosis in farm animals, which could be used to minimize the risk of importation of infected livestock. There must also be increased awareness of the possible occurrence of biological strains of the parasite that might be of greater or lower infectivity for humans.

At present no data are available on the actual prevalence of *E. granulosus* eggs in food or in drinking water in general. Even less is known about that which is traded internationally. Greater consideration of the possible occurrence of parasite strains that might be of greater or lower infectivity for humans may be important. However, the development of specific DNA detection techniques would provide an important diagnostic tool.

Action in definitive hosts is an effective means to strengthen the prevention of the introduction of the disease due to importation of dogs, cats and wild carnivores. Indeed, the World Organisation for Animal Health (OIE) has issued important recommendations in this regard:

> "Veterinary Authorities of importing countries should require the presentation of an international veterinary certificate attesting that the animals were treated against echinococcosis/hydatidosis prior to shipment, and that the treatment used is recognized as being effective" (OIE, 2012).

Impact of CE on economically vulnerable populations

As a cosmopolitan disease, CE represents an increasing public health and socio-economic concern in many areas of the world ((Eckert, Conraths and Tackmann, 2000; Garippa, Varcasia and Scala, 2004), and already results in a high disease burden in underdeveloped regions of the world, including areas of North Africa, the Near East, South America, Central Asia, and China (Wang, Wang and Liu, 2008). It affects both human and animal health and has important socio-economic consequences. However, the socio-economic impact of the disease is not fully understood in most endemic countries because it is necessary to consider not only human and animal health, but also agriculture, trade and market factors. Evaluation of the costs to national economies has been reviewed by Budke, Deplazes and Torgerson (2006). However, the true impact of CE may still be substantially under-represented.

In humans, costs associated with CE have been shown to have a great impact on affected individuals, their families, and the community as a whole (Budke, Deplazes and Torgerson, 2006; Torgerson, 2003). CE represents a substantial burden on the human population, and current estimates suggest that the disease results in the loss

of 1 to 3 million disability-adjusted life years (DALYs) per annum (Torgerson and Craig, 2011). The World Health Organization (WHO) considered CE as: "… not only one of the most widespread parasitic diseases, but also one of the most costly to treat and prevent in terms of public health." (Eckert *et al.,* 2001). Furthermore, in most reports, between 1 and 4% of CE cases are fatal (Budke, Deplazes and Torgerson, 2006; Dakkak, 2010; Torgerson, 2003).

In livestock, there is a direct cost (mainly the loss of revenue through offal condemnation) and indirect costs (reductions in the growth, fecundity and milk production of infected animals) that are included in the estimate of the total costs associated with CE. According to Benner *et al.* (2010), indirect losses account for almost 99% of the total cost associated with CE. Torgerson and Craig (2011) estimated that the annual cost of treating cases and economic losses to the livestock industry probably amounts to US$ 2 billion.

References

Barnes, T.S., Deplazes, P., Gottstein, B., Jenkins, D.J., Mathis, A., Siles-Lucas, M., Torgerson, P.R., Ziadinov, I.D. & Heath, D. 2012. Challenges for diagnosis and control of cystic hydatid disease. *Acta Tropica,* 123: 1–7

Benner, C., Carabin, H., Sánchez-Serrano, L.P., Budke, C.M. & Carmena, D. 2010. Analysis of the economic impact of cystic echinococcosis in Spain. *Bulletin of the World Health Organization*, 88: 49–57.

Boubaker, G., Macchiaroli, N., Prada L., Cucher, M.A., Rosenzvit, M.C., Ziadinov, I., Deplazes, P., Saarma, U., Babba, H., Gottstein, B. & Spiliotis, M. 2013. A Multiplex PCR for the simultaneous detection and genotyping of the *Echinococcus granulosus* Complex. *PLoS Neglected Tropical Diseases,* 7(1): e2017. Online. See doi:10.1371/journal.pntd.0002017

Bouraoui, H., Trimeche, B. & Mahdhaoui, A. 2005. Echinococcosis of the heart: clinical and echocardiographic features in 12 patients. *Acta Cardiologica*, 60(1): 39–41.

Budke, C.M., Deplazes, P. and Torgerson, P.R. 2006. Global socioeconomic impact of cystic echinococcosis. *Emerging Infectious Diseases*, 12: 296–303.

Dakkak, A. 2010. Echinococcosis/Hydatidosis: a severe threat in Mediterranean countries. *Veterinary Parasitology,* 174: 2–11.

Eckert J., Conraths F.J. & Tackmann K. 2000. Echinococcosis: an emerging or re-emerging zoonosis? *International Journal of Parasitology*, 30(12-13): 1283–1294.

Eckert, J., Kutzer, E., Romel, M., Bürger, H.J. & Körting, W. (editors). 1992. *Veterinärmedizinische Parasitologie.* 4th edition. Verlag Paul Parey, Berlin, Germany. 905 p.

Eckert, J., Schantz, P.M., Gasser, R.B., Torgerson, P.R., Bessonov, A.S., Movsessian, S.O., Thakur, A., Grimm, F. & Nikogossian, M.A. 2001. Geographic distribution and prevalence of cystic echinococcosis. pp. 20–66, in: J. Eckert, M.A. Gemmel, F.X. Meslin and Z.S. Pawlowski (editors). *WHO/OIE Manual on Echinococcus in humans and animals: A public health problem of global concern.* World Health Organization, Geneva, Switzerland, and World Organization for Animal Health, Paris, France.

Garippa, G., Varcasia, A. & Scala, A. 2004. Cystic echinococcosis in Italy from the 1950s to present. *Parassitologia*, 46(4): 387–391.

Gemmell, M.A. & Lawson, J.R. 1986. Epidemiology and control of hydatid disease. pp 189–216, in: R.C.A. Thompson (editor). *The biology of Echinococcus and hydatid disease.* Allen & Unwin, London, UK.

Grosso, G., Gruttadauria, S., Biondi, A., Marventano, S., Mistretta, A., Grosso, G., Gruttadauria, S., Biondi, A., Marventano, S. & Mistretta, A. 2012. Worldwide epidemiology of liver hydatidosis including the Mediterranean area. *World Journal of Gastroenterology,* 18: 1425–1437.

Moro, P. & Schantz, P.M. 2009. Echinococcosis: a review. *International Journal of Infectious Diseases,* 13(2): 125–133.

Nazirov, F.G., Ilkhamov, I.L. & Ambekov, N.C. 2002. Echinococcosis in Uzbekistan: types of problems and methods to improve treatment. *Medical Journal of Uzbekistan,* 23: 2–5.

OIE (World Organisation for Animal Health). 2012. Echinococcosis/Hydatidosis. Recommendations applicable to OIE Listed diseases and other diseases of importance to international trade. Volume 2, Chapter 8.4, art. 8.4.2, in: *Terrestrial Animal Health Code.* OIE, Paris, France.

Pawlowski, Z., Eckert, J. & Vuitton, D. 2001. Echinococcosis in humans: clinical aspects, diagnosis and treatment. pp. 20–66, in: J. Eckert, M.A. Gemmel, F.X. Meslin and Z.S. Pawlowski (editors). *WHO/OIE Manual on Echinococcus in humans and animals: A public health problem of global concern.* World Health Organization, Geneva, Switzerland, and World Organization for Animal Health, Paris, France.

Serra, I., Garcia, V., Pizzaro, A., Luzoro, A., Cavada, G. & Lopez, J.A. 1999. [A universal method to correct underreporting of communicable diseases. Real incidence of hydatidosis in Chile, 1985-1994] [Article in Spanish]. *Revista Médica de Chile*, 127(4): 485–492.

Spruance, L. 1974. Latent period of 53 years in a case of hydatid cyst disease. *Archives of Internal Medicine,* 1: 741–742.

Thompson, R.C. & McManus, D.P. 2002. Towards a taxonomic revision of the genus *Echinococcus*. *Trends in Parasitology*, 18: 452–457.

Torgerson P.R. 2003. Economic effects of echinococcosis. *Acta Tropica*, 85: 113–118.

Torgerson, P.R. & Craig, P. 2011. Updated global burden of cystic and alveolar echinococcosis. p. 1, in: Report of the WHO Informal Working Group on cystic and alveolar echinococcosis surveillance, prevention and control, with the participation of FAO and OIE, Geneva, 22–23 June 2011. Available at http://whqlibdoc.who.int/publications/2011/9789241502924_eng.pdf Accessed 2013-06-20.

Torgerson, P.R. & Macpherson, C.N. 2011. The socioeconomic burden of parasitic zoonoses: global trends. *Veterinary Parasitology,* 182: 79–95.

Torgerson, P.R., Karaeva, R.R., Corkeri, N., Abdyjaparov, T.A., Kuttubaev, O.T. & Shaikenov, B.S. 2003. Human cystic echinococcosis in Kyrgystan: an epidemiological study. *Acta Tropica*, 85: 51–61.

Wang, Z., Wang, X. & Liu, X. 2008. Echinococcosis in China, a review of the epidemiology of *Echinococcus* spp. *Ecohealth*, 5: 115–126.

Zhang, W., Ross, A.G. & McManus, D.P. 2008. Mechanisms of immunity in hydatid disease: implications for vaccine development. *Journal of Immunology,* 181: 6679–6685.

A7.8 *ECHINOCOCCUS MULTILOCULARIS*

General information

The fox tapeworm, *Echinococcus multilocularis* (Cestoda: Cyclophyllidea: Taeniidae) is mostly associated with a sylvatic life cycle, with foxes of the genera *Vulpes* and *Alopex* usually serving as definitive hosts, although other wild canids (e.g. raccoon dogs, wolves, coyotes) may also act as definitive hosts. A synanthropic cycle also occurs, in which domestic dogs usually act as definitive hosts; although domestic cats (and possibly wild felids) may serve as definitive hosts, experimental infections suggest that cats would appear to have only a minor role in the maintenance of *E. multilocularis* in endemic areas, and infections in cats may be of minimal public health significance (Thompson *et al.,* 2006).

For both sylvatic and synanthropic cycles, various different genera of rodents and lagomorphs may act as intermediate hosts, being infected by ingestion of the eggs released from the tapeworms in the faeces of the definitive hosts. The most common potential intermediate hosts include rodents in the genera *Microtus*, *Arvicola* and *Ondatra*, and lagomorphs in the genera *Ochotona*, depending on location. A number of other mammals, including humans and pigs, may also be infected with the eggs of the parasite; in humans, this may result in the disease state known as alveolar echinococcosis (AE). However, as metacestode development in these non-rodent mammals seems to be incomplete or retarded, and also as these animals are less likely to be later consumed by the definitive hosts, they do not seem to play a role in the perpetuation of the life cycle, and they are usually referred to as aberrant or accidental intermediate hosts (Böttcher *et al.,* 2013).

Geographical distribution

Data on the prevalence of AE in humans is scattered and patchy, probably partly due to diagnostic challenges, particularly in early stages of infection. However, improved diagnostics, such as specific serological tests in combination with imaging techniques, have increased diagnostic possibilities.

In North America, only a couple of cases of human AE have been recorded, despite a high prevalence and intensity of infection in wild canids and despite some populations, such as fox and coyote trappers, being highly exposed. In 2008, the EU reported an annual incidence of 1 case per 10 million inhabitants (EFSA, 2010), whereas reports from the United States of America indicate a much lower incidence (Bristow *et al.,* 2012). It has been suggested that this difference in incidence may represent genetic differences between strains of parasites, rather than differences in exposure risks or diagnostic capabilities between populations (Davidson *et al.,* 2012). Although *E. multilocularis* infections in wildlife in Europe appear to be increasing and expanding in prevalence, and the pattern of prevalence in humans

is following the same trend (Schweiger *et al.,* 2007), human infection nevertheless continues to be considered as rare. For example, the mean annual incidence of human cases per 100 000 population, recorded with consistent methods, more than doubled in Switzerland, from 0.10 between 1993 and 2000, to 0.26 between 2001 and 2005 (Moro and Schantz, 2009), while in Latvia and Lithuania patient numbers seem to have been rising since 2002 (Bruzinskaite *et al.,* 2007; Keis *et al.,* 2007), indicating emergence of this infection in some parts of Europe. Expanding fox populations associated with rabies vaccination in some areas may contribute to the spread of this infection.

While *E. multilocularis* infection apparently does not occur in Australia, Africa, South or Central America, countries in Asia and Europe, as well as North America, remain important endemic areas. In particular, Russia and adjacent countries (Belarus, Ukraine, Moldova, Turkey, Armenia, Azerbaijan, Kazakhstan, Turkmenistan, Uzbekistan, Tajikistan, Kyrgyzstan and Mongolia), nine provinces or autonomous regions in China (Tibet, Sichuan, Inner Mongolia, Gansu, Ningxia, Qinghai, Xinjiang, Heilongjiang and Shaanxi) and the Japanese island of Hokkaido are important endemic foci (Davidson *et al.,* 2012). Indeed, by far the largest numbers of human cases are reported from three main foci in China, with prevalences ranging from 0.2% in northwestern Xinjiang to 4% in Gansu and Northwestern Sichuan (Craig, 2006). Specific individual villages report even higher prevalence, with 16% reported from the village of Ban Ban Wan, Gansu (Vuitton *et al.,* 2011).

Disease

Adult *E. multilocularis* tapeworms normally cause little harm to the definitive host and infection is asymptomatic. In intermediate hosts, including humans, ingested eggs develop to oncospheres, which penetrate the intestinal wall and are carried via blood to the liver in particular, but also to other organs, where they form multilocular cysts causing the disease, AE. From ingestion of eggs to onset of clinical symptoms (incubation time) in people may be from months to years, or even decades, depending on the location of the cysts and their speed of growth. In the vast majority of human AE cases, metacestodes of *E. multilocularis* initially develop in the liver (Kern, 2010), with cysts varying from a few millimetres up to 15–20 cm or more in diameter. These cysts can also reproduce aggressively by asexual lateral budding. This gradual invasion of adjacent tissue in a tumour-like manner is the basis for the severity of this disease. Metacestodes may also spread from the liver to other internal organs, such as the lungs, spleen, heart and kidney. Symptoms of severe hepatic dysfunction appear in the advanced clinical stage, in addition to symptoms from other affected organs.

The proportion of cases of AE that are actually food-borne is difficult to estimate, as diagnosis usually occurs long after infection and it may be difficult to associate

an infection with a food-borne event many years previously. It should be noted that the tapeworm eggs excreted in the faeces of definitive hosts may contaminate various types of edible plants, including fruits and vegetables, as well as drinking water. The eggs are extremely tolerant of environmental conditions, as the oncosphere membrane surrounds and protects the infective part of the egg from the environment. *E. multilocularis* eggs are also extremely freeze-tolerant; freezing the eggs at -20°C does not affect their infectivity. However, the eggs are sensitive to desiccation and heat. Thus, although there is a large potential for food-borne infection via raw produce, it is difficult to obtain evidence for this, and consumption of raw outdoor produce did not emerge as an important risk factor for AE in a German study in which other factors had considerably higher odds ratios (Kern *et al.,* 2004). Other reports suggest that owning pet dogs with access to the outdoors may be the highest risk factor for AE (Stehr-Green *et al.,* 1988; Kreidl *et al.,* 1998). Nevertheless, the severity of the chronic morbidity associated with AE, and the potential for food-borne transmission without it necessarily being recognized, means that food-borne transmission should not be dismissed.

While there is negligible acute morbidity associated with AE, its chronic morbidity is severe and infection is potentially fatal. Most patients suffering from a chronic carrier status need continuous medical treatment and follow-up examinations. Surgery and various endoscopic or percutaneous interventions are required. In addition to anti-infective therapy with benzimidazoles, earlier diagnosis and long-term medical care has increased patients survival time during the last 35 years (Kern, 2010).

Trade relevance

Although globalization of trade suggests that *E. multilocularis* could also be introduced to countries via fresh produce, particularly with respect to the longevity of the infective eggs, a risk assessment from Norway concluded that import of *E. multilocularis* to mainland Norway (currently *E. multilocularis*-free) via fresh produce is unlikely (VKM, 2012). Import of this parasite to currently *E. multilocularis*-free regions seems to be more likely to occur via transport in either definitive or intermediate hosts, as has previously been documented (for example, introduction to Svalbard; Davidson *et al.,* 2012).

Different regions of the world have veterinary regulations for treatment of dogs, wild canids and cats to avoid the import of the infection. For example, within the EU there is a specific regulation regarding preventive health measures for the control of *E. multilocularis* infection in dogs (EU, 2003). From an international perspective, the OIE terrestrial code provides recommendations for the importation of dogs, wild canids and cats from an infected country.

Impact on economically vulnerable populations

It should be noted that in communities where access to either diagnosis or prolonged (life-long) treatment, or both, is limited, then the potential impact of infection is considerable. AE is a serious public health problem mainly in the more sparsely populated regions of China (including the Tibetan plateau and Inner Mongolia) and is often associated with pastoral minority communities. Failure to diagnose AE (or its misdiagnosis) leads to advanced disease, making treatment difficult and prognosis poor; cases studies in rural China have indicated that poor public health infrastructure may result in diagnostic and treatment challenges for AE (McManus *et al.,* 2011). Thus, although the prognosis for AE is reasonable when treatment is available, the prognosis is bleak in the absence of treatment or with failure for diagnosis (Torgerson *et al.,* 2010), and in economically vulnerable populations annual mortality may be similar to the incidence. The disease burden from AE has been compared to that of rabies (Torgerson *et al.,* 2010), with annual AE mortality estimated as being approximately one-third of that due to rabies, which has been estimated at approximately 55 000. The authors note that, unlike with rabies, there is no vaccine for AE, and therefore although AE is rare globally, in some highly endemic communities in China (and possibly other economically vulnerable populations) it imposes high burden, and is likely to be one of the leading causes of death.

References

Böttcher, D., Bangoura, B., Schmäschke, R., Müller, K., Fischer, S., Vobis, V., Meiler, H., Wolf, G., Koller, A., Kramer, S., Overhoff, M., Gawlowska, S. & Schoon, H.A. 2013. Diagnostics and epidemiology of alveolar echinococcosis in slaughtered pigs from large-scale husbandries in Germany. *Parasitology Research*, 112(2): 629–636.

Bristow, B.N., Lee, S., Shafir, S., Sorvillo, F. 2012. Human echinococcosis mortality in the United States, 1990-2007. *PLoS Neglected Tropical Diseases*, 6(2): e1524. Online. doi: 10.1371/journal.pntd.0001524

Bruzinskaite, R., Marcinkute, A., Strupas, K., Sokolovas, V., Deplazes, P., Mathis, A., Eddi, C. & Sarkūnas, M. 2007. Alveolar echinococcosis, Lithuania. *Emerging Infectious Diseases*, 13(10): 1618–1619.

Craig, P.S. 2006. Epidemiology of human alveolar echinococcosis in China. *Parasitology* International, 55: S221–S225.

Davidson, R.K., Romig, T., Jenkins, E., Tryland, M. & Robertson, L.J. 2012. The impact of globalization on distribution of *Echinococcus multilocularis. Trends in Parasitology,* 28(6): 239–247.

EFSA (European Food Safety Authority). 2010. The community summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in the European Union in 2008. EFSA *Journal*, 8: 1496.

EU (European Union). 2003. Commission Delegated Regulation (EU) No 1152/2011 of 14 July 2011 supplementing Regulation (EC) No 998/2003 of the European Parliament and of the Council as regards preventive health measures for the control of *Echinococcus multilocularis* infection in dogs (Text with EEA relevance). Available at http://eur-lex.europa.eu/LexUriServ/ LexUriServ.do?uri=OJ:L:2011:296:0006:0012:EN:PDF Accessed 2013-06-20.

Keiss, J., Sondore, V., Cernusenko, A., Viksna, L. & Rozentale, B. 2007. Current trends in echinococcosis in Latvia. Abstract number: 1733_48 presented at the 17th European Congress of Clinical Microbiology and Infectious Diseases, ICC, Munich, Germany, 31 March - 04 April 2007. *International Journal of Antimicrobial Agents*, 29(Special issue: Problem Pathogens): S122–S123.

Kern, P. 2010. Clinical features and treatment of alveolar echinococcosis. *Current Opinion in Infectious Diseases,* 23: 505–512.

Kern, P., Ammon, A., Kron, M., Sinn, G., Sander, S., Petersen, L.R., Gaus, W. & Kern, P. 2004. Risk factors for alveolar echinococcosis in humans. *Emerging Infectious Diseases,* 10(12): 2088–2093.

Kreidl, P., Allerberger, F., Judmaier, G., Auer, H., Aspöck, H. & Hall, A.J. 1998. Domestic pets as risk factors for alveolar hydatid disease in Austria. *American Journal of Epidemiology,* 147(10): 978–981.

McManus, D.P., Li, Z., Yang, S., Gray, D.J. & Yang, Y.R. 2011. Case studies emphasising the difficulties in the diagnosis and management of alveolar echinococcosis in rural China. *Parasites & Vectors,* 4: Article 196. Online. DOI: 10.1186/1756-3305-4-196

Moro, P. & Schantz, P.M. 2009. Echinococcosis: a review. *International Journal of Infectious Diseases,* 13(2): 125–133.

Schweiger, A., Ammann, R.W., Candinas, D., Clavien, P.A., Eckert, J., Gottstein, B., Halkic, N., Muellhaupt, B., Prinz, B.M., Reichen, J., Tarr, P.E., Torgerson, P.R. & Deplazes, P. 2007. Human alveolar echinococcosis after fox population increase, Switzerland. *Emerging Infectious Diseases,* 13(6): 878–882

Stehr-Green, J.K., Stehr-Green, P.A., Schantz, P.M., Wilson, J.F. & Lanier, A. 1988. Risk factors for infection with *Echinococcus multilocularis* in Alaska. *American Journal of Tropical Medicine and Hygiene,* 38(2): 380–385.

Thompson, R.C., Kapel, C.M., Hobbs, R.P. & Deplazes, P. 2006. Comparative development of *Echinococcus multilocularis* in its definitive hosts. Parasitology, 132(5): 709–716.

Torgerson, P.R., Keller, K., Magnotta, M. & Ragland, N. 2010. The global burden of alveolar echinococcosis. *PLoS Neglected Tropical Diseases,* 4(6): e722. Online. doi:10.1371/journal.pntd.0000722

VKM (Vitenskapskomitteen for Mattrygghet/Norwegian Scientific Committee for Food Safety). 2012. Assessment of risk of introduction and establishment of *Echinococcus multilocularis* to mainland Norway. Prepared by L. Robertson, J. Lassen, M. Tryland and R.K. Davidson. Available at http://vkm.no/dav/d35674e4f0.pdf Accessed 2013-06-20.

Vuitton, D.A., Wang, Q., Zhou, H.X., Raoul, F., Knapp, J., Bresson-Hadni, S., Wen, H. & Giraudoux, P. 2011. A historical view of alveolar echinococcosis, 160 years after the discovery of the first case in humans: part 1. What have we learnt on the distribution of the disease and on its parasitic agent? *China Medical Journal (English)*. 124(18): 2943–2953.

A7.9 *ENTAMOEBA HISTOLYTICA*

General information

Entamoeba histolytica is an intestinal protozoan and causes amoebic colitis, dysentery, and extraintestinal abscesses. Amoebiasis is the second leading cause of death from protozoan disease worldwide (Haque *et al.,* 2003; Stanley, 2003). *E. histolytica* has a life cycle consisting of the infectious cyst form and the trophozoite, the invasive and disease causing stage. The incidence of amoebiasis was previously overestimated as two or more morphologically indistinguishable species were thought to be responsible for disease. However, differentiation by molecular diagnosis such as PCR (rRNA, peroxiredoxin, tRNA-linked short tandem repeats) led to the consensus that only *E. histolytica* (and maybe *E. moshkovskii*) is invasive and causes disease, whereas *E. dispar* is commensal and non-invasive. The current estimation of the disease burden is approximately 50 million infections, resulting in an estimated 40 000 to 110 000 deaths annually (PAHO, 1998). Infection mostly occurs by ingestion of food or water contaminated with faeces containing *E. histolytica* cysts. However, direct ingestion of faeces by oral and anal sex, particularly among men who have sex with men, and also by faecal smearing among persons with intellectual disabilities, are considered to be the major route of infection in industrialized countries (Weinke *et al.,* 1990; Nozaki, 2000). Since waterborne routes are primarily important in developing countries, the exact proportion of food-borne association with amoebiasis is not known.

Geographical distribution

Amoebiasis is distributed throughout the world and is a potential health risk in all countries where water and food are not adequately separated from faecal contamination. In Mexico, serological studies showed that >8% of the population had amoebiasis (Caballero-Salcedo *et al.,* 1994). In Hue City, Viet Nam, the annual incidence of amoebic liver abscess was reported to be 21 cases per 100 000 inhabitants (Blessmann *et al.,* 2002). In the United States of America, about three thousand cases of amoebiasis were recorded in 1993, comprising mostly immigrants from Central and South America, Asia and the Pacific Islands (MMWR, 1994). Travellers to endemic countries and regions are also at risk of amoebiasis infections. For instance, 10% of about 500 individuals with diarrhoea after travelling to a developing country were diagnosed with amoebiasis (Jelinek *et al.,* 1996), and 3% of about 3000 German travellers returning from the tropical regions were infected with *E. histolytica* (Weinke *et al.,* 1990).

Disease

Less than 10% of individuals infected with *E. histolytica* develop symptoms (Haque *et al.,* 2003; Stanley, 2003; Ali and Nozaki, 2007). Clinical symptoms of amoebic colitis include bloody diarrhoea with multiple mucoid stools, abdominal pain and

tenderness. Fulminant amoebic colitis is characterized by profuse bloody diarrhoea, fever, pronounced leucocytosis, and severe abdominal pain, and occasionally seen in individuals at risk, including pregnant women, immunocompromised individuals, including those with AIDS, diabetes or alcoholism. Amoebic liver abscess is the most common extraintestinal manifestation of an amoebic infection. Symptoms associated with amoebic liver abscess are fever, right upper quadrant pain and hepatic tenderness, and sometimes include cough, anorexia and weight loss. Pleuropulmonary amoebiasis, amoebic brain abscess and amoebic skin abscess also occasionally occur. In most cases, amoebic infection is cured by drug treatment or is self-limiting, and persistent and chronic infection does not usually occur. Protective acquired immunity against amoebiasis does not last long, particularly in children, which leads to repeated infections. The case fatality rate of amoebiasis is not well known. However, in Japan, 10 deaths were reported among the 2574 confirmed cases in 2003–2006 (IASR, 2007). The case fatality rate in developing countries may be significantly higher.

Trade relevance

As mentioned above, attribution of food-borne association with overall incidence of amoebiasis is not very clear. As transmission occurs through consumption of fresh produce, trade involving all endemic countries and regions may have an impact on transmission of the parasite. However, amoebiasis is considered to be mostly irrelevant to international trade. It is important to improve hygiene and awareness of potential food-borne transmission in food handlers.

Impact on economically vulnerable populations

Children, particularly malnourished children, are more susceptible than adults (Haque *et al.,* 2003). Trade-associated impact to these populations is not known.

References

Ali, V. & Nozaki, T. 2007. Current therapeutics, their problems, and sulfur-containing-amino-acid metabolism as a novel target against infections by "amitochondriate" protozoan parasites. *Clinical Microbiology Reviews*, 2007, 20:164-87.

Blessmann, J., Van Linh, P., Nu, P.A., Thi, H.D., Muller-Myhsok, B., Buss, H. & Tannich, E. 2002. Epidemiology of amebiasis in a region of high incidence of amebic liver abscess in central Vietnam. *American Journal of Tropical Medicine and Hygiene*, 66(5): 578–583.

Caballero-Salcedo, A., Viveros-Rogel, M., Salvatierra, B., Tapia-Conyer, R., Sepulveda-Amor, J., Gutierrez, G. & Ortiz-Ortiz, L. 1994. Seroepidemiology of amebiasis in Mexico. *American Journal of Tropical Medicine and Hygiene*, 50(4): 412–429.

Haque, R., Huston, C.D., Hughes, M., Houpt, E. & Petri, W.A. Jr. 2003. Amebiasis. *New England Journal of Medicine*, 348: 1565–1573.

IASR (Infectious Agents Surveillance Reports). 2007. Amoebiasis 2003–2006. *Infectious Agent Surveillance Reports*, 28: 103–104.

Jelinek, T., Peyerl, G., Loånscher, T. & Nothdurft, H.D. 1996. Evaluation of an antigen-capture enzyme immunoassay for detection of *Entamoeba histolytica* in stool samples. *European Journal of Clinical Microbiology and Infectious Disease*, 15: 752–755.

MMWR (Morbidity and Mortality Weekly Report). 1994. Summary of notifiable diseases, United States. *Morbidity and Mortality Weekly Report*, 42: 1–73.

Nozaki, T. 2000. Current problems of amebiasis in Japan and recent advances in amebiasis research. *Japan Journal of Infectious Disease*, 53: 229–237.

PAHO (Pan American Health Organization). 1998. Mexico. pp. 357–378, in: *Health in the Americas*. Pan American Health Organization, Washington DC, USA.

Stanley, S.L. Jr. 2003. Amoebiasis. *Lancet*, 361(9362): 1025–1034.

Weinke, T., Friedrich-Jaenicke, B., Hopp, P. & Janitschke, K. 1990. Prevalence and clinical importance of *Entamoeba histolytica* in two high-risk groups: travellers returning from the tropics and male homosexuals. *Journal of Infectious Diseases*, 161: 1029–1031.

A7.10 *FASCIOLA* SPP.

General information

Over 80 different species of food-borne trematodes have been reported from human infections (Fürst, Keiser, and Utzinger. 2012; Chai, 2007). Worldwide, about 56.2 million people were infected with food-borne trematodes (including *Fasciola*) in 2005: 7.9 million presented severe sequelae and 7158 died (Fürst, Keiser, and Utzinger. 2012).

Fasciola (Fasciolidae) is a plant-borne trematode. Two species have been found to affect humans: *Fasciola hepatica* and *F. gigantica*. Fascioliasis is an important disease in sheep, cattle and humans and is chiefly confined to the liver, where the most important pathogenic sequelae are hepatic lesions and fibrosis, and chronic inflammation of the bile ducts (Mas-Coma, Esteban and Bargues, 1999; Mas-Coma, Bargues and Valero, 2005).

The emergence of fascioliasis appears to be partly related to climate change, where mainly anthropogenic modifications of the environment have increased the geographical range of intermediate hosts (aquatic snails) and livestock (WHO, 1995; Mas-Coma, Valero and Bargues, 2009). The World Health Organization includes human fascioliasis on its list of priorities among neglected tropical diseases (NTDs) (WHO, 2008)

Geographical distribution

Fascioliasis is widely distributed among herbivorous animals and humans, throughout most of the world. Human fascioliasis infection estimates increased from the 2000 reported in 1990 to 17 million people in 1992, and in 51 different countries in 1998 (Esteban, Bargues and Mas-Coma, 1998). Fascioliasis occurs worldwide in over 50 countries, especially where sheep or cattle are reared. In general, *F. hepatica* is present in Europe, Africa, Asia, the Americas and Oceania, and *F. gigantica* is mainly distributed in Africa and Asia (WHO, 2007). Fürst, Keiser, and Utzinger (2012) reported 2 646 515 fascioliasis patients globally, including North, Central and Latin America; North and Eastern Africa; Near East; Asia; and Europe. It has been reported, in Viet Nam, that fascioliasis is an emerging problem, increasing from 12 provinces with 500 cases in 2000, to 52 provinces with over 20 000 cases in 2012 (De *et al.,* 2003; De, Le and Waikagul, 2006; De, 2012).

Disease

People usually become infected from eating raw watercress or other water plants contaminated with immature *Fasciola* larvae (metacercariae). On ingestion, the larval flukes migrate through the intestinal wall, into the abdominal cavity, migrate to the liver and finally into the bile ducts, where they develop into mature, egg-

laying adult flukes (Mas-Coma, Valero and Bargues, 2009; Esteban, Bargues and Mas-Coma, 1998).

Acute morbidity

In the liver the most important pathogenic sequelae are hepatic lesions such as liver tumours or abscesses, and in some cases, bleeding, and the occurrence of ectopic lesions when immature flukes deviate during migration and enter into other organs (Mas-Coma, Esteban and Bargues, 1999). The major clinical symptoms are abdominal pain, fever, dyspepsia, fatty food intolerance, weight loss, digestive disorders, jaundice, allergy, enlarged liver, lithiasis of the bile duct or the gall bladder, urticaria, and respiratory symptoms. The usual signs are hepatomegaly and splenomegaly, ascites, anaemia, chest signs, jaundice, vomiting and bleeding from the bile duct (De, 2011; Chen and Mott, 1990; Esteban, Bargues and Mas-Coma, 1998). The major sub-clinical symptoms are tumours or liver abscesses detected by ultrasound, CT scans or MRI; eosinophilia; and positive ELISA test by *Fasciola* antigen.

The pathology typically is most pronounced in the bile ducts and liver. However, fascioliasis is treatable, for example with Triclabendazole (Egaten) (WHO, 2007) (see also CDC, 2013).

Chronic morbidity

Chronic infection may cause expansion and thickening of the bile duct wall, and degenerative lesions in liver tissue resulting in liver cirrhosis. In some cases, parasites in the liver tissue may be calcified or become incorporated in a granuloma (Mas-Coma, Esteban and Bargues, 1999; Esteban, Bargues and Mas-Coma, 1998). Fascioliasis patients may experience weight loss, fever, and abdominal pain, which may result in a loss of strength and physical activity; high case fatality rates are reported (Mas-Coma, Esteban and Bargues, 1999).

Trade relevance

The import of domesticated livestock such as sheep, goats, oxen, zebu cattle, buffaloes, pigs, donkeys, horses, mules, yaks, camels, dromedaries, llamas and alpacas can lead to introduction of *Fasciola* into non-endemic areas (Mas-Coma, Esteban and Bargues, 1999;; Mas-Coma, Bargues and Valero, 2005). Because of this, export activity may be negatively affected, but there are no international restrictions known.

Impact on economically vulnerable populations

Fascioliasis may have a major impact on community human health due to the associated mortality, morbidity and disability. The costs for diagnosis, hospitalization and treatment are expensive, especially for rural populations in low income

countries. Farm income can be affected because of direct effects on animal health and on economic value of livestock and their products. It is important to recognize that because of climate change the distribution of vector snails, reservoir hosts and suitable ecological habitats may increase, thereby leading to greater public health problems and economic impact on livestock producers and their communities. Increasing parasite resistance to the most effective drug, Triclabendazole, may also exacerbate these impacts.

References

CDC (Centers for Disease Control). 2013. Fact sheet: Parasites - Fascioliasis (*Fasciola* infection). Web page. Available at http://www.cdc.gov/parasites/fasciola/index.html Accessed 2013-06-23.

Chai, J.-Y. 2007. Intestinal flukes. pp. 53–115, in: K.D. Murrell and B. Fried (editors). *World Class Parasites.* Vol. 11. Springer, Dordrecht, The Netherlands.

Chen, M.G. & Mott, K.E. 1990. Progress in assessment of morbidity due to *Fasciola hepatica* infection: a review of recent literature. *Tropical Diseases Bulletin*, 87: R1–R38.

De, N.V. 2011. Fascioliasis infection in tumour liver patients in Hanoi hospitals 2006–2010. *Tropical Medicine and International Health*, 16: 274.

De, N.V. 2012. An update on the parasitic diseases in Vietnam. pp. 9–21, in: International Scientific Proceeding of Mekong-Sante-110, 10–12 May 2012, Hanoi Medical University, Viet Nam.

De, N.V., Le, T.H. & Waikagul, J. 2006. Plant-borne trematodes and fascioliasis in Vietnam. Presented at 5th Seminar on Food- and Water-borne Parasitic Zoonoses (5th FBPZ), 28–30 November 2006, Bangkok, Thailand.

De, N.V., Murrell, K.D., Cong, le D., Cam, P.D., Chau, le V., Toan, N.D. & Dalsgaard, A. 2003. The food-borne trematode zoonoses of Vietnam. *Southeast Asian Journal of Tropical Medicine and Public Health,* 34(Suppl. 1): 12–34.

Esteban, J.G., Bargues, M.D. & Mas-Coma, S. 1998. Geographical distribution, diagnosis and treatment of human fascioliasis: a review. *Research and Reviews in Parasitology*, 58: 13–42.

Fürst, T., Keiser, J. & Utzinger, J. 2012. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 12(3): 210–221.

Mas-Coma, S. 2004. Human fascioliasis: Epidemiological patterns in human endemic areas of South America, Africa and Asia. *Southeast Asian Journal of Tropical Medicine and Public Health*, 35(Suppl. 1): 1–11.

Mas-Coma, S. & Bargues, M.D. 1999. Human liver flukes: a review. pp. 411–434, in: J.P. Dalton (editor). *Research Reviews in Parasitology*. CAB International Publishing, Wallingford, UK.

Mas-Coma, S., Bargues, M.D. & Valero, M.A. 2005. Fascioliasis and other plant-borne trematode zoonoses. *International Journal of Parasitology*, 35(11-12): 1255–1278.

Mas-Coma, M.S., Esteban, J.G. & Bargues, M.D. 1999. Epidemiology of human fascioliasis: a review and proposed new classification. *Bulletin of the World Health Organization*, 77(4): 340–346.

Mas-Coma, S., Valero, M.A. & Bargues, M.D. 2009. *Fasciola*, lymnaeids and human fascioliasis, with a global overview on disease transmission, epidemiology, evolutionary genetics, molecular epidemiology and control. *Advances in Parasitology*, 69: 41–146.

WHO (World Health Organization). 1995. Control of food-borne trematode infections. *WHO Technical Reports Series,* No. 849. 157 p.

WHO. 2007. Report of the WHO Informal Meeting on use of triclabendazole in fascioliasis control. Geneva, Switzerland, 17–18 October 2006. Available at http://www.who.int/neglected_diseases/ preventive_chemotherapy/WHO_CDS_NTD_PCT_2007.1.pdf Accessed 2013-06-21.

WHO. 2008. Fact sheet on fascioliasis. Action Against Worms, WHO, Geneva, Switzerland.

A7.11 *GIARDIA DUODENALIS*

General information

Giardia duodenalis, Giardia intestinalis, and *Giardia lamblia* are the names used to refer to the same flagellated, binucleated protozoan, but opinions differ regarding the name *G. intestinalis*. Recently, numerous biological and genetic analyses have shown that the same *Giardia* species present in humans are also found in a range of other mammalian species, so there is no taxonomic basis for the use of the name *G. lamblia*. For purposes of consistency we will use *G. duodenalis*.

The protozoan *G. duodenalis* is the most frequent intestinal parasite for humans in many countries [1]. Although *G. duodenalis* is the only species found in humans and many other mammals, including pets and livestock, it is now considered a multispecies complex whose members can be assigned to at least seven distinct assemblages or groups of strains (Feng and Xiao, 2011; Cacciò and Ryan, 2008). Only assemblages A and B have been detected in humans and in a wide range of other mammalian hosts, whereas the remaining assemblages, C to H, are likely to be host specific and have not yet been described infecting humans. One sub-assemblage of the A assemblage, the AII, has been described as infecting only humans (Feng and Xiao, 2011; Cacciò and Ryan, 2008).

Geographical distribution

G. duodenalis has a global distribution, causing an estimated 8×10^8 cases per year, and is the most common intestinal parasite of humans in many countries. In Asia, Africa and Latin America, about 200 million people have symptomatic giardiasis, with some 500 000 new cases reported each year (Lal *et al.*, 2013). Infection rates for giardiasis in humans are generally lower in developed countries. Food-borne transmission could occur through manure application to cropland; irrigation with contaminated water; and infected consumables such as meat and milk (Nash *et al.*, 1987). Most food-borne outbreaks of giardiasis has been related to direct contamination by a food handler, but a role for zoonotic transmission is also suggested (e.g. the consumption of a Christmas pudding contaminated with rodent faeces, and tripe soup made from the offal of an infected sheep) (Nash *et al.*, 1987). Unfortunately, no information is available on the proportion of food-borne sources for total *G. duodenalis* human infections (Nash *et al.*, 1987).

Disease

Severity of acute morbidity

Approximately 50% of exposed individuals clear the infection without clinical symptoms, and approximately 5% to 15% of individuals shed cysts asymptomatically (Caeiro *et al.*, 1999). The remaining 35% to 45% of individuals have symptomatic infection (Caeiro *et al.*, 1999). *Giardia* causes a generally self-limited clinical

illness characterized by diarrhoea, abdominal cramps, bloating, weight loss and malabsorption. It is not fully understood why some individuals develop clinical giardiasis while others remain asymptomatic. Host factors and strain variation of the parasite are both likely to be involved.

Severity of chronic morbidity

Chronic giardiasis may follow the acute phase of illness or may develop in the absence of an antecedent acute illness. Symptoms of chronic giardiasis may include loose stools but usually not diarrhoea; steatorrhoea; profound weight loss; malabsorption; or malaise. The manifestations may wax and wane over many months. Even in cases of otherwise asymptomatic infection, malabsorption of fats, sugars, carbohydrates and vitamins may occur. This can lead to hypoalbuminaemia and deficiencies of vitamin A, B12 and folate. Acquired lactose intolerance occurs in up to 40% of patients; clinically, this manifests as exacerbation in intestinal symptoms following ingestion of dairy products (Cantey *et al.,* 2011). Recovery can take many weeks, even after clearance of the parasite (Cantey *et al.,* 2011). In some patients, persistence of infection is associated with development of malabsorption and weight loss (Ortega and Adam, 1997; Ish-Horowicz *et al.,* 1989). Children with chronic giardiasis may present growth retardation, protuberance of the abdomen, spindly extremities, oedema and pallor. Hypochromic microcytic anaemia is common. One study among Columbian children suggested that giardiasis was a strong predictor of stunted growth (Botero-Garcés *et al.,* 2009).

Chronic illness fraction

Chronic symptoms can develop in up to half of symptomatic individuals. In one study of experimentally infected individuals, 84% had a self-limited illness (mean duration 18 days); the remainder became chronically infected (Nash *et al*., 1987).

Case fatality rates

No mortality has been reported

Increase in human illness potential

Cultural practices and trends drive food selection and preparation, influencing the extent of exposure to parasitic protozoa through food. In Morocco, where untreated wastewater is traditionally used for irrigation, crops were contaminated with *Giardia* cysts (Amahmid, Asmama and Bouhoum, 1999). Giardiasis in resident children was linked to the use of raw wastewater in agriculture (Melloul *et al*., 2002). In some high-income countries, the popularity of raw salads, sushi and other seafood, and of drinks prepared from imported berries, has increased the risk of food-borne cryptosporidiosis and giardiasis (Graczyk, Graczyk and Naprawska, 2011).

Trade relevance

Currently *Giardia* is not considered relevant for trade. However, raising awareness of potential transmission through food, implementing appropriate food safety measures, and the development of cross-border transport protocols may need to be discussed in correspondence with new knowledge and information available about this parasite and its diversity. Consequently, it can be anticipated that food groups, such as fresh fruits and vegetables, may require new food safety controls for these parasites.

Impact on economically vulnerable populations

Children are more frequently infected than adults, particularly those from developing countries and those malnourished. *Giardia* infection in early childhood is associated with poor cognitive function and failure to thrive (Berkman *et al*., 2002).

References

Amahmid, O., Asmama, S. & Bouhoum, K. 1999. The effect of waste water reuse in irrigation on the contamination level of food crops by *Giardia* cysts and *Ascaris* eggs. *International Journal of Food Microbiology,* 49(1-2): 19–26.

Berkman, D.S., Lescano, A.G., Gilman, R.H., Lopez, S. & Black, M.M. 2002. Effects of stunting, diarrhoeal disease, and parasitic infection during infancy on cognition in late childhood: a follow-up study. *Lancet*, 359(9306): 564–571.

Botero-Garcés, J.H., García-Montoya, G.M., Grisales-Patiño, D., Aguirre-Acevedo, D.C. & Alvarez-Uribe, M.C. 2009. *Giardia intestinalis* and nutritional status in children participating in the complementary nutrition program, Antioquia, Colombia, May to October 2006. *Revista do Instituto de Medicina Tropical de São Paulo*, 51(3): 155–162.

Cacciò, S.M. & Ryan, U. 2008. Molecular epidemiology of giardiasis. *Molecular and Biochemical Parasitology*, 160(2): 75–80.

Caeiro, J.P., Mathewson, J.J., Smith, M.A., Jiang, Z.D., Kaplan, M.A. & Dupont, H.L. 1999. Etiology of outpatient pediatric nondysenteric diarrhea: a multicenter study in the United States. *Pediatric Infectious Disease Journal*, 18(2): 94–97.

Cantey, P.T., Roy, S., Lee, B., Cronquist, A., Smith, K., Liang, J. & Beach, M.J. 2011. Study of nonoutbreak giardiasis: novel findings and implications for research. *American Medical Journal*, 124(12): 1175.e1-8. Online. doi: 10.1016/j.amjmed.2011.06.012.

Feng, Y. & Xiao, L. 2011. Zoonotic potential and molecular epidemiology of *Giardia* species and giardiasis. *Clinical Microbiology Reviews*, 24(1): 110–140.

Graczyk, Z., Graczyk, T.K. & Naprawska, A. 2011. A role of some food arthropods as vectors of human enteric infections. *Central European Journal of Biology*, 6(2): 145–149.

Ish-Horowicz, M., Korman, S.H., Shapiro, M., Har-Even, U., Tamir, I., Strauss, N. & Deckelbaum, R.J. 1989. Asymptomatic giardiasis in children. *Pediatric Infectious Disease Journal*, 8(11): 773–779.

Lal, A., Baker, M.G., Hales, S. & French, N.P. 2013. Potential effects of global environmental changes on cryptosporidiosis and giardiasis transmission. *Trends in Parasitology*, 29(2): 83–90

Melloul, A., Amahmid, O., Hassani, L. & Bouhoum, K. 2002. Health effect of human wastes use in agriculture in El Azzouzia (the wastewater spreading area of Marrakesh city, Morocco). *International Journal of Environmental Health Research,* 12(1): 17–23.

Nash, T.E., Herrington, D.A., Losonsky, G.A. & Levine, M.M. 1987. Experimental human infections with *Giardia lamblia*. *Journal of Infectious Diseases,* 156(6): 974–984.

Ortega, Y.R. & Adam, R.D. 1997. *Giardia*: overview and update. *Clinical Infectious Diseases,* 25(3): 545–549.

A7.12 HETEROPHYIDAE AND HETEROPHYIDIASIS

General information

Fish-borne intestinal trematodes (flukes), predominately the Heterophyidae, have many biological and epidemiological traits in common with the liver flukes and usually co-occur (Chai, Murrell and Lymbery, 2005). More than 35 species are reported to be zoonotic; species of *Metagonimus, Haplorchis, Heterophyes* and *Centrocestus* are the most prevalent. The number of species of fish (intermediate host) reported to be susceptible to infection with infective metacercariae is very large, more than 70, including both freshwater and marine species (Chai, 2007). An important epidemiological feature is the wide variety of reservoir hosts for these flukes, including fish-eating birds and wild and domestic mammals, especially cats, dogs and pigs. Human fondness for raw or lightly prepared fish foods is the primary human risk factor, and responsible for the wide geographical distribution of the human infections.

Geographical distribution

Heterophyid infections occur worldwide because of the wide distribution of reservoir and fish host species, and risky human food behaviours that include consuming raw or lightly processed or cooked fish, especially in Asia, but also Europe, Africa, Near East, and North and South America (WHO, 1995).

It has been estimated by WHO (2004) that heterophyids infect 40 to 50 million people worldwide, and that approximately 600 million are at risk for fish-borne flukes. Importantly, it is not possible to accurately determine the number of cases based on clinical and epidemiological data because of diagnostic confusion in distinguishing between heterophyid faecal eggs (the primary detection procedure) and those of the liver flukes in clinical and prevalence surveys. It is likely that under-reporting of intestinal flukes and the over-reporting of the liver flukes (commonly *Clonorchis sinensis* and *Opisthorchis* spp., especially in SE Asia and China). A second reason is that the milder clinical picture with intestinal infections may result in many "hidden infections".

Disease

Disease caused by intestinal flukes (heterophyidiasis) is generally not considered as significant in clinical importance as that of liver fluke infections. This may not be an accurate assessment because heterophyid infections, until recently, have not been widely recognized. More recent reports demonstrate that several heterophyid species can cause significant pathology, although infrequently fatal, in the heart, brain and spinal cord of humans (which may be related to invasion of the circulatory system by worm eggs). Disease is usually related to worm burdens (generally true for most helminth infections in the intestine) and although many infections

are probably sub-clinical, heavy infections are often associated with diarrhoea, mucus-rich faeces, catarrhal inflammation, abdominal pain, dyspepsia, anorexia, nausea and vomiting, the most prominent symptoms being malabsorption and diarrhoea. A recent report on *Haplorchis taichui* infection in Thailand revealed that mucosal ulceration, mucosal and sub-mucosal haemorrhages, fusion and shortening of villi, chronic inflammation, and fibrosis of the sub-mucosa can occur.

Because the extent of intestinal fluke infections have only recently been recognized, there is little basis on which to estimate overall health impact. Case fatality rates especially have not been estimated because disease is usually related to worm burdens and while serious in heavy infections, the majority of epidemiological data suggests most infections are moderate to light, and hence most are probably sub-clinical. A recent estimate of intestinal trematode infections suggested morbidity estimates for DALYs as 83 699 (Fürst, Keiser and Utzinger, 2012). However, this was based on aggregation of all intestinal fluke infections, fish-borne and otherwise, and not specific to just heterophyids.

Trade relevance

Importing countries apply the regulatory standards for safety and quality relevant to parasite contamination similar to that imposed for anisakids and cestodes. For example of these regulations, these are detailed in the US FDA and EC-EUFSA regulations (EU, no date; and Chapter 5 in FDA, no date).

Impact on economically vulnerable populations

Impact is not easily estimated because the communities most at risk consume locally produced fish and are not commonly involved in the large-scale aquaculture that accounts for most exports of fish. However, as poverty levels are reduced in rural areas, the awareness and demand for higher quality and safer fish can be expected to rise; this could have a negative impact on fish farmers who produce for the local or national markets (WHO, 2004).

Other relevant information

Because of the importance in heterophyid epidemiology of non-human reservoir hosts (e.g. fish-eating birds, dogs, cats) (Anh *et al.,* 2009), attempts to change long-entrenched food behaviours of people (i.e. consumption of raw fish) or the application of human mass drug treatment strategies are not likely to have a sustainable impact on fish infections. Instead, efforts should be made to improve fish production practices to control risk of fish infections.

References

Anh, L.T.N., Phuong, T.N., Murrell, K.D., Johansen, M.V., Dalsgaard A., Thu, T.L, Chi, K.T.B. & Thamsborg, S.M. 2009. Animal reservoir hosts and fish-borne zoonotic trematode infections on fish farms, Vietnam. *Emerging Infectious Diseases*, 15: 540–546.

Chai, J.Y. 2007. Intestinal flukes. pp. 53–115 (Ch. 2), in: K.D. Murrell and B. Fried (editors). *Food-borne Parasitic Zoonoses*. Springer, New York, USA.

Chai, J.Y., Murrell, K.D. & Lymbery, A. 2005. Fishborne zoonoses: status and issues. *International Journal of Parasitology*, 35: 1233–1254.

Chai, J.Y., Murrell, K.D. & Lymbery, A.J. 2005. Fish-borne parasitic zoonoses: status and issues. *International Journal for Parasitology,* 35(11-12): 1233–1254.

EU (European Union). No date. EU import conditions for seafood and other fishery products. Available at http://ec.europa.eu/food/international/trade/im_cond_fish_en.pdf Accessed 2013-06-21.

FDA (Federal Drug Administration). No date. Chapter 5 – Parasites, in: *Fish and Fishery Products Hazards and Controls Guidance*. 4th Edition, November 2011. Available at http://www.fda.gov/ downloads/Food/GuidanceRegulation/UCM252393.pdf Accessed 2013-08-24

Fürst, T., Keiser, J. & Utzinger, J. 2012. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 12(3): 210–221.

WHO (World Health Organization). 1995. Control of food-borne trematode infections. *WHO Technical Reports Series,* No. 849. 157 p.

WHO. 2004. Report of the Joint WHO/FAO Workshop on food-borne trematode infections in Asia. Ha Noi, Viet Nam, 26–28 November 2002. World Health Organization Regional office for the Western Pacific. 158 p. Available at http://whqlibdoc.who.int/wpro/2004/RS_2002_GE_40(VTN).pdf Accessed 2013-06-21.

A7.13 OPISTHORCHIIDAE

General information

Opisthorchiidae is a group of fish-borne zoonotic trematodes that includes the liver flukes *Opisthorchis viverrini*, *Clonorchis sinensis* and *O. felineus*. The life cycle of the liver fluke involves freshwater snails (*Bithynia* spp.) as first intermediate hosts, cyprinid fish as second intermediate hosts, humans as the definitive hosts, and cats and dogs as reservoir hosts. Humans are infected by consumption of undercooked fish containing viable metacercariae, and the infection induces hepatobiliary pathology that eventually leads to bile duct cancer, cholangiocarcinoma (CCA), the leading cause of death in Asia. Because of a strong link to CCA, *O. viverrini* and *C. sinensis* are known as type 1 carcinogens (IARC, 2012).

It is estimated that the number of people infected with liver fluke may be as many as 25 million with 10 million for *O. viverrini*, 15 million for *C. sinensis* and about 1 million for *O. felineus* (WHO 1995). Up to 700 million (10% of the global population) are at risk of infection when the third species, *O. felineus*, is considered (Keiser and Utzinger, 2005). Their contribution to the global disease burden in terms of disability-adjusted life years (DALYs) reflects substantial impact on health and well-being of the infected victims in developing countries (Fürst, Keiser and Utzinger, 2012). Infection by the liver fluke causes various non-specific gastrointestinal symptoms in some infected individuals, which are related to the intensity of infection. In *C. sinensis* alone, an estimated 2.5 million people may have some form of illness (Hong and Fang, 2012).

Geographical distribution (endemic regions)

Human liver flukes cause public health problems in many parts of the world, particularly in Asia and Europe. *C. sinensis* is endemic in southern China, Korea, Taiwan, northern Viet Nam and also in Russia. *O. viverrini* is endemic in the Lower Mekong Basin, including Thailand, Lao People's Democratic Republic (Lao PDR), Cambodia and central Viet Nam (WHO, 1995). *O. felineus* is found in the former USSR and in Central Eastern Europe, and a recent review indicated that it is endemic in 13 European countries (Pozio *et al.,* 2013).

Disease

Liver fluke infections primarily induce chronic inflammatory diseases of the hepatobiliary system and may subsequently cause bile duct cancer (cholangiocarcinoma). Benign hepatobiliary diseases are characterized by cholangitis, obstructive jaundice, hepatomegaly, periductal fibrosis, cholecystitis, and cholelithiasis. Most of these manifestations are mild and asymptomatic. However, once advanced CCA develops, clinical manifestation such as jaundice occurs in approximately half of the cases, while the other half may have no specific symptoms.

Severity of acute morbidity

There is little evidence of acute morbidity and it is rarely reported. This is probably due to the nature of low dose infection over many years rather than a heavy or massive infection. Acute symptoms may occur in cases with heavy infection, including epigastric pain and tenderness, fever, jaundice and diarrhoea.

Severity of chronic Morbidity

Chronic morbidity is more common in liver fluke infections since the parasite survives more than 10 years in humans. The illness may occur in a small percentage of infected individuals and includes weakness, flatulence or dyspepsia, and abdominal pain in the right upper quadrant (Upatham *et al.,* 1984). However, preclinical hepatobiliary abnormalities can be determined by radiological examination such as ultrasonography, MRI and CT. These include advanced periductal fibrosis, chronic cholecystitis, gall stones, pyogenic cholangitis, abscesses and cholangiocarcinoma.

Chronic illness fraction

Chronic illness occurs in a small fraction of infected people and some of the infected individuals (less than 10%) may develop severe disease and also cholangiocarcinoma (CCA). CCA is a complication of a liver fluke infection (opisthorchiasis or clonorchiasis) but once it develops, it is fatal and curative treatment is not available. Unlike hepatocellular carcinoma (hepatoma), a specific early marker or biomarker for diagnosis is not available for CCA. Several risk factors for CCA are documented and in addition to the liver fluke infection by *O. viverrini* or *C. sinensis*, cholangiocarcinoma associates with other conditions such as primary schlerosing cholangitis, gall stones as well as viral hepatitis.

Case fatality rates

Case fatality as a result of CCA is high and in the endemic areas of opisthorchiasis, such as in northeast Thailand, the district-based incidence of CCA varied from 90 to 300 per 100 000 (Sriamporn *et al.,* 2004). Most CCA cases have poor prognosis and even with surgical treatment survival is short, depending on the stage of cancer and also the health care system. Most CCA patients survive for less than 5 years.

Increase in human illness potential

Generally the risk of infection is confined to the endemic localities where active transmission occurs with ongoing transmission in human and intermediate hosts (snail and fish). However, with cross-border migration and aquaculture trading, there is a possibility that it may pose a threat outside endemic areas. Moreover, infection of the liver fluke is normally contracted by ingestion of native fish species (mostly cyprinid), but aquaculture fishery has been increasing and several species of cyprinid carps are cultured, and hence may have potential for transmission of the liver flukes.

Trade relevance

Currently, the liver fluke has little trade relevance because the main sources of infection are native species of fish circulated locally in endemic countries. Aquaculture of fresh-water cyprinid or fin fish (low-value aquaculture) are often operated by small-scale farmers to serve domestic consumers. Generally, this farm practice does not meet export standards set by importing countries such as EU, Japan and United States of America, and thus may have low or little relevance for international trade. However, evidence in aquaculture in Viet Nam and China indicated potential contamination with zoonotic fish-borne trematodes, including *C. sinensis* in aquaculture for international trade. Therefore, import of fishery products from the liver fluke-endemic areas, particularly Asia, may create a risk of infection to consumers. As such, prevention is required from the farm level and throughout the market chain.

Impact on economically vulnerable populations

The impact on vulnerable populations in endemic areas is high. There are potentially severe socio-economic consequences if the infected people finally develop CCA and if they are income earners in the family and community. Currently, no data on healthcare costs for CCA treatment in endemic countries (i.e. Thailand and Lao PDR) are available, although it can be expected that the cost of such healthcare might be high since treatment of CCA either by surgery or palliative care is costly.

Other relevant information

Concerted and comprehensive effort is required for sustainable prevention and control of the liver flukes and is vital for reduction of CCA. Although the liver fluke is recognized as one of the Neglected Tropical Diseases, the problem is difficult to solve because it links not only with public health aspects but also socio-economic and cultural dimensions. Therefore, in addition to conventional chemotherapy by mass drug administration, health education, including on food safety issues, to raise awareness starting at school-age-level as well as to community members is needed for successful outcomes.

References

Fürst, T., Keiser, J. & Utzinger, J. 2012. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 12(3): 210–221.

Hong, S.T. & Fang, Y. 2012. *Clonorchis sinensis* and clonorchiasis: an update. *Parasitology International,* 61(1): 17–24.

IARC (World Health Organization International Agency for Research On Cancer). 2012. A review of human carcinogens (6 vols). Monographs on the Evaluation of Carcinogenic Risks to Humans. *IARC Monograph*, 100.

Keiser, J. & Utzinger, J. 2005. Emerging food-borne trematodiasis. *Emerging Infectious Diseases,* 11(10): 1507–1514.

Pozio, E., Armignacco, O., Ferri, F. & Gomez-Morales, M.A. 2013. *Opisthorchis felineus,* an emerging infection in Italy and its implication for the European Union. *Acta Tropica*, 126(1): 54–62.

Sriamporn, S., Pisani, P., Pipitgool, V., Suwanrungruang, K., Kamsa-ard, S., & Parkin, D.M. 2004. Prevalence of *Opisthorchis viverrini* infection and incidence of cholangiocarcinoma in Khon Kaen, northeast Thailand. *Tropical Medicine & International Health,* 9(5): 588–594.

Upatham, E.S., Viyanant, V., Kurathong, S., Rojborwonwitaya, J., Brockelman, W.Y., Ardsungnoen, S., Lee, P. & Vajrasthira, S. 1984. Relationship between prevalence and intensity of *Opisthorchis viverrini* infection, and clinical symptoms and signs in a rural community in northeast Thailand. *Bulletin of the World Health Organization,* 62(3): 451–461.

WHO (World Health Organization). 1995. Control of food-borne trematode infections. *WHO Technical Reports Series,* No. 849. 157 p.

A7.14 *PARAGONIMUS* SPP.

General information

Paragonimiasis, also recognized as endemic haemoptysis, oriental lung fluke infection, etc., is a food-borne parasitic infection caused by the lung fluke of the family Paragonimidae that triggers a sub-acute to chronic inflammatory disease of the lung. Among the 30 species of trematodes (flukes) of the genus *Paragonimus* that are able to infect humans and animals, the most common agent for human infection is *P. westermani* (John and Petri, 2006: 198).

There are about 15 species of *Paragonimus* known to infect humans. *P. heterotremus* is the aetiologic agent of human paragonimiasis in P.R. China, Lao PDR, Viet Nam and Thailand. Species of *Paragonimus* are reported to infect humans in other places, including *P. africanus* in Africa and *P. kellicotti* in North America.

P. westermani was reported for the first time in the lungs of a human followed by recognition of the eggs in the sputum in 1880. The intermediate host and details of the parasite's life cycle were reported between 1916 and 1922 (Manson, 1881; Cox, 2002).

Paragonimus has two agents of intermediate hosts as well as humans in its life cycle. Intermediate hosts are various snails and crab species. Transmission of the parasite *P. westermani* to humans primarily occurs through the consumption of raw or undercooked seafood. Diagnosis is based on stool or sputum examination for the parasite's eggs until 2 to 3 months after infection. However, eggs are also occasionally encountered in effusion fluid or biopsy material. Antibody detection is useful in light infections and in the diagnosis of extrapulmonary paragonimiasis. Praziquantel is the drug of choice, with recommended dosage of 75 mg/kg per day, divided into 3 doses over 2 days (Pachucki *et al.*, 1984).

Geographical distribution

Human paragonimiasis occurs in three endemic focal areas: Asia (P.R. China, Japan, Korea, Lao PDR, Philippines, Viet Nam, Taiwan and Thailand); South and Central America (Ecuador, Peru, Costa Rica and Columbia); and Africa (Cameroon, Gambia and Nigeria) (Sripa *et al.*, 2010). There have been some reports of the disease in the United States of America during the past 15 years because of the increase in immigrants.

Approximately 200 million people have been exposed and 20 million people have been infected worldwide with this parasite (WHO, 1995). The total number of infections can be seen in Table 1. Some detailed prevalences (Sripa *et al.*, 2010) are: China, 4.1–5.1% in 24 provinces; Viet Nam, 0.5–15% in 10/64 provinces; Thailand,

cases reported in 23/68 provinces; Japan, cases reported with over 200 cases; Philippines, 27.2–40% in some areas; and India, endemic to northeastern states, up to 50%.

Disease

Severity of acute morbidity

The acute phase consists of various manifestations, including diarrhoea, abdominal pain, fever, cough, urticaria, hepatosplenomegaly, pulmonary abnormalities and eosinophilia (CDC, no date).

Severity of chronic morbidity

The chronic phase might embrace pulmonary manifestations such as cough, expectoration of discoloured sputum, haemoptysis and chest radiographic abnormalities. It is possible that the disease could be confused with TB. Flukes occasionally invade and reside in the pleural space without parenchymal lung involvement. Extra-pulmonary locations of the adult worms result in more severe manifestations, especially when the brain is involved. Extra-pulmonary paragonimiasis is rarely seen in humans because the worms migrate to the lungs, but cysts can develop in the brain and abdominal adhesions resulting from infection have been reported. Haemoptysis is the most common sign of the disease.

Table 1 shows the number of cerebral infections in patients infected with paragonimiasis. Accordingly, the three parameters of Years Lost to Disability (YLD), Years of Life Lost (YLL) and Disbility-adjusted Life Years (DALYs) can be seen in this table which shows the importance of the disease.

Chronic illness fraction

No reports could be found on chronic illness cases, but column 3 in Table 1 depicts an estimation of cases that might result in chronic infection.

Case fatality rates

According to Table 1 and based on Global Burden of Disease (GBD) 2010 study regions, in 2005 the number of global deaths would have been 244 cases (Fürst, Keiser and Utzinger, 2012).

Increase in human illness potential

There are many reports that show the increasing risk of illness potential in endemic regions. Many cases of eating roast crabs in the field amongst schoolchildren have been reported, as well as frequent consumption of seasoned crabs by adult villagers, and papaya salad with crushed raw crab (Stanford University, no date; Song *et al.,* 2008). In addition to this characteristic feature of the villagers' food culture, area residents drink fresh crab juice as a traditional cure for measles, and this was also

TABLE 1 Summary of parasite-specific and region-specific modelled point estimates for paragonimiasis in 2005, based on Global Burden of Disease (GBD) 2010 study regions

Regions	Total no. infected	No. of heavy infections	No. of cerebral infections	No. of deaths	YLD	YLL	DALYs
Asia, east (China)	22 320 640	4 909 332	159 953	235	175 997	12 442	188 439
Latin America, Andean (Ecuador, Peru)	630 173	131 345	4420	8	6 960	443	7 403
Asia, southeast (Laos)	203 334	43 876	1 467	1	780	87	867
Asia Pacific, high income (South Korea)	957	176	20	0	1	0	1
Global	23 155 105	5 084 729	165 860	244	183 738	12 972	196 710

Notes: YLD = Years Lost to Disability; YLL = Years of Life Lost; DALY = Disbility-adjusted Life Years.
Source: Fürst, Keiser and Utzinger, 2012.

thought to constitute a route for infection. *Kung Plah*, *Kung Ten* (raw crayfish salad) and *Nam Prik Poo* (crab sauce) are popular and widely consumed dishes in Thailand. *Kinagang*, which is semi-cooked fresh-water mountainous crabs, are eaten as an appreciated dish in the Philippines. In Viet Nam, people have the habit of eating undercooked crabs. All these data show the increasing risk of the disease in regions where eating crab is a part of the culture.

When live crabs are crushed during preparation, the metacercariae may contaminate the fingers or utensils of the kitchen staff. Accidental transfer of infective cysts can occur via food preparers who handle raw seafood and subsequently contaminate cooking utensils and other foods (Yokogawa, 1965). Consumption of animals that feed on crustaceans can also transmit the parasite, such as eating raw boar meat. Food preparation techniques such as pickling and salting do not neutralize the causative agent. In some countries, crabs are soaked in wine for 3–5 minutes, and so called "drunken crabs" are eaten by people or cats and dogs; hence it is an important risk factor for transmission of the disease (Yokogawa, 1965). In the United States of America, significant behavioural and recreational risk factors

include eating raw crayfish while on canoeing trips on local rivers, eating raw crayfish while on canoeing trips in Missouri, and eating raw crayfish while intoxicated (Diaz, 2011).

In addition, raw or undercooked meat of paratenic hosts such as boar, bear, wild pig or rat, where juvenile worms can survive in the muscles for years, is also an important source of human infection. Animals such as pigs, dogs and a variety of feline species can also harbour *P. westermani* (CDC, No date).

Trade relevance

Paragonimiasis is a neglected disease that has received relatively little attention from public health authorities. Interest in *Paragonimus* species outside endemic areas is increasing because of the risk of infection through consumption of crustaceans traded far from their point of origin in today's globalized food supply. No trade limitations currently exist with regard to *Paragonimus* spp., but it might be of importance for the international trade of seafood from endemic areas.

Impact on economically vulnerable populations

In many countries endemic for paragonimiasis, it is very difficult to change the habits of consuming raw or semi-cooked crabs and crayfish. Unfortunately, in some poor countries involved with this disease, intersectoral collaboration between governmental sectors, such as agriculture, aquaculture, public health and education and finance, is weak and this can cause an increase in the disease rate.

References

CDC (Centers for Disease Control). No date. Parasites and Health: Paragonimiasis. Available at http://www.dpd.cdc.gov/DPDx/html/Frames/MR/Paragonimiasis/body_Paragonimiasis_page2.htm Accessed 2013-06-21.

Cox, F.E.G. 2002. History of human parasitology. *Clinical Microbiology Reviews*, 15(4): 595–612.

Diaz, J.H. 2011. Boil before eating: paragonimiasis after eating raw crayfish in the Mississippi River Basin. *Journal of Louisiana State Medical Society*, 163(5): 261–266.

Fürst, T., Keiser, J. & Utzinger, J. 2012. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infectious Diseases,* 12(3): 210–221.

John, D.T. & Petri, W.A. (editors). 2006. *Markell and Voge's Medical Parasitology.* 9th edition. Elsevier. 480 p.

Manson, P. 1881. *Distoma ringeri*. *Medical Times Gazette*, 2: 8–9.

Pachucki, C.T., Levandowski, R.A., Brown, V.A., Sonnenkalb, B.H. & Vruno, M.J. 1984. American Paragonimiasis treated with praziquantel. *New England Journal of Medicine*, 311: 582–583.

Song, H.-Y., Min, D.-Y., Rim, H.-J., Vonghachack Youthanavanh, Bouakhasith Daluny, Vongsouvan Sengdara, Banouvong Virasack & Phommasak Bounlay. 2008. Skin test for paragonimiasis among schoolchildren and villagers in Namback District, Luangprabang Province, Lao PDR. *Korean Journal of Parasitology,* 46(3): 179–182.

Sripa, B., Kaewkes, S., Intapan, P.M., Maleewong, W. & Brindley, P.J. 2010. Food-borne trematodiases in Southeast Asia epidemiology, pathology, clinical manifestation and control. *Advances in Parasitology*, 72: 305–350.

Stanford University. No date [online]. *Paragonimus westermani*. http://www.stanford.edu/group/parasites/ParaSites2009/FatimaHassan_Paragonimus/FatimaHassan_Paragonimus%20westermani.htm Accessed 2013-08-24.

WHO (World Health Organization). 1995. Control of food-borne trematode infections. *WHO Technical Reports Series,* No. 849. 157 p.

Yokogawa, M. 1965. *Paragonimus* and paragonimiasis. *Advances in Parasitology*, 3: 99–158.

A7.15 *SARCOCYSTIS* SPP.

General information

The genus *Sarcocystis* consists of obligate intracellular protozoan parasites with a two-host life cycle described as a prey-predator, herbivore-carnivore or intermediate-definitive host relationship. Humans can serve as intermediate hosts for some species of *Sarcocystis* and as definitive hosts for other species. Care must be taken to understand these roles and the potential sources of infection for each.

In the intermediate host, sarcocysts develop in skeletal muscles, tongue, oesophagus, diaphragm and cardiac muscle, and occasionally in spinal cord and brain (Fayer, 2004a, b). Mature sarcocysts of different species vary in size from microscopic to macroscopic, and in the structure of the wall that surrounds 100s to 1000s of crescent-shaped bodies called bradyzoites. After flesh (meat) from the intermediate host is eaten by the carnivore definitive host the sarcocyst wall is digested, bradyzoites are liberated and enter cells in the intestine. Each bradyzoite develops into a sexual stage and after fertilization the oocyst stage is formed. Mature oocysts (containing two sporocysts each with four sporozoites) are excreted in the faeces and contaminate the environment. When a susceptible intermediate host ingests the oocysts in water or food they pass to the small intestine, where the sporozoites are released. Sporozoites penetrate the gut epithelium and enter endothelial cells in blood vessels throughout the body giving rise to several generations of asexual stages. The number of asexual generations and their primary sites of development differ for each species of *Sarcocystis*. The terminal generation of asexual development occurs in muscle cells. Maturation varies with the species and can take 2 months or more until bradyzoites form and sarcocysts become infectious for the definitive host. Sarcocysts may persist for months or years.

Geographical distribution

Sarcocystis species have been found as sarcocysts in the muscles of fish, reptiles, birds, and mammals worldwide.

Prevalence in food animals

Prevalence data for all *Sarcocystis* infections must be interpreted carefully. They often reflect the findings of physicians, public health workers, veterinarians or scientists with specific interests. Much data are unreported and no truly large-scale population surveys have been conducted. Based on examination of tissues from abattoirs, a high percentage of cattle worldwide have been found infected with *S. cruzi* (infectious from cattle only to canines), the most prevalent species. Because *S. hominis* (infectious from cattle to humans) and *S. hirsuta* (infectious from cattle to felines) are difficult to distinguish except by electron microscopy, some prevalence data may be erroneous. *S. hominis* has not been detected in the United States

of America, whereas up to 63% of cattle in Germany have been reported to be infected. *S. suihominis* (infectious from pigs to humans) was found more prevalent in Germany than Austria, but little information is available from other countries. In Brazil, all 50 samples of raw *kibbe* (beef) from 25 Arabian restaurants in Sao Paulo contained sarcocysts (Pena, Ogassawara and Sinhorini, 2001). Based on wall structure, *S. hominis, S. hirsuta* and *S. cruzi* were found in 94, 70 and 92% of the samples. The overall prevalence of *Sarcocystis* in pigs appears low, at 3–36% worldwide. *S. suihominis* and *S. hominis* have been reported in slaughtered pigs and cattle, respectively, raised in Japan (Saito *et al.,* 1998, 1999).

Although humans acquire gastrointestinal sarcocystosis by ingesting raw or undercooked meat from cattle or pigs harbouring mature cysts of *S. hominis* or *S. suihominis*, other species of meat animals that harbour *Sarcocystis* include sheep, goats, bison, water buffalo, yaks, a variety of wild ruminants, horses, camels, llamas and species of pigs other than the domesticated *Sus scrofa* (Dubey, Speer and Fayer, 1989). Many species of reptiles, birds, and mammals that harbour sarcocysts serve as food animals in various parts of the world (Dubey, Speer and Fayer, 1989).

Prevalence in humans

Based on limited, somewhat focal surveys, intestinal sarcocystosis in humans was reported as more prevalent in Europe than any other continent (Dubey, Speer and Fayer, 1989). A prevalence of 10.4% of faecal specimens was found in children in Poland and 7.3% of samples from Germany. Of 1228 apprentices from the Hanoi-Haiphong area of Viet Nam who worked in Central Slovakia in 1987–1989, 14 (1.1%) had sporocysts of *Sarcocystis* spp. detected in their stool (Straka *et al.,* 1991). *Kibbe* positive for *S. hominis* was fed to 7 human volunteers; 6 excreted sporocysts, 2 developed diarrhoea (Pena, Ogassawara and Sinhorini, 2001). After eating raw beef, a patient in Spain with abdominal discomfort, loose stools, and sporulated oocysts in the faeces was diagnosed with *S. hominis* (Clavel *et al.,* 2001). In Tibet, where *Sarcocystis* was detected in 42.9% of beef specimens examined from the marketplace, *S. hominis* and *S. suihominis* were found in stools from 21.8% and 0–7% of 926 persons, respectively (Yu *et al.*, 1991).

Muscular sarcocystosis in humans is rarely reported, with only about 100 cases until recently (Fayer 2004a, b). In such cases, humans harbour the sarcocyst stage and therefore serve as the intermediate host. Based on all other *Sarcocystis* life cycles, infected human tissues must be eaten by a carnivore to complete the life cycle. Because there is no known predatory or scavenging cycle in nature in which human tissues are eaten regularly by carnivores, humans most likely become infected accidentally by ingestion of food or water contaminated with faeces from a carnivore that participates in a primate-carnivore cycle involving an unknown

species of *Sarcocystis*. Most have been from Asia and Southeast Asia, although cases from Central and South America, Africa, Europe and the United States of America have been reported (McLeod *et al.,* 1980; Mehrotra *et al.,* 1996). An outbreak in 7 persons of a 15 member military team occurred in Malaysia (Arness *et al.,* 1999). During 2011, 32 patients 21–59 years of age, all residents in Europe, complained of mild to severe myalgia with onset a median of 11 days after departing Tioman Island, Malaysia (Esposito, 2011). All cases consumed ice in beverages, 7 (70%) brushed teeth with tap water, and 6 (60%) ate fresh produce.

Disease

Humans serve as definitive hosts after eating undercooked or raw meat containing mature cysts. *S. hominis* is acquired from eating beef, and *S. suihominis* is acquired from eating pork. The cycles must be human-cattle-human and human-pig-human. Like most other species of *Sarcocystis*, *S. hominis* and *S. suihominis* are genetically programmed to complete their life cycles in specific intermediate hosts or within closely related host species. For example, sporocysts of *S. hominis* infect cattle and not pigs whereas those of *S. suihominis* infect pigs but not cattle.

Human volunteers that ate raw beef containing *S. hominis* became infected and shed oocysts in their faeces. One person who became ill 3 to 6 hours after eating the beef had nausea, stomach ache and diarrhoea (Aryeetey and Piekarski, 1976; Rommel and Heydorn, 1972). Other volunteers who ate raw pork containing *S. suihominis* had signs after 6 to 48 hours, including bloat, nausea, loss of appetite, stomach ache, vomiting, diarrhoea, difficult breathing and rapid pulse (Rommel and Heydorn, 1972; Heydorn, 1977).

Humans can also serve as intermediate hosts with asexual stages developing throughout the body and cysts forming in striated muscles. In such cases, humans apparently are accidental hosts because it is extremely rare that carnivores eat humans and unless that happens frequently a cycle cannot be maintained. Vasculitis, fever, myalgias, bronchospasm, pruritic rashes, lymphadenopathy, and subcutaneous nodules associated with eosinophilia, elevated erythrocyte sedimentation rate, and elevated creatinine kinase levels can last for weeks to several months (Fayer, 2004a, b). An American who, 4 years earlier, travelled extensively in Asia, had for over a year intermittent lesions on his arms, legs, soles of his feet, and trunk, beginning as subcutaneous masses associated with overlying erythaema (MacLeod *et al.,* 1980).

Trade relevance

Only those meat products that contain grossly visible cysts are recognized as infected. Although rarely reported in recent decades, they have been found predominantly in sheep in North America and recently in alpacas in Peru, but the

impact on trade is unknown. Eosinophilic myositis (a greenish sheen on portions of beef carcasses that resulted in condemnation of parts or entire carcasses) was once attributed solely to *Sarcocystis* infections, but other causes may be possible. Some countries might have import restrictions related to sarcocysts in meat, which might complicate trade in animals or meat due to the lack of diagnostic tools.

Impact on economically vulnerable populations

Sarcocysts have been identified in carcasses of alpacas in the altiplano of Peru, which have been found unfit for consumption and of no commercial value, resulting in economic loss to local farmers (Vitaliano Cama, 2013, pers. comm.). Documentation of the impact is not available.

References

Arness, M.K., Brown, J.D., Dubey, J.P., Neafie, R.C. & Granstrom, D.E. 1999. An outbreak of acute eosinophilic myositis due to human *Sarcocystis* parasitism. *American Journal of Tropical Medicine and Hygiene,* 61: 548–553.

Aryeetey, M.E. & Piekarski, G. 1976. Serologische *Sarcocystis*-studien an Menschen und Ratten. *Zeitschrift fur Parasitenkunde*, 50: 109–124.

Clavel, A., Doiz, O., Varea, M., Morales, S., Castillo, F.J., Rubio, M.C. & Gomez-Lus, R. 2001. Molestias abdominales y heces blandas en consumidor habitual de carne de vacuno poco cocinada. *Enfermedades Infecciosas y Microbiología Clínica,* 19: 29–30.

Dubey, J.P., Speer, C.A. & Fayer, R. 1989. Sarcocystis *of animals and man.* CRC Press, USA. 215 p.

Esposito, D.H. 2011. Muscular sarcocystosis in travelers returning from Tioman Island, Malaysia – 2011. Presented at International Congress on Emerging Infectious Disease (Abstract).

Fayer, R. 2004a. *Sarcocystis* of humans. In: D.S. Lindsay and L.M. Weiss (editors). *Opportunistic Infections:* Toxoplasma*,* Sarcocystis *and* Microsporidia. Kluwer Academic Publishers, Boston, USA. 256 p.

Fayer, R. 2004b. *Sarcocystis* in human infections. *Clinical Microbiology Reviews,* 17(4): 894–902.

Heydorn, A.O. 1977. Sarkosporidien enfiziertes Fleisch als mogliche Krankheitsurache fur den Menschen. *Archiv für Lebensmittelhygiene,* 28: 27–31.

McLeod, R., Hirabayashi, R.N., Rothman, W. & Remington, J.R. 1980. Necrotizing vasculitis and *Sarcocystis*: a cause and effect relationship? *Southern Medical Journal*, 73(10): 1380–1383.

Mehrotra, R., Bisht, D., Singh, P.A., Gupta, S.C. & Gupta, R.K. 1996. Diagnosis of human *Sarcocystis* infection from biopsies of the skeletal muscle. *Pathology*, 28: 281–282.

Pena, H.F., Ogassawara, S. & Sinhorini, I.L. 2001. Occurrence of cattle *Sarcocystis* species in raw kibbe from Arabian food establishments in the city of Sao Paolo, Brazil, and experimental transmission to humans. *Journal of Parasitology*, 87: 1459–1465.

Rommel, M. & Heydorn, A.O. 1972. Beitrage zum Lebenszyklus der Sarkosporidien. III. *Isospora hominis* (Railiet und Lucet, 1891) Wenyon, 1923, eine Dauerform des Sarkosporidien des Rindes und des Schweins. *Berliner und Münchener Tierärztliche Wochenschrift*, 85: 143–145.

Saito, M., Shibata, Y., Ohno, A., Kubo, M., Shimura, K. & Itagaki, H. 1998. *Sarcocystis suihominis* detected for the first time from pigs in Japan. *Japan. Journal of Veterinary Medical Science,* 60: 307–309.

Saito, M., Shibata, Y., Kubo, M., Sakakibara, I., Yamada, A. & Itagaki, H. 1999. First isolation of *Sarcocystis hominis* from cattle in Japan. *Japan. Journal of Veterinary Medical Science*, 61: 307–309.

Straka, S., Skracikova, J., Konvit, I., Szilagyiova, M. & Michal, L. 1991. *Sarcocystis* species in Vietnamese workers. *Ceskoslovenska Epidemiologie Mikrobiologie Immunologie*, 40: 204–208.

Yu, S. 1991. [Field survey of *Sarcocystis* infection in the Tibet autonomous region] [In Chinese] *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*, 13: 29–32.

A7.16 *SPIROMETRA* SPP.

General information

Sparganosis is one of the rare forms of metacestode infections caused by the pseudophyllidean tapeworms of the genus *Spirometra*. The plerocercoid larvae of three species of *Spirometra* namely *Spirometra mansoni* (or *Spirometra erinaceieuropaei*), *S. mansonoides* and *S. proliferum* are implicated in human disease (Khurana *et al.,* 2012).

The adult worm inhabits the small intestine of felines, which are the usual definitive hosts, although adult worms have also been reported in the human intestinal tract (Wang, Tang and Yang, 2012). The adult cestode worms are hermaphrodites and consist of scolex with a pair of grooves resembling lips and several proglottids. The terminal proglottid releases numerous ovoid eggs through the uterine pore. The eggs hatch in water to liberate the ciliated, free swimming larva called the coracidium. The coracidium is ingested by the freshwater crustacean *Cyclops*, the first intermediate host in which the procercoid larva is formed. The procercoid larva develops into the plerocercoid larva in the second intermediate hosts, the amphibians or reptiles that acquire the infection on ingesting the infected *Cyclops*. Humans contract sparganosis either by drinking water containing infected copepods or by the ingestion of inadequately cooked meat of the infected amphibians or reptiles containing the plerocercoid larva. Practices such as application of frog flesh or blood as poultices on open wounds can also cause sparganosis (Parija, 2011).

Geographical distribution

Although cases of sparganosis has been reported sporadically from numerous countries across the world, China and a few South East Asian countries, including Thailand, South Korea and Viet Nam, contribute the majority of the case load. From 1927 to 2011, more than 1000 cases of sparganosis have been reported from China (Li *et al.*, 2011). Thailand reported 52 cases in the period 1943 to 2010. The major reason for this geographical predilection is the local social and cultural practices (Anantaphruti, Nawa and Vanvanitchai, 2011).

Studies from China show that around 30% of the wild frogs and 30% of the frogs sold in markets for consumption were infected with any of the three species of *Spirometra*. Also, faecal examination of stray dogs and cats in one of the provinces of China showed that around 20% of the stray dogs and over 30% of the stray cats had eggs of *Spirometra* (Cui *et al.,* 2011).

Even though the worm, its hosts and the favourable ecological setting are present, sparganosis is a rare entity in India (Saleque, Juyal and Bhatia, 1990). Only five cases of sparganosis have been reported to date from India: two cases of cerebral

sparganosis, two cases of visceral sparganosis and a case of ocular sparganosis. (Khurana *et al.,* 2012; Sundaram, Prasad and Reddy, 2003; Duggal *et al.,* 2011; Kudesia *et al.,* 1998; Sen *et al.,* 1989). The most probable reason for the low prevalence in India would be the absence of practices such as consumption and poulticing of frog meat.

Disease

The disease in humans is due to the migration of the plerocercoid larvae from the intestine to different sites of the body. Most common localizations of sparganum are in the subcutaneous connective tissue and superficial skeletal muscles, where it forms nodular lesions that are usually painful and associated with pruritis (Qin, Feng and Zheng, 2011). Other manifestations include ocular, cerebral and visceral sparganosis.

Ocular sparganosis clinically presents as redness and oedema of the eyelids and conjunctivas; forward displacement of the eyeball from the orbit (proptosis); subconjunctival granulomatous lesions; and migratory hyperaemic masses of the eyelid or conjunctiva (Ye *et al.,* 2012). The clinical manifestations of cerebral sparganosis resemble that of brain tumour, with seizures, headache or focal neurological disturbances (Finsterer and Auer, 2012). Migration of the larvae to internal organs leads to visceral sparganosis. Although the preferred localizations are the intestinal wall, perirenal fat and the intestinal wall, along with its peritoneal attachments (mesentry), virtually any organ can be affected. Sparganosis of liver, lung, pericardium, breast and scrotum have been reported (Khurana *et al.,* 2012; Huang, Gong and Lu, 2012; Lee *et al.*, 2011; Hong *et al.*, 2010). Disseminated sparganosis is a rare entity caused by *S. proliferum*, whose sparganum is pleomorphic with irregular branches and proliferative buds that detach and migrate to different sites, where they repeat the process and invade other organs (Stief and Enge, 2011).

While sparganosis is rarely fatal, it causes significant morbidity, which manifests acutely as in ocular and visceral forms, while cerebral sparganosis can result in chronic neurological sequelae (Qin, Feng and Zheng, 2011). In mainland China and Guangdong province, where most cases of the disease has been reported, sparganosis has been associated with significant morbidity and work absenteeism (Li *et al.*, 2011). Treatment includes the surgical removal of worm or nodule, with or without administration of anti-parasitic agents such as pyquiton or metronidazole (Anon., 1990).

Trade relevance and impact on vulnerable populations

Sparganosis is a significant disease of the eastern world due to the habit of eating frog meat and the usage of frog muscles as poultices. In other parts of the world it occurs as a result of drinking raw water containing infected *Cyclops*. As the disease

has a wide variation in clinical presentation, it is often misdiagnosed or neglected (Cui *et al.,* 2011). Increased public awareness about the risks associated with eating or poulticing raw frog and strengthened food safety measures are needed to control the disease transmission in endemic regions (Li *et al.*, 2011). Export of frog meat from endemic regions to other parts of the world might be restricted due to *Spirometra* infections.

References

Anantaphruti, M.T., Nawa, Y. & Vanvanitchai, Y. 2011. Human sparganosis in Thailand: an overview. *Acta Tropica*, 118(3): 171–176.

Anon[ymous]. 1990. Helminthic infections. pp. 235–236, in: *Review of Parasitic Zoonoses*. 1st ed. A.I.T.B.S. Publishers Distributors, New Delhi, India.

Cui, J., Lin, X.M., Zhang, H.W., Xu, B.L. & Wang, Z.Q. 2011. Sparganosis, Henan Province, central China. *Emerging Infectious Diseases,* 17(1): 146–147.

Duggal, S., Mahajan, R.K., Duggal, N. & Hans, C. 2011. Case of sparganosis: a diagnostic dilemma. *Indian Journal of Medical Microbiology,* 29(2): 183–186.

Finsterer, J. & Auer, H. 2012. Parasitoses of the human central nervous system. *Journal of Helminthology,* 10: 1–14.

Hong, S.J., Kim, Y.M., Seo, M. & Kim, K.S. 2010. Breast and scrotal sparganosis: sonographic findings and pathologic correlation. *Journal of Ultrasound Medicine,* 29(11): 1627–1633.

Huang, F., Gong, H.Y. & Lu, M.H. 2012. Pulmonary sparganosis mansoni: a case report. *Tropical Biomedicine,* 29(2): 220–223.

Khurana, S., Appannanavar, S., Bhatti, H.S. & Verma, S. 2012. Sparganosis of liver: a rare entity and review of literature. *BMJ Case Reports* published online 6 December 2012. doi: 10.1136/bcr-2012-006790

Kudesia, S., Indira, D.B., Sarala, D., Vani, S., Yasha, T.C., Jayakumar, P.N. & Shankar, S.K. 1998. Sparganosis of brain and spinal cord: unusual tapeworm infestation (report of two cases). *Clinical Neurology and Neurosurgery,* 100(2): 148–152.

Lee, J.H., Kim, G.H., Kim, S.M., Lee, S.Y., Lee, W.Y., Bae, J.W., Shin, K.S., Hwang, K.K., Kim, D.W., Cho, M.C. 2011. A case of sparganosis that presented as a recurrent pericardial effusion. *Korean Circulation Journal*, 41(1): 38–42.

Li, M.-W., Song, H.-Q., Li, C., Lin, H.-Y., Xie, W.-T., Lin, R.-Q. & Zhu, X.-Q. 2011. Sparganosis in mainland China. *International Journal of Infectious Diseases*, 15(3): e154–156. Online. doi: 10.1016/j.ijid.2010.10.001

Parija, S.C. 2011. Helminthic infections. pp. 203–204, in: *Textbook of Medical Parasitology*. 3rd ed. All India Publishers and Distributors, New Delhi, India.

Qin, Y., Feng, Y. & Zheng, L. 2011. [A case of sparganosis mansoni] [In Chinese]. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi*, 29(4): 246.

Saleque, A., Juyal, P.D. & Bhatia, B.B. 1990. *Spirometra* sp. in a domestic cat in India. *Veterinary Parasitology*, 35(3): 273–276.

Sen, D.K., Muller, R., Gupta, V.P. & Chilana, J.S. 1989. Cestode larva (*Sparganum*) in the anterior chamber of the eye. *Tropical Geographic Medicine*, 41(3): 270–273.

Stief, B. & Enge, A. 2011. Proliferative peritonitis with larval and cystic parasitic stages in a dog. *Veterinary Pathology,* 48(4): 911–914.

Sundaram, C., Prasad, V.S.S.V. & Reddy, J.J.M. 2003. Cerebral sparganosis. *Journal of the Association of Physicians of India,* 51: 1107–1109.

Wang, H., Tang, Y. & Yang, Y. 2012. [A case of *Spirometra mansoni* infection with both plerocercoid larvae and adult worm] [In Chinese]. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi*, 30(1): 40.

Ye, H., Du, Y., Liu, G., Luo, X. & Yang, H. 2012. Clinical features of 8 cases of orbital sparganosis in southern China. *Canadian Journal of Ophthalmology*, 47(5): 453–457.

A7.17 *TAENIA SAGINATA*

General information

Taenia saginata is an intestinal zoonotic cestode with humans as definitive hosts. Formerly defined as *Cysticercus bovis*, the metacestode larval stage occurs in the intermediate host (cattle) as cysts, causing *T. saginata* cysticercosis (Abuseir *et al.,* 2007). Upon ingestion of these cysticerci, an adult tapeworm will develop in the host's small intestine and will reach maturity within two to three months. An adult tapeworm can measure 3 m up to 12 m and will release gravid proglottids that contain between 30 000–50 000 eggs (Murrell *et al.,* 2005). These proglottids leave the host by active migration through the anus or in the stools. The eggs contain a larva (oncosphere) and are infective for the intermediate host (cattle) immediately after release from the human host. Cattle become infected orally during grazing when the environment is contaminated with eggs shed by human faeces directly (animal care takers) or via sewage plants after flooding or sewage sediment distributed on pastures (Cabarat, Geerts and Madeline, 2002). Eggs hatch in the intestine and the oncospheres liberated from the eggs, penetrate the intestinal wall and circulate through the lymphatic system and blood stream. Following migration in the animal's body, the larvae will develop into cysticerci after 8 to 10 weeks in muscle tissues, including the heart, and other predilection sites such as tongue, diaphragm and the masseter muscles (Abuseir *et al.,* 2007). Humans acquire the infection by consumption of raw or undercooked beef containing live cysticerci of *T. saginata*.

Geographical distribution

Globally, *T. saginata* is the most widely distributed human *Taenia* tapeworm, with an estimated 60 million human infections worldwide (Craig and Ito, 2007). Human tapeworm infections occur wherever cattle husbandry is prevalent and where human faeces are not disposed of properly. Despite this, *T. saginata* is also present in industrialized countries with good sanitary systems, because indirect transmission to cattle pastures via contaminated sewage sludge might also occur (Cabarat, Geerts and Madeline, 2002). (Cabarat, Geerts and Madeline, 2002) reported global human taeniasis prevalence results from the last 25 years ranging from less than 0.01 to 10% in Europe and up to 36% in Dagestan. It is unclear whether the data available reflects only *T. saginata* or also includes *T. solium* infections, since *Taenia* eggs of all species are morphologically alike.

Not many studies have been conducted in humans in many African countries, and in many instances there is difficulty in differential diagnoses with *T. solium* eggs. Bovine cysticercosis occurs in most of the African countries, but the epidemiological patterns in the African countries are far from being completely understood because there is a lack of surveillance systems, with consequent unavailability of data with which to quantify the disease burden.

In the Near East, the prevalence of human *T. saginata* (taeniasis) is infrequently reported, as is bovine cysticercosis from meat inspection. In Europe, every single carcass of bovines above 6 weeks of age needs to be examined for bovine cysticercosis, but this does not lead to accurate data of the prevalence in cattle due to low sensitivity of the method and poor reporting systems. In addition, no prevalence data have been reported in humans.

T. saginata has a global distribution, but the number of global food-borne illnesses is still not very clear due to difficulties in differential diagnosis with other *Taenia* infections, the asymptomatic nature of most of the infections, and rare complications, such as bowel obstructions (Craig and Ito, 2007). There are an estimated 12 million carriers in Africa, and an incidence up to 30% in some regions has been stated (Gracey, Collins and Huey, 1999). Based on meat inspection data in various European countries, the prevalence in cattle ranges between 0.01 and 7% (Abuseir *et al.,* 2007), but due to the lack of sensitivity of the post-mortem meat inspection there is an underestimation of the prevalence by a factor of 5 to 50 times (Dorny *et al.,* 2000).

In conclusion, despite the global distribution of *T. saginata*, the real prevalence of this tapeworm in humans and in cattle is underestimated due to imperfect diagnostic testing and poor reporting systems in cattle and the asymptomatic character of the disease in humans.

Disease

Patients harbouring adult *T. saginata* tapeworms are either asymptomatic or suffer from anal pruritis and discharge faecal proglottids. In some cases there might be non-specific symptoms like vomiting, nausea, epigastric pain, diarrhoea and weight loss. *T. saginata* is also a rare cause of ileus, pancreatitis, cholecystitis and cholangitis. In some endemic countries, *T. saginata* can cause an acute cholangitis (Uygur-Bayramiçli *et al.,* 2012).

Severity of acute morbidity

Low, with most infected people asymptomatic. In some cases there is more severe illness due to epigastric fullness, nausea, diarrhoea and vomiting. Rare cases of acute cholangitis have been reported.

Severity of chronic morbidity

Low. Weight loss can occur. In some patients there are more severe symptoms, as *T. saginata* have been reported as the cause of ileus, pancreatitis, cholecystitis and cholangitis.

Chronic illness fraction
Unknown, but asymptomatic carriers are most frequent.

Case fatality rate
Not known, but probably non-existent.

Increase in human illness
Unknown.

Trade relevance

In Europe, bovine carcasses require mandatory meat inspection under EC regulation No. 854/2004. In the event of positive findings during meat inspection, positive carcasses are condemned (heavily infected) or frozen if lightly infected, to inactivate cysticerci before consumption. Therefore, economic losses occur and, due to the global distribution of the parasite, might be relevant.

Impact on economically vulnerable populations

The impact in terms of number of infections might be high when beef is eaten raw or undercooked. This is of particular relevance in the absence of adequate hygienic conditions and appropriate veterinary public health control measures. However, since most infections in humans are asymptomatic, the impact in terms of number of reported illnesses is rather low.

The economic losses might be relevant due to carcass devaluation or condemnation in those vulnerable communities with poor hygiene when beef is traded, although data are lacking to show the relevance of this point.

References

Abuseir, S., Kuhne, M., Schnieder, T., Klein, G. & Epe, C. 2007. Evaluation of a serological method for the detection of *Taenia saginata* cysticercosis using serum and meat juice samples. *Parasitology Research*, 101: 131–137.

Cabarat, J., Geerts, S. & Madeline, M. 2002. The use of urban sewage sludge on pastures: the cysticercosis threat. *Veterinary Research*, 33: 575–597

Craig, P. & Ito, A. 2007. Intestinal parasites. *Current Opinions in Infectious Diseases*, 20: 524–532.

Dorny, P., Vallée, I., and 19 others. 2010. Development of harmonised schemes for the monitoring and reporting of *Cysticercus* in animals and foodstuffs in the European Union. Scientific Report submitted to EFSA. 30 p. Available at http://www.efsa.europa.eu/en/supporting/doc/34e.pdf Accessed 2013-06-22.

Gracey, J.F., Collins, D.S. & Huey, R. 1999. Diseases caused by helminth and arthropod parasites. pp. 243–259, 635–699, in: J.F. Gracey, D.S. Collins and R.J. Huey (Authors). *Meat Hygiene.* 10th edition. Saunders, UK.

Murrell, K.D., Dorny, P., Flisser, A., Geerts, S., Kyvsgaard, N.C., McManus, D.P., Nash, T.E. & Pawlowski, Z.S. (Editors). 2005. *WHO/FAO/OIE Guidelines for the surveillance, prevention and control of taeniosis/cysticercosis.* OIE, Paris, France. 139 p. Available at http://www.oie.int/doc/ged/d11245.pdf Accessed 2013-08-24

Uygur-Bayramiçli, O., Ak, O., Dabak, R., Demirhan, G., Ozer, S. 2012. *Taenia saginata* a rare cause of acute cholangitis: a case report. *Acta Clinica Belgia,* 67(6): 436–437.

A7.18 *TAENIA SOLIUM*

General information on the parasite

Humans are definitive hosts of *Taenia solium* and will shed eggs in their stool (taeniasis). Ingestion of *T. solium* eggs will lead to the development of cysticerci in pigs, and also in humans (cysticercosis). Cysticerci can develop in almost any tissue, but involvement of the central nervous system, known as neurocysticercosis, is the clinically most important manifestation of the disease in humans and may lead to epilepsy and death (Sorvillo, DeGiorgio and Waterman, 2007). The presence of cysticerci in pork also makes pork unsafe for human consumption and greatly reduces its market value.

Humans acquire taeniasis (adult tapeworm infection) by eating raw or undercooked pork with cysticerci, the larval form of *T. solium* (Sorvillo, DeGiorgio and Waterman, 2007). The cysticerci evaginate and attach to the intestinal wall of the small intestine and within approximately two months develop into adult tapeworms, which can grow to more than 3 m long (Flisser, 1994). The distal proglottids detach from the worm when their eggs are mature and pass out into the environment with the human faeces. These eggs are infective to the same (auto-infection) or other humans as well as pigs if they are ingested following direct contact with tapeworm carriers, ingestion of infected faecal matter or from consuming water or food contaminated with human faeces (Garcia *et al.,* 2003).

Geographical distribution

T. solium cysticercosis is one of the most common parasitic diseases worldwide and the estimated prevalence is greater than 50 million people (Psarros, Zouros and Coimbra. 2003; Hawk *et al.,* 2005).

The prevalence of *T. solium* infection varies greatly according to the level of sanitation, pig husbandry practices and eating habits in a region. The parasite is endemic in several developing countries, including in Central and South America, sub-Saharan Africa, South East Asia and Western Pacific (Schantz, 2002). In developed countries, such as the United States of America and parts of Europe, *T. solium* cysticercosis is considered as an emerging disease due to increased immigration and international travel (Schantz, 2002; Pal, Carpio and Sander, 2000).

Disease

Clinical manifestations of *T. solium* cysticercosis are related to individual differences in the number, size, and topography of lesions, and the efficiency of the host's immune response to the parasites (Nash and Neva, 1984). Neurocysticercosis and ophthalmic cysticercosis are associated with substantial morbidity (Garcia, Gonzalez and Gilman, 2011). Epileptic seizures are the commonest presentation of neurocysticercosis and generally represent the primary or sole manifestation of

the disease. Seizures occur in 50–80% of patients with parenchymal brain cysts or calcifications, but are less common in other forms of the disease (Schantz, Wilkins and Tsang, 1998; Chopra, Kaur and Mahajan, 1981; Del Brutto *et al.,* 1992).

Severity of acute morbidity

T. solium neurocysticercosis is considered responsible for over 10% of acute case admissions to the neurological ward of countries where it is endemic (Montresor and Palmer, 2006).

Severity of chronic morbidity

Seizure disorders raise the risk of injuries, and in New Guinea the introduction of cysticercosis was followed by an epidemic of serious burns when convulsions caused people to fall into open cooking fires (Bending and Cartford, 1983). The estimated economic consequences due to chronic disability are heavy (Flisser, 1988; Carabin *et al.,* 2006; Praet *et al.,* 2009).

Case fatality rates

Several large facility-based case series studies have reported that the number of deaths from cysticercosis is relatively low and that the case-fatality rate is <1% (Sorvillo, DeGiorgio and Waterman, 2007). Global deaths due to cysticercosis were estimated in 1990 to be 700 (Range (0 to 2800) and in 2010 1200 (Range 0 to 4300) for all ages and both sexes combined (Lozano *et al.,* 2012).

Increase in human illness potential

With the introduction of pigs into rural farming communities by donor agencies in most countries in Africa and the short reproductive cycle of pigs, human infection with *T. solium* should be considered emergent, and is spreading rapidly in this region. Public health efforts for its control in pig and human populations are active in many countries.

Trade relevance

Veterinary public health efforts for control of this parasite in pigs are active in many endemic countries. In most African countries carcasses may not be released even for domestic market unless they have been inspected or tested, or both, to ascertain the absence of infection. The challenge is in the enforcement of legislations on meat inspection in resource-poor communities rearing outdoor pigs.

In non-endemic regions veterinary public health measurements are in place.

Impact on economically vulnerable populations

Neurocysticercosis due to *T. solium* infection is one of the main causes of epilepsy in rural African communities (Pal, Carpio and Sander, 2000). This comes with

social stigma to those affected by the parasite (Placencia *et al.,* 1995) and the disease has substantial global impact in terms of disability adjusted life years (DALYs) and monetary losses (Carabin *et al.,* 2006; Praet *et al.,* 2009; Lozano *et al.,* 2012).

T. solium is considered to have economic impact when it comes to monetary loss due to carcass devaluation or condemnation (Carabin *et al.,* 2006). The parasite has high prevalence in both pigs and humans where sanitation is poor, pigs are allowed to roam freely (free-range), or meat inspection is absent or inadequate (Garcia *et al.,* 2003; Bern *et al.,* 1999). These features are mainly associated with resource-poor communities or small-holder livestock farmers in the developing countries.

References

Bending, J.J. & Catford, J.C. 1983. Epidemic of burns in New Guinea due to cerebral cysticercosis [letter]. *Lancet*, 1(8330): 922.

Bern, C., Garcia, H.H., Evans, C., Gonzalez, A.E., Verastegui, M., Tsang, V.C.W. & Gilman, R.H. 1999. Magnitude of the disease burden from neurocysticercosis in a developing country. *Clinical Infectious Diseases*, 29: 1203-9.

Carabin, H., Krecek, R.C., Cowan, L.D., Michael, L., Foyaca-Sibat, H., Nash, T. & Willingham, A.L. 2006. Estimation of the cost of *Taenia solium* cysticercosis in Eastern Cape Province, South Africa. *Tropical Medicine and International Health,* 11: 906–916.

Chopra, J.S., Kaur, U. & Mahajan, R.C. 1981. Cysticerciasis and epilepsy: a clinical and serological study. *Transaction of Royal Society of Tropical Medicine and Hygiene,* 75: 518–520.

Del Brutto, O.H., Santibanez, R., Noboa, C.A., Aguirre, R., Diaz, E. & Alarcon, T.A. 1992. Epilepsy due to neurocysticercosis: analysis of 203 patients. *Neurology*, 42: 389–392.

Flisser, A. 1988. Neurocysticercosis in Mexico. *Parasitology Today*, 4: 131–137.

Flisser, A. 1994. Taeniasis and Cysticercosis due to *Taenia solium*. pp. 77–116, *In:* Tsieh Sun (editor). *Progress in Clinical Parasitology*. CRC Press, Boca Raton, FL, USA.

García, H.H., Gonzalez, A.E. & Gilman, R.H. 2011. Cysticercosis of the central nervous system: how should it be managed? *Current Opinion in Infectious Diseases,* 24(5): 423–427.

García, H.H., Gonzalez, A.E., Evans, C.A.W. & Gilman, R.H. 2003. *Taenia solium* cysticercosis. *Lancet*, 362(9383: 547–556.

Hawk, M.W., Shahlaie, K., Kim, K.D. & Theis, J.H. 2005. Neurocysticercosis: a review. *Surgery and Neurology*, 63: 123–132.

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K. and the Working Group. 2012. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859): 2095–2128. See also same authors, 2013, *Lancet*, 381(9867): 628–628.

Montresor, A. & Palmer, K. 2006. Taeniasis/cysticercosis trend worldwide and rationale for control. *Parasitology International*, 55: 301–303.

Nash, T.E. & Neva, F.A. 1984. Recent advances in the diagnosis and treatment of cerebral cysticercosis. *New England Journal of Medicine*, 311: 1492–1496.

Pal, D.K., Carpio, A. & Sander, J.W. 2000. Neurocysticercosis and epilepsy in developing countries. *Journal of Neurology, Neurosurgery and Psychiatry,* 68: 137–143.

Placencia, M., Farmer, P.J., Jumbo, L., Sander, J.W. & Shorvon, S.D. 1995. Levels of stigmatization of patients with previously untreated epilepsy in northern Ecuador. *Neuroepidemiology*, 14: 147–154.

Praet, N., Speybroeck, N., Manzanedo, R., Berkvens, D., Nsame Nforninwe, D., Zoli, A., Quet, F., Preux, P.M., Carabin, H. & Geerts, S. 2009. The disease burden of *Taenia solium* cysticercosis in Cameroon. *PLoS Neglected Tropical Diseases*, 3(3): e406. Online. doi: 10.1371/journal.pntd.0000406.

Psarros, T.G., Zouros, A. & Coimbra, C. 2003. Neurocysticercosis: a neurosurgical perspective. *Southern Medical Journal*, 96: 1019–1022.

Schantz, P.M. 2002. Overview of global distribution and transmission. *In:* G. Singh and S. Prabhakar (editors). *Taenia solium Cysticercosis: from basic to clinical science.* CAB International, Wallingford, UK

Schantz, P.M., Wilkins, P.P. & Tsang, V.C.W. 1998. Immigrants, imaging and immunoblots: the emergence of neurocysticercosis as a significant public health problem. pp. 213–241, *in:* W.M. Scheld, W.A. Craig and J.M. Hughes (editors). *Emerging Infections 2*. ASM Press, Washington DC, USA.

Sorvillo, F.J., DeGiorgio, C. & Waterman, S.H. 2007. Deaths from Cysticercosis, United States. *Emerging Infectious Diseases*, 13: 230–235.

A7.19 *TOXOCARA* SPP.

General information

Human toxocariasis is a zoonotic helminth infection caused by the migration of the larvae of *Toxocara canis* (mainly) and *T. cati* from dogs and cats respectively. Eggs of the parasite are shed in the faeces of dogs and cats, and the infective larvae then develop within the environmentally robust eggs until maturation of the infective stage larvae. Infective eggs can survive in soil for several years. Human infection primarily occurs upon ingestion of embryonated eggs. The larvae hatch in the intestine, penetrate the intestinal wall and migrate through the liver, lungs and heart, ultimately disseminating to other organs and the central nervous system (Hotez and Wilkins, 2009). The larvae do not develop further in humans, but remain under developmental arrest and can survive for many years. During their migrations they release antigens that result in systematic immune and local inflammatory responses, and commonly elicit eosinophilia and immunoglobulin E antibodies.

Other routes of infection include the consumption of raw vegetables grown in kitchen gardens contaminated with faeces of dogs and cats containing embryonated eggs, which may result in chronic low-dose infections. Rarely, the infection is associated with consumption of raw meat from potential paratenic hosts (in non-canid hosts, during migration, the larvae encyst in muscles and are infective), such as chicken (Nagakura *et al.*, 1989), lamb (Salem and Schantz, 1992) or rabbit (Stürchler, Weiss and Gassner, 1990).

Geographical distribution

Toxocariasis is a worldwide zoonosis (Utzinger *et al.,* 2012*).* Eggs of *T. canis* and *T. cati* are found worldwide in soil that is open to contamination by dogs and cats. The eggs of these species occur in 2 to 88% of soil samples collected in various countries and regions.

Seroprevalence surveys in Western countries of apparently healthy adults from urban areas indicate from 2 to 5% infection compared with 14.2–37% of adults in rural areas (Magnaval, Glickman and Dorchies, 1994a). In tropical countries the seroprevalence of *Toxocara* infection has been found to be higher, ranging from 63.2% (Chomel *et al.,* 1993) to 92.8% (Magnaval *et al.*, 1994b).

The proportion of human illness attributable to a food source is very low compared with that due to contact with soil (geophagia) and the global burden of disease attributable to toxocariasis is unknown (Utzinger *et al.,* 2012).

Disease

Toxocariasis manifests itself in three syndromes, namely visceral larval migrans (VLM), ocular larval migrans (OLM) and neurological toxocariasis. Ocular toxocariasis occurs when *Toxocara* larvae migrate to the eye. Symptoms and signs include vision loss, eye inflammation or damage to the retina. Typically, only one eye is affected. It can be mistakenly diagnosed as childhood retinoblastoma, with consequent inappropriate enucleation of the eye. Visceral toxocariasis occurs when *Toxocara* larvae migrate to various body organs, such as the liver or central nervous system. Symptoms of visceral toxocariasis include fever, fatigue, coughing, wheezing or abdominal pain. The clinical signs of neurological toxocariasis, as with VLM, are non-specific (Magnaval *et al.*, 1997), leading to possible under-diagnosis of this condition. Quattrocchi *et al.* (2012) has shown that there is a highly significant association ($p<0.001$) between people with epilepsy and levels of antibodies to *Toxocara* (Odds Ratio of 1.92). In addition, there have been studies associating *Toxocara* infections with allergic asthma (Tonelli, 2005; Pinelli *et al.,* 2008).

Severity of acute morbidity

Many people who are infected with *Toxocara* are asymptomatic, while others present mild or more severe symptoms after the infection, and may develop overt ocular and visceral toxocariasis**.** The most severe cases are rare, but are more likely to occur in young children, who often play in contaminated areas, or eat soil (pica) contaminated by dog or cat faeces (CDC, 2013).

Severity of chronic morbidity

Because of the occult nature of the infection and the non-specificity of the symptoms, the global scale of chronic morbidity is not known. Ocular toxocariasis is a particular exception to this, although prevalence appears to be relatively low and no data exists in many countries. In the United States of America between September 2009 and September 2010, 68 patients were diagnosed with ocular toxocariasis (CDC, 2011). Of these 30 had clinical data and of these 25 (83%) reported vision loss and 17 (68%) of these had permanent vision loss. VLM involving the brain is thought to be rare, but this may merely be because of under-recognition and -detection. Because toxocariasis tends to be an occult infection, the true incidence of infection and morbidity is probably greatly underestimated.

Increase in human illness potential

One of the main drawbacks to diagnosis of toxocariasis has been lack of diagnostic tools and clinical symptoms that are not specific to the disease condition in humans. Considering that dogs and cats are the hosts of *T. canis* and *T. cati*, the reporting of human cases may continue to increase as diagnostic methods improve and infection in dogs (e.g. 25% (Barriga, 1988) and cats 30-60% (Petithory *et al.,*

1996) remain high. In western countries, the above quoted seroprevalence surveys clearly demonstrate high infection rates, especially in children.

Trade relevance

Toxocariasis may have little trade relevance at present because the main vehicle of transmission remains through raw vegetables and meats from paratenic hosts. The embryonated eggs of *Toxocara* canis could develop at a low threshold temperature of 11.8°C and have been shown to survive for 6 weeks between +1 and –2°C (Azam *et al.,* 2012). The fact that the larval stages and eggs can survive under these environmental conditions and the increase in international trade of the food vehicles mentioned above would pre-empt the trade relevance for this food-borne parasite.

Impact on economically vulnerable populations

The population at risk is children under 7 years with geophagic or pica characteristics. In this section of the population, infection, though rarely resulting in death, can cause untold suffering if it develops into ocular and neurological forms. The costs of treatment and chronic disabilities associated with these two forms are the major losses to affected populations.

References

Azam, D., Ukpai, O.M., Said, A., Abd-Allah, G.A. & Morgan, E.R. 2012. Temperature and the development and survival of infective *Toxocara canis* larvae. *Parasitology Research*, 110(2): 649–656.

Barriga, O.O. 1988. A critical look at the importance, prevalence and control of toxocariasis and the possibilities of immunological control. *Veterinary Parasitology*, 29: 195–234.

CDC (Centers for Disease Control). 2011. Ocular Toxocariasis – United States, 2009–2010. *Morbidity and Mortality Weekly Report*, 60, No. 22.

CDC. 2013. Parasites – Toxocariasis (also known as Roundworm Infection). Web page, last updated 2013-01-10. Available at http://www.cdc.gov/parasites/toxocariasis/index.html Accessed 2013-06-23.

Chomel, B.B., Kasten, R., Adams, C., Lambillotte, D., Theis, J., Goldsmith, R., Koss, J., Chioino, C., Widjana, D.P. & Sutisna, P. 1993. Serosurvey of some major zoonotic infections in children and teenagers in Bali, Indonesia. *Southeast Asian Journal of Tropical Medicine and Public Health,* 24(2): 321–326.

Hotez, P.J. & Wilkins, P.P. 2009. Toxocariasis: America's most common neglected infection of poverty and a helminthiasis of global importance? *PLoS Neglected Tropical Diseases,* 3(3): e400. Online doi:10.1371/journal.pntd.0000400

Magnaval, J.-F., Glickman, L.T. & Dorchies, P. 1994a. La toxocarose, une zoonose helminthique majeure. *Revue de Medecine Veterinaire,* 145(9): 611–627.

Magnaval, J.-F., Michault, A., Calon, N., Charlet, J.P. 1994b. Epidemiology of human toxocariasis in La Reunion. *Transaction of Royal Society of Tropical Medicine and Hygiene,* 88: 531–533.

Magnaval, J.-F., Galindo, V., Glickman, L.T. & Clanet, M. 1997. Human *Toxocara* infection of the central nervous system and neurological disorders: a case-control study. *Parasitology*, 115(5): 537–543.

Magnaval, J.F., Glickman, L.T., Dorchies, P. & Morassin, B. 2001 Highlights of human toxocariasis. Review. *Korean Journal of Parasitology*, 39(1): 1–11.

Nagakura, K., Tachibana, H., Kaneda, Y. & Kato, Y. 1989. Toxocariasis possibly caused by ingesting raw chicken. *Journal of Infectious Diseases,* 160: 735–736.

Petithory, J.C., Vandemeule Broucke, E., Jousserand, P. & Bisognani, A.C. 1996. Prevalence de *Toxocara cati* chez le chat en France. *Bulletin de la Societe Francaise de Parasitologie*, 14: 179–184.

Pinelli, E., Brandes, S., Dormans, J., Gremmer, E. & van Loveren, H. 2008. Infection with the roundworm *Toxocara canis* leads to exacerbation of experimental allergic airway inflammation. *Clinical and Experimental Allergy*, 38(4): 649–658.

Quattrocchi, G., Nicoletti, A., Marin, B., Bruno, E., Druet-Cabanac, M. & Preux, P.M. 2012. Toxocariasis and epilepsy: systematic review and meta-analysis. *PLoS Neglected Tropical Diseases,* 6(8): e1775. Online. doi:10.1371/journal.pntd.0001775.

Salem, G. & Schantz, P. 1992. Toxocaral visceral larva migrans after ingestion of raw lamb liver. *Clinical Infectious Diseases,* 15: 743–744.

Stürchler, D., Weiss, N. & Gassner, M. 1990. Transmission of toxocariasis. *Journal of Infectious Diseases,* 162: 571.

Tonelli, E. 2005. [Toxocariasis and asthma: a relevant association] [In Portuguese]. *Journal Pediatrics (Rio Janeiro).* 81(2): 95–96.

Utzinger, J., Becker, S.L., Knopp, S., Blum, J., Neumayr, A.L., Keiser, J. & Hatz, C.F. 2012. Neglected tropical diseases: diagnosis, clinical management, treatment and control. *Swiss Medical Weekly*, 142: w13727. Online 142:w13727. doi: 10.4414/smw.2012.13727

A7.20 *TOXOPLASMA GONDII*

General Information

Toxoplasma is a protozoan parasite belonging to the Phylum Apicomplexa and is infectious to practically all warm-blooded animals, including humans, livestock, birds and marine mammals. There is only one species in the *Toxoplasma* genus: *Toxoplasma gondii*. Based on molecular analyses, in conjunction with mouse virulence information, *T. gondii* from Europe and North America has been classified into 3 genetic types (I, II, III), of which type I isolates are lethal to mice, irrespective of dose, while types II and III are generally avirulent for mice. In Europe, genotype II is predominant in humans and animals. Strains that did not fall into these three clonal types were previously considered atypical, but a fourth clonal type has been recently recognized, mostly in wildlife (Khan *et al.,* 2011). In South America, particularly Brazil, a greater diversity of genotypes has been detected that also tend to be more virulent (Clementino Andrade *et al.,* 2013; Carneiro *et al.,* 2013), with a heavier burden of clinical disease (Dubey *et al.,* 2012a, b).

The overall life cycle of *Toxoplasma* contains two distinct cycles: the sexual enteroepithelial cycle and the asexual cycle. The definitive hosts of *T. gondii* are members of the cat family (Felidae), thus the sexual cycle of the parasite occurs only within the intestinal epithelial cells of felids. Oocysts are the zygotic stage of the life cycle, and are excreted unsporulated in cat faeces. Speed of oocyst sporulation in the environment depends on factors such as temperature and humidity, but usually takes around three days. The oocysts are environmentally robust, and can retain infectivity in a cool damp environment for months (Guy, Dubey and Hill, 2012).

The asexual cycle occurs when consumption of tissue cysts (see below) or oocysts results in infection of the intestine, and the tachyzoite form of the parasite multiplies asexually in the cells of lamina propria by repeated divisions until the cells rupture. Tachyzoites from ruptured cells are released into surrounding tissues resulting in systemic infection. Circulating tachyzoites infect new cells throughout the body, with cells in cardiac and skeletal muscle and the central nervous system more often infected. After several more rounds of asexual division, tissue cysts are formed and these remain intracellular. Tissue cysts of *T. gondii* range from 5 µm to over 100 µm in size and contain bradyzoites, which are infectious when ingested with the tissue surrounding them. If ingested by a felid, then the sexual enteroepithelial cycle occurs; if ingested by any other host, then the asexual cycle, as described in the previous paragraph occurs. Additionally, if a female host is pregnant when first infected, then circulating tachyzoites may move through the placenta to the foetus (intrauterine or congenital transmission).

Geographical distribution

Toxoplasma gondii is perhaps the most widespread protozoan parasite affecting humans, and it has been estimated that between 1 and 2 billion of the world's population is infected at any one time (Montoya and Liesenfeld, 2004). It should be emphasized that the majority of these do not manifest clinical illness (see later).

Infection in humans occurs worldwide, but prevalence varies significantly between populations. Between 11 and 40% of adults in the United States of America and UK have been found to be seropositive, but in other countries in western Europe, typical seroprevalence rates vary from 11 to 28% in Scandinavia, to 42% in Italy, and up to 67% in Belgium (Guy, Dubey and Hill, 2012). In some regions of Brazil, infection rates of over 70% have been reported, while rates of around 40% have been reported from various African countries. In Asia, infection rates vary from less than 10% to over 70% (Guy, Dubey and Hill, 2012). With the exception of congenital transmission, the majority of infections with *T. gondii* are considered to be food-borne, as described below, although waterborne outbreaks can also be of local importance, and water-borne infection has been suggested to be the major source of *Toxoplasma* infection in developing countries (Petersen, Kijlstra and Stanford, 2012).

There are three potentially infectious stages of *Toxoplasma*: tachyzoites, bradyzoites and oocysts, two of which (bradyzoites and oocysts) are of particular relevance to food-borne transmission. Bradyzoites may be ingested with the tissue of an infected intermediate host, while oocysts may be ingested with any produce that has the potential to be contaminated with the faeces of an infected felid. In addition, though probably of less significance, tachyzoites excreted in the milk might result in milk-borne infection. Outbreaks of toxoplasmosis associated with consumption of unpasteurized goats' milk have been reported (Guy, Dubey and Hill, 2012), and consumption of such milk is considered a risk factor for *T. gondii* infection in the United States of America (Jones *et al.*, 2009).

Human infection via bradyzoites in meat is dependent on various factors, including prevalence of *Toxoplasma* infection in meat animals, cultural factors regarding meat consumption and meat preparation, and factors (such as age and immunological status) of the person exposed. Parasite factors are probably of relevance also. Virtually all edible portions of an animal can harbour viable *T. gondii* tissue cysts, and most species of livestock are susceptible to infection (Dubey, 2009a; Guy, Dubey and Hill, 2012). In some countries sheep and goats are the most important hosts of *T. gondii*, and the main source of infection to humans (Dubey, 2009b). In other countries, for example United States of America, lamb and mutton are considered relatively minor food commodities (Guy, Dubey and Hill, 2012). Of

the major meat animal species investigated in United States of America to date, pig is the only species that has been found to frequently harbour the parasite (Dubey and Jones, 2008), although prevalence has declined in areas where they are predominantly raised indoors (Guy, Dubey and Hill, 2012). However, elevated infection in organic pigs indicates that consumption of under-cooked organic pork may represent an increasing infection route (Dubey *et al.*, 2012a, b). The risk of acquiring toxoplasmosis from beef also demonstrates regional variability, with some European studies suggesting that it can be a significant contributor to human infection (Cook *et al.,* 2000; Opsteegh *et al.,* 2011). Although poultry are also susceptible to infection with *T. gondii*, and theoretically pose a source of infection to humans, the relatively limited lifespan of poultry and the fact that they tend to be well-cooked before consumption, limits their importance as sources of infection for humans (Kijlstra and Jongert, 2008). Indeed, chickens have not been indicated as a source of human infection in the United States of America, despite high infection rates in some flocks (Guy, Dubey and Hill, 2012). Game animals are also considered to be potentially important sources of meat-borne toxoplasmosis, particularly as such meat is often consumed undercooked (Opsteegh *et al.,* 2011), with wild boar and venison particularly implicated in Europe (Kijlstra and Jongert, 2008). In other parts of the world, other game meats may be of equal or greater importance; for example, kangaroos are considered to be highly susceptible to *T. gondii* infection (Kijlstra and Jongert, 2008). In Arctic regions, consumption of undercooked game meat, particularly from marine mammals, seems to be an important risk factor for human infection (Davidson *et al.,* 2011).

Human infection via oocysts occurs when a person ingests something that has been contaminated with faeces from an infected cat. As *Toxoplasma* oocysts are not infective at excretion, direct infection from handling an infected cat or cleaning the litter box daily is unlikely. As oocysts are very hardy (and, unlike bradyzoites, can survive freezing), contamination of produce provides a route for transmission. It is possible that the importance of the oocyst infection route has been generally under-estimated previously. In various outbreaks, as well as individual infections, use of a test detecting sporozoites has indicated that oocysts have been the source of infection rather than bradyzoites, indicating the importance of this route of infection (Boyer *et al.,* 2012). Oocysts may also contaminate water, and can result in water-borne infections and outbreaks, or may contaminate fresh produce or other food items.

Disease

The clinical picture of infection with *Toxoplasma* is greatly influenced by the immune status of the infected person, and also by the virulence of the strain of parasite. In the immunocompetent, *T. gondii* infection is usually asymptomatic,

but may cause a mild to moderate illness, in which typical symptoms include low grade fever, lymphadenopathy, fatigue, muscle pain, sore throat and headache. In some cases, ocular toxoplasmosis may occur, which may be accompanied by partial or total loss of vision. The rate of ocular toxoplasmosis seems to differ according to unknown factors, but is more common in South America, Central America, the Caribbean and parts of tropical Africa than in Europe and North America, and is quite rare in China (Petersen, Kijlstra and Stanford, 2012). In addition, ocular disease appears to be more severe in South America than in other continents, presumably due to the presence of extremely virulent genotypes of the parasite.

Although latent *Toxoplasma* infection is generally accepted as being generally benign in the immunocompetent, some studies have suggested that the parasite may affect behaviour (Flegr, 2007), perhaps being a contributory, or even causative, factor in various psychiatric disorders, including depression, anxiety and schizophrenia (Henriquez *et al.,* 2009; Flegr, 2013). It has been proposed that *Toxoplasma* may affect dopamine levels within the brain, resulting in alterations in CNS function (Flegr, 2013). Should the association between *Toxoplasma* infection and psychiatric dysfunction be proven, then the overall burden of disease and risk to health and well-being due to this parasite should be re-evaluated (Guy, Dubey and Hill, 2012; Flegr, 2013).

In the immunocompromised and immunodeficient (such as HIV-patients and those receiving profound immunosuppressive therapy), severe or life-threatening disease can result either from acute *Toxoplasma* infection or re-activation of a previously latent infection. Here, encephalitis is the most clinically significant manifestation, but retinochoroiditis, pneumonitis and other systemic disease may also occur. In patients with acquired immunodeficiency syndrome (AIDS), toxoplasmic encephalitis is the most common cause of intracerebral mass lesions and ranks highly on the list of diseases resulting in the death of AIDS patients.

Congenital toxoplasmosis is another serious potential manifestation of *T. gondii* infection; this is not food-borne infection *per se*, but may result from food-borne infection of the mother. In an immunocompetent mother, it is generally accepted that *Toxoplasma* is passed on to the foetus from an infection acquired immediately before or during pregnancy, i.e. prior to onset of the latent phase of infection. However, rare cases of transplacental infection have been reported in which the mother has had a previous latent infection. The risk of transplacental infection increases throughout pregnancy, but the risk of severe disease or foetal death decreases. Symptoms commonly associated with transplacental infection include spontaneous termination, foetal death, ventricular dilatation and intracranial calcification (Guy, Dubey and Hill, 2012). Neonates may present with hydrocephalus,

seizures, retinochoroiditis, spasticity, deafness, hepatosplenomegaly, jaundice or rash, and children that are asymptomatic at birth, may suffer from mental retardation or retinochoroidal lesions later in life. Children who have been infected late on in the pregnancy are usually asymptomatic or have only mild complications. Again, there is variation according to strain of *Toxoplasma*, with more severe symptoms apparently associated with congenital toxoplasmosis in South America (Gómez-Marin *et al.,* 2011).

Trade relevance and Impact on economically vulnerable populations

As toxoplasmosis has a global distribution, the trade relevance is generally considered minimal. However, import and export of chilled (non-frozen) meat (including beef and horse) may enable spread of the different genotypes of *Toxoplasma*, with particular concern being the import of more virulent strains into new areas (Pomares *et al.,* 2011).

An elevation in vulnerable populations (e.g. immunologically compromised) who are more likely to experience clinical illness from infection with *T. gondii* may indicate that this parasite is of increasing importance.

Thus, the main concerns appear to be that populations that are vulnerable to clinical toxoplasmosis may be increasing, while more virulent strains may have the potential to spread with traded produce, meat, and animals.

References

Boyer, K., Hill, D., Mui, E., Wroblewski, K., Karrison, T., Dubey, J.P., Sautter, M., Noble, A.G., Withers, S., Swisher, C., Heydemann, P., Hosten, T., Babiarz, J., Lee, D., Meier, P., McLeod, R. and the Toxoplasmosis Study Group. 2011. Unrecognized ingestion of *Toxoplasma gondii* oocysts leads to congenital toxoplasmosis and causes epidemics in North America. *Clinical and Infectious Diseases,* 53(11): 1081–1089.

Carneiro, A.C., Andrade, G.M., Costa, J.G., Pinheiro, B.V., Vasconcelos-Santos, D.V., Ferreira, A.M., Su, C., Januário, J.N. & Vitor, R.W. 2013. Genetic characterization of *Toxoplasma gondii* revealed highly diverse genotypes for isolates from newborns with congenital toxoplasmosis in south-eastern Brazil. *Journal of Clinical Microbiology*, 51(3): 901–907.

Clementino Andrade, M.M., Pinheiro, B.V., Cunha, M.M., Carneiro, A.C., Andrade Neto, V.F. & Vitor, R.W. 2013. New genotypes of *Toxoplasma gondii* obtained from farm animals in northeast Brazil. *Research in Veterinary Science,* 94(3): 587–589.

Cook, A.J., Gilbert, R.E., Buffolano, W., Zufferey, J., Petersen, E., Jenum, P.A., Foulon, W., Semprini, A.E. & Dunn, D.T. 2000. Sources of *Toxoplasma* infection in pregnant women: European multicentre case-control study. European Research Network on Congenital Toxoplasmosis. *British Medical Journal*, 321(7254): 142–147.

Davidson, R., Simard, M., Kutz, S.J., Kapel, C.M., Hamnes, I.S. & Robertson, L.J. 2011. Arctic parasitology: why should we care? *Trends in Parasitology*, 27(6): 239–245.

Dubey, J.P. 2009a. *Toxoplasmosis of Animals and Humans.* 2nd ed. CRC Press, Boca Raton, FL, USA.

Dubey, J.P. 2009b. Toxoplasmosis in sheep – the last 20 years. *Veterinary Parasitology*, 163(1-2): 1–14.

Dubey, J.P. & J.L. Jones. 2008. *Toxoplasma gondii* infections in humans and animals in the United States. *International Journal of Parasitology*, 38: 1257–1278.

Dubey, J.P., Hill, D.E., Rozeboom, D.W., Rajendran, C., Choudhary, S., Ferreira, L.R., Kwok, O.C. & Su, C. 2012a. High prevalence and genotypes of *Toxoplasma gondii* isolated from organic pigs in northern United States of America. *Veterinary Parasitology*, 188(1-2): 14–18.

Dubey, J.P., Lago, E.G., Gennari, S.M., Su, C. & Jones, J.L. 2012b. Toxoplasmosis in humans and animals in Brazil: high prevalence, high burden of disease, and epidemiology. *Parasitology*, 139(11):1375-424.

Flegr, J. 2007. Effects of *Toxoplasma* on human behaviour. *Schizophrenia Bulletin*, 33(3): 757–760.

Flegr, J. 2013. How and why *Toxoplasma* makes us crazy. *Trends in Parasitology*, 29(4): 156–163.

Gómez-Marin, J.E., de la Torre, A., Angel-Muller, E. and 30 others. 2011. First Colombian multicentric newborn screening for congenital toxoplasmosis. *PLoS Neglected Tropical Diseases,* 5(5): e1195 Online doi: 10.1371/journal.pntd.0001195.

Guy, E., Dubey, J.P. & Hill, D.E. 2012. *Toxoplasma gondii.* pp. 167–188 (Ch. 6), in: L.J. Robertson and H.V. Smith (editors). *Food-borne Protozoan Parasites.* Nova Biomedical.

Henriquez,, S.A., Brett, R., Alexander, J., Pratt, J. & Roberts, C.W. 2009. Neuropsychiatric disease and *Toxoplasma gondii* infection. *Neuroimmunomodulation*, 16: 122–133.

Jones, J.L., Dargelas, V., Roberts, J., Press, C., Remington, J.S. & Montoya, J.G. 2009. Risk factors for *Toxoplasma gondii* infection in the United States. *Clinical Infectious Diseases*, 49(6): 878–884.

Khan, A., Dubey, J.P., Su, C., Ajioka, J.W., Rosenthal, B.M. & Sibley, L.D. 2011. Genetic analyses of atypical Toxoplasma gondii strains reveal a fourth clonal lineage in North America. *International Journal of Parasitology*, 41: 645–655.

Kijlstra, A. & Jongert, E. 2008. Control of the risk of human toxoplasmosis transmitted by meat. *International Journal of Parasitology*, 38(12): 1359–1370.

Montoya, J. & Liesenfeld, O. 2004. Toxoplasmosis. *Lancet,* 363: 965–976.

Opsteegh, M., Prickaerts, S., Frankena, K. & Evers, E.G. 2011. A quantitative microbial risk assessment for meat-borne *Toxoplasma gondii* infection in The Netherlands. *International Journal of Food Microbiology*, 150(2-3): 103–114.

Petersen, E., Kijlstra, A. & Stanford, M. 2012 Epidemiology of ocular toxoplasmosis. *Ocular Immunology and Inflammation*, 20(2): 68–75.

Pomares, C., Ajzenberg, D., Bornard, L., Bernardin, G., Hasseine, L., Dardé, M.-L. & Marty, P. 2011, Toxoplasmosis in horse meat. 2011. *Emerging Infectious Diseases*, 17(7): 1327–1328.

A7.21 *TRICHINELLA* SPP. OTHER THAN *T. SPIRALIS*

General information

Nematodes of the genus *Trichinella* are maintained in nature by sylvatic or domestic cycles. The sylvatic cycle is widespread on all continents, from frigid to torrid zones except Antarctica, and it is maintained by cannibalism and the scavenging behaviour of carnivorous and omnivorous animals. Twelve taxa are recognized in the genus *Trichinella*, three of them (*T. pseudospiralis, T. papuae, T. zimbabwensis*) are clustered in the non-encapsulated clade, and the other nine are in the encapsulated clade (*T. spiralis, T. nativa, T. britovi, T. murrelli, T. nelsoni, T. patagoniensis, Trichinella* T6, T8 and T9). All taxa infect mammals, while whereas, *T. pseudospiralis* infects also birds, and *T. papuae* and *T. zimbabwensis* infect also reptiles) (Pozio *et al.,* 2009).

Only humans show the clinical disease, trichinellosis, whereas animals are generally asymptomatic and only those experimentally infected with a huge number of larvae can develop the signs of the disease. Humans acquire the infection by the ingestion of raw or poorly cooked meat of domestic and wild swine, bears, walruses, horses, badgers, dogs, cougars, jackals and turtles. Meat and meat-derived products of all *Trichinella*-susceptible animals are a risk for humans if consumed raw or semi-raw (Pozio and Murrell, 2006).

Geographical distribution

Trichinella parasites are widespread in all continents, except Antarctica, with varying prevalence according to the environmental conditions (low temperature and high humidity versus high temperature and low humidity), wildlife, and human behaviour. For example, the common habit of hunters to leave animal carcasses in the field after skinning, or removing and discarding the entrails, increases the probability of transmission to new hosts (Pozio and Murrell, 2006). *T. spiralis* and *T. pseudospiralis* are the only two species with a cosmopolitan distribution for two different reasons: *T. spiralis* has been spread in the world by humans, while *T. pseudospiralis* is spread by birds. All the other taxa show a well defined distribution area: *T. nativa* in arctic and sub-arctic regions; *T. britovi* in Europe, western Asia, North and West Africa; *T. murrelli* in United States of America, southern Canada and northern Mexico; *T. nelson* in eastern and southern Africa; *T. patagoniensis* in South America; *Trichinella* T6 in arctic and sub-arctic regions of North America; *Trichinella* T8 in southwest Africa; and *Trichinella* T9 in Japan (Pozio *et al.,* 2009).

In 1998, it was estimated that the global prevalence of trichinellosis was about 11 million (Dupouy-Camet, 2000). This estimate was based on the assumption that the number of trichinellosis cases was similar to that of people affected by taeniasis/cysticercosis, because both diseases are transmitted through pork consumption. In

2007, an estimate of the yearly incidence suggested around 10 000 infections. This number was estimated by aggregating the highest incidence rate reported in the countries of the world in a ten-year period (Pozio, 2007). However, because of problems related to incomplete data from some regions, and to the quality of diagnostic criteria of infection, the World Health Organization's Food-borne Disease Burden Epidemiology Reference Group (FERG) requested a systematic review of the global incidence. The systematic review of the literature available worldwide from 1986 to 2009 founds reports of 65 818 cases and 42 deaths from 41 countries (Murrell and Pozio, 2011). Most of the infections (87%) have been documented in Europe, with about half of those being from Romania.

Disease

Severity of acute morbidity

In most persons, the onset of the acute stage is sudden, with general weakness, chills, headache, fever (up to 40°C), excessive sweating and tachycardia. In nearly all cases, symmetrical eyelid and periocular oedema occur, and oedema frequently affects the entire face. The blood vessels of conjunctivae become inflamed, and in some persons petechiae, intraconjunctival haemorrhages and haemorrhages of nail beds occur. These symptoms are accompanied by eosinophilia, and usually by leucocytosis. This symptomatology is followed by pain in various muscle groups, which may restrict motility. The intensity of muscle pain reflects the severity of the disease. Pain develops in nuchal and trunk muscles, in the muscles of the upper and lower extremities, and, less frequently, in masseter muscles. Pain occurs upon movement (Pozio, Gomez Morales and Dupouy-Camet, 2003).

Severity of chronic morbidity

It is quite difficult to distinguish what may be considered as "chronic trichinellosis". Nonetheless, there have been reports of persons who, months or even years after the acute stage, continued to suffer from chronic pain, general discomfort, tingling, numbness and excessive sweating, and who showed signs of paranoia and a syndrome of persecution. The persistence of these symptoms has been more frequently observed among persons who had suffered severe trichinellosis. Up to ten years from infection, there have been reports of impaired muscle strength, conjunctivitis, impaired coordination and the presence of IgG antibodies, and live larvae have been detected in muscles up to 39 years after infection, yet without clinical signs or symptoms (Pozio, Gomez Morales and Dupouy-Camet, 2003).

Chronic illness fraction

Chronic trichinellosis is very rarely documented; however, all cases in which trichinellosis has been defined as "chronic" have been reported in persons who had not been treated in a timely manner (i.e. early in the invasion of the muscles by larvae) (Pozio, Gomez Morales and Dupouy-Camet, 2003).

Case fatality rates

In a 24-year period (1986–2009), 42 deaths were reported worldwide, of which 24 were documented in Europe (Murrell and Pozio, 2011).

Increase in human illness potential

Social, political and economic factors; food behaviour; increase in animal populations susceptible to *Trichinella*; and the common habit of hunters to leave animal carcasses in the field after skinning or removing and discarding the entrails, are responsible for the reemergence of trichinellosis in humans.

Trade relevance

Trade was of important relevance for horse meat in the past (Liciardi *et al.,* 2009). Game meat (mainly from wild boar and bear) illegally imported from endemic to non-endemic countries was the source of infection for hundreds of people. Since *Trichinella*-infected pigs are backyard or free-ranging, they are consumed at the local level and do not reach the market. Most marketed pigs are reared in high containment-level farms and consequently are *Trichinella* free.

Impact on economically vulnerable populations

Trichinella spp. circulate at relatively high prevalence in backyard or free-ranging pigs of poor rural areas without efficient veterinary services. However, the behaviour of the human population and the environmental conditions play an important role in the circulation of these zoonotic parasites. In addition, since *Trichinella* spp. circulate in wildlife, the hunters, their relatives and friends consuming game meat of *Trichinella*-susceptible animals can be exposed to the infection regardless of their economic and social status if game is not tested by the veterinary services.

References

Dupouy-Camet, J. 2000. Trichinellosis: a worldwide zoonosis. *Veterinary Parasitology*, 93: 191–200.

Liciardi, M., Marucci, G., Addis, G., Ludovisi, A., Gomez Morales, M.A., Deiana, B., Cabaj, W. & Pozio, E. 2009. *Trichinella britovi* and *Trichinella spiralis* mixed infection in a horse from Poland. *Veterinary Parasitology,* 161: 345–348.

Murrell, K.D. & Pozio, E. 2011. Worldwide occurrence and impact of human trichinellosis, 1986–2009. *Emerging Infectious Diseases,* 17: 2194–2202.

Pozio, E. 2007. World distribution of *Trichinella* spp. infections in animals and humans. *Veterinary Parasitology,* 149: 3–21.

Pozio, E., Gomez Morales, M.A. & Dupouy-Camet, J. 2003. Clinical aspects, diagnosis and treatment of trichinellosis. *Expert Reviews in Anti-infection Therapy*, 1: 471–482.

Pozio, E., Hoberg, E., La Rosa, G. & Zarlenga, D.S. 2009. Molecular taxonomy, phylogeny and biogeography of nematodes belonging to the *Trichinella* genus. *Infection Genetics and Evolution,* 9(4): 606–616.

Pozio, E. & Murrell, K.D. 2006. Systematics and epidemiology of *Trichinella*. *Advances in Parasitology*, 63: 367–439.

A7.22 *TRICHINELLA SPIRALIS*

General information

Trichinella spiralis is an intracellular parasitic nematode of mammalian striated muscles. It is responsible for trichinellosis, a zoonosis resulting from consumption of raw or undercooked meat from infected animals (e.g. pork, game animals). Human outbreaks have been regularly reported during the last century (Ancelle *et al.,* 2005; Khumjui *et al.,* 2008). Trichinellosis is regarded as an emerging or re-emerging disease in some parts of the world (particularly in Eastern Europe, Asia, etc.). *Trichinella* infections are mainly due to food or culinary habits, with pork being the major source of contamination for humans (Devine, 2003; Blaga *et al.,* 2009). The *Trichinella* genus is divided in two clades (Gottstein, Pozio and Noeckler, 2009) with (i) encapsulated species due to the production of a collagen capsule surrounding the parasite: *T. spiralis, T. nativa, T. britovi, T. murrelli*, *T. nelsoni, T. patagoniensis* (Krivokapich *et al.,* 2012) and 3 genotypes; and (ii) the non-encapsulated species that do not form a thick collagen capsule in muscle: *T. pseudospiralis, T. papuae* and *T. zimbabwensis*. Most of these species and genotypes are involved in human infections and clinical signs.

Geographical distribution

It was estimated that more than 11 million people are infected worldwide (Dupouy-Camet, 2000), but this figure should be carefully used as it is based on serological studies.

Even if *Trichinella* can be found worldwide in wild animals, the parasite is endemic in pig breeding in several countries in eastern Europe, Russia (in some areas), China (in various provinces), South Asia (Laos, Thailand) and in South America (except Brazil). For example, an overall study in China described more than 500 human outbreaks, numbering 25 161 reported cases with 240 deaths (Liu and Boireau, 2002). It was underlined that this reported quantity was probably significantly underestimated because adequate diagnostic techniques might not have been available in China at the time.

Disease

Severity of acute morbidity

In animals the disease is considered as asymptomatic, whereas in humans, trichinellosis is a serious disease that can cause much suffering and rarely may result in death. The symptoms follow the parasitic life cycle, with an enteric phase, a migratory phase and a muscle phase. During the invasion of intestinal epithelium by the worms, intestinal pains and diarrhoea can be observed (Gottstein, Pozio and Noeckler, 2009). Severe signs and symptoms such as fever (39–40°C) and facial oedema may result from the migration of the larvae within blood vessels.

The establishment of new-born larvae within the muscle cell and the encystment of muscle larvae (ML) are responsible for myalgia and asthenia. The most frequently affected muscles are the muscles of the cervix, trunk, upper and lower extremities, and also less frequently the masseters. Severe myalgia generally lasts for two to three weeks.

Severity of chronic morbidity and chronic illness fraction

A small percentage of trichinellosis cases become "clinically chronic" and may be associated with recurrent muscle pain, a difficulty in eye accommodation, and intestinal disorders in the case of repeated infection. Brain abnormalities were also reported by several authors (Gottstein, Pozio and Noeckler, 2009). The fraction of chronic illness is difficult to establish precisely as it depends on the initial infective dose of ML ingested and the density of ML spread in the organism. During large outbreaks, like those reported following the consumption of contaminated horse meat, less than 10% of human cases become chronic.

Case fatality rates

A study on the reported trichinellosis cases in China (Liu and Boireau, 2002) allowed for an estimate of mortality (0.9%). This figure confirmed the previous estimation for human mortality.

Increase in human illness potential

A recent report in India underlines the possibility of reaching 30% mortality in the absence of treatment during severe infection (Sethi *et al.,* 2012).

Trade relevance

Domestic pigs, horses and susceptible wild animals intended for human consumption are submitted to compulsory veterinary controls to ensure the meat is *Trichinella* free. The method for *Trichinella* detection is based on direct identification of the parasite after artificial digestion of muscle sample harvested on carcasses (Gajadhar *et al.,* 2009). The reference method is described in both EU regulation and ICT (EU, 2005; ICT, no date) recommendations. Briefly, EU regulation requests that pigs must be systematically sampled at slaughterhouses and submitted to *Trichinella* detection (1 g for domestic swine, 2 g for breeding sows and boars, taken in the pillar of the diaphragm). Other animals (horse meat, wild game meat and other species sensitive to *Trichinella* infection) must be analysed with at least 5 g of muscle from tongue or jaw muscle for horsemeat and at least 5 g of muscle from foreleg, tongue or diaphragm for wild boar. Derogations for meat of domestic swine are possible when pig holdings have been officially recognized as being controlled housing as defined by the competent authorities.

Impact on economically vulnerable populations

Few studies on trichinellosis have been performed in low- or middle-income countries and there is a need for research in this field.

Other relevant information

Critical control points in pre- and post-harvest raising of pigs are described in OIE and ICT guidelines and also derogations are given in the EU regulation. The main points are:

- *Prevention of livestock contamination* Feed must be purchased from an approved company that produces feed following good production practices. Feed and feed storage must be maintained in closed silos where rodents cannot enter. Feeding livestock with uncooked food waste, rodents or other wildlife are practices that expose animals to a risk of contamination by *Trichinella*.
- *Meat processing* Meat of domestic swine that has undergone a freezing treatment according to EU regulation or ICT recommendations and under the supervision of competent authorities can be exempted from *Trichinella* examination. For example, pork of a thickness up to 15 cm needs to be frozen at -15°C for at least 20 days to be considered safe. However, *Trichinella* found in game meats (mainly *T. nativa* and to a lesser extent *T. britovi*) may be resistant to freezing and therefore frozen meat may still pose a public health risk. If meat cannot be controlled by a fully implemented direct examination, ICT recommends adequate treatment by cooking the meat to an internal temperature of 71°C. Appropriate treatment of meat cannot be ensured by the use of microwaves, drying or smoking.

Prevention of human infection is accomplished by meat inspection, by meat processing and by prevention of exposure of food animals to infected meat. Game meats should always be considered as a potential source of infection, and therefore game meats should be tested or cooked thoroughly.

References

Ancelle, T., De Bruyne, A., Poisson, D. & Dupouy-Camet, J. 2005. Outbreak of trichinellosis due to consumption of bear meat from Canada. France, September 2005. *Eurosurveillance*, 10(10: e051013.3)

Blaga, R., Durand, B., Antoniu, S., Gherman, C., Cretu, C., Cozma, V. & Boireau, P. 2007. A dramatic increase in the incidence of human trichinellosis in Romania over the past 25 years: impact of political changes and regional food habits. *American Journal of Tropical Medicine and Hygiene,* 76: 983–986

Devine, R. 2003. La consommation des produits carnés. *INRA Productions Animales,* 16: 325–327.

Dupouy-Camet, J. 2000. Trichinellosis: a worldwide zoonosis. *Veterinary Parasitology*, 93: 191–200.

EU (European Union). 2005. Commission Regulation (EC) No 2075/2005 of 5 December 2005 laying down specific rules on official controls for *Trichinella* in meat. Available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:338:0060:0082:EN:PDF Accessed 2013-06-23.

Gajadhar, A.A., Pozio, E., Gamble, H.R., Nockler, K., Maddox-Hyttel, C., Forbes, L.B., Vallee, I., Rossi, P., Marinculic, A. & Boireau, P. 2009. *Trichinella* diagnostics and control: mandatory and best practices for ensuring food safety. *Veterinary Parasitology*, 159: 197–205.

Gottstein, B., Pozio, E. & Noeckler, K. 2009. Epidemiology, diagnosis, treatment, and control of trichinellosis. *Clinical Microbiology Reviews*, 22: 127–145.

ICT (International Commission on Trichinellosis). No date. Recommendations on methods for the control of *Trichinella* in domestic and wild animals intended for human consumption. Prepared by the ICT Standards for Control Guidelines Committee. 22 p. Available at http://www.trichinellosis.org/uploads/ICT_Recommendations_for_Control_English.pdf Accessed 2013-06-23.

Khumjui, C., Choomkasien, P., Dekumyoy, P., Kusolsuk, T., Kongkaew, W., Chalamaat, M. & Jones, J.L. 2008. Outbreak of trichinellosis caused by *Trichinella papuae,* Thailand, 2006. *Emerging Infectious Diseases*, 14: 1913–1915.

Krivokapich, S.J., Pozio, E., Gatti, G.M., Gonzalez Prous, C.L., Ribicich, M., Marucci, G., La Rosa, G. & Confalonieri, V. 2012. *Trichinella patagoniensis* n.sp. (Nematoda), a new encapsulated species infecting carnivorous mammals in South America. *International Journal for Parasitology,* 42: 903–910

Liu, M. & Boireau, P. 2002. Trichinellosis in China: epidemiology and control. *Trends in Parasitology*, 18: 553–556.

Sethi, B., Butola, K.S., Kumar, Y. & Mishra, J.P. [2012]. Multiple outbreaks of trichinellosis with high mortality rate. *Tropical Doctor*, 42(4): 243–243.

A7.23 *TRICHURIS TRICHIURA*

General information

Trichuris trichiura is a nematode commonly known as the whipworm due to its particular shape (it looks like a whip with wider "handles" at the posterior end). Females are approximately 35–50 mm long, males 30–45 mm. The female *T. trichiura* produces 2000–10 000 single-celled eggs per day. Eggs are deposited from human faeces to soil where, after two to three weeks depending on the temperature and humidity (hot and humid climatic conditions are optimal for their development), they become embryonated and enter the "infective" stage. When these embryonated infective eggs are ingested by humans, they hatch in the small intestine, exploiting the intestinal microflora as hatching stimulus, where they grow and moult. The young worms move to the caecum and penetrate the mucosa with the cephalic end, and there they complete their development to adult worms. The life cycle from time of ingestion of eggs to development of mature worms takes approximately three months. During this time, there may be limited signs of infection in stool samples due to lack of egg production and shedding. The female *T. trichiura* begin to lay eggs after three months of maturity, and worms can live up to two to three years.

Geographical distribution

T. trichiura, together with *Ascaris lumbricoides, Ancylostoma duodenal* and *Necator americanus*, is a soil-transmitted helminth. It is distributed worldwide, infecting an estimated 600 million people, especially in tropical and subtropical areas, with the greatest numbers occurring in Africa, southern India, China, Southeast Asia and the Americas. In 2010, the global population at risk was estimated at 5 023 million (Asian Group Report, this publication), with a Global Burden of Disease (GBD) estimated at 1.0–6.4 million DALYs (WHO, 2102a) in the world (236 000 DALYs in Africa) (African Group Report, this publication).

Infection occurs through ingestion of eggs by eating raw, unwashed vegetables, by drinking contaminated water, or by not washing the hands after handling contaminated soil (a common transmission route for children).

Disease

Morbidity is related to the number of worms harboured (WHO, 2012b). Light infections (<100 worms) are frequently asymptomatic, while bloody diarrhoea and dysentery may occur in heavy infections, with rectal prolapse possible in severe cases. Vitamin A deficiency may also result due to infection. Mechanical damage to the mucosa may occur, as well as toxic or inflammatory damage to the intestines of the host. Trichuriasis is one of the seven most common Neglected Tropical Diseases (NTDs) (GNNTD, 2012).

Intensity of infection is classified by WHO according to the number of eggs per gram (epg) of faeces, excreted by infected persons: from 1–999 epg the infection is considered light, from 1000–9999 epg moderate, and >10 000 epg the infection is heavy intensity (WHO, 2011).

The burden of disease due to *T. trichiura* is mainly attributed to its chronic and insidious impact on the health and quality of life of those infected, rather than to the mortality it causes. Infections of heavy intensity impair physical growth and cognitive development and are a cause of micronutrient deficiencies, leading to poor school performance and absenteeism in children, reduced work productivity in adults and adverse pregnancy outcomes.

In countries of high endemicity of the soil-transmitted helminth parasites, preventive chemotherapy (i.e. repeated administration of anthelmintic drugs to at-risk populations) is the main strategy to control morbidity. However, rapid re-infection of humans occurs after successful de-worming, and therefore effective preventive measures are required to achieve public health goals with optimal efficiency and sustainability.

In 2001, the World Health Organization endorsed preventive chemotherapy as the global strategy to control soil-transmitted helminthiasis (WHO, 2012b). The key component of this strategy is regular administration of anthelmintic drugs to at-risk groups: children, women of childbearing age, and adults in high-risk occupations, such as nightsoil re-use and farming. Although this strategy reduces illness caused by soil-transmitted helminths, it does not prevent rapid re-infection. To interrupt transmission and to achieve local elimination of helminthiasis, integrated control approaches that include access to sanitation and other complementary interventions of a primary prevention nature are needed (Ziegelbauer, 2012).

Trade relevance

Currently this parasite is not considered an issue in trade. Due to the faecal-oral route of transmission for *T. trichiura*, the primary production and pre-harvest stage of the food chain are critical in terms of control of this parasite, and areas for cultivation of fresh produce, particularly for raw consumption, need to be assessed in terms of their susceptibility to faecal contamination.

Impact on economically vulnerable populations

Poor hygiene, especially lack of sanitation occurring wherever there is poverty, is associated with soil-transmitted helminthiases, such as *T. trichiura*, and also contributes to the faecal contamination of foods. People infected with soil-transmitted helminths have parasite eggs in their faeces. In areas where there are no latrine

systems, the soil (and water) around the village or community becomes contaminated with faeces containing worm eggs. Children are especially vulnerable to infection due to their high exposure risk.

References

GNNTD (Global Network on Neglected Tropical Diseases). 2012. Web site. http://www.globalnetwork.org/trichuriasis Accessed 2013-06-23.

WHO (World Health Organization). 2011. Helminth control in school age children. A guide for managers of control programmes. 2nd ed. 90 p. Available at http://whqlibdoc.who.int/publications/2011/9789241548267_eng.pdf Accessed 2013-06-23.

WHO. 2012a. Research priorities for helminth infections. Technical report of the TDR disease reference group on helminth infections. *WHO Technical Report Series*, no. 972. 174 p. Available at http://apps.who.int/iris/bitstream/10665/75922/1/WHO_TRS_972_eng.pdf Accessed 2013-06-23.

WHO. 2012b. Soil-transmitted helminthiases: eliminating soil-transmitted helminthiases as a public health problem in children. Progress report 2001–2010 and strategic plan 2011–2020. 79 p. Available at http://whqlibdoc.who.int/publications/2012/9789241503129_eng.pdf Accessed 2013-06-23.

Ziegelbauer, K., Speich, B., Mäusezahl, D., Bos, R., Keiser, J. & Utzinger, J. 2012. Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Medicine*, 9(1): e1001162. Online; doi: 10.1371/journal.pmed.1001162.

A7.24 *TRYPANOSOMA CRUZI*

General information

Chagas disease, or American trypanosomiasis, a primarily vector-borne parasitic disease in the Americas, is a human infection caused by the protozoan parasite *Trypanosoma cruzi*. The disease can also be transmitted through transfusion, through transplant, congenitally and by oral transmission (WHO, 2003; Bern *et al.,* 2011). *T. cruzi* is a flagellate that belongs to the Kinetoplastida order, Trypanosomatidae family, characterized by the presence of one flagellum and a single mitochondrion, where the kinetoplast is located. The parasite *T. cruzi* is not a homogeneous population and is composed of a pool of strains which circulate both in the domestic and sylvatic cycles involving humans, vectors and animal reservoirs of the parasite (Bern *et al.,* 2011).

Geographical distribution

According to information from 21 countries located throughout Mexico, Central America and South America, where the disease is endemic, the number of infected people today is estimated at 7 694 500 (1.448% of the population) (PAHO/WHO, 2012). The number of new cases per year due to vector transmission is estimated at 41 200 (7775 per 100 000) and the number of new cases of congenital Chagas disease per year has been estimated at 14 385. In addition, in 2008, 11 000 people died from the disease (WHO, 207; PAHO/WHO, 2012; WHO. 2010).

Animal reservoirs

To date, over 100 mammalian species have been reported as natural hosts for *T. cruzi*, and all mammals are considered to be susceptible to infection. The epidemiologically important reservoirs vary geographically according to the biology and ecology of mammals and vectors, and how these interactions translate to risk of human exposure. Although *T. cruzi* has a wide host range, opossums and armadillos are important reservoirs throughout the Americas (Bern *et al.,* 2011).

Vectors

There are more than 130 triatomine species (blood sucking reduviid insects) in the Americas, many of which can be infected by and transmit *T. cruzi*. However, a small number of highly domiciliated vectors are important in the human epidemiology of the disease. The major triatomine species that colonize domestic and peridomestic environments and play an important role in the epidemiology of Chagas disease in Latin America are: *Triatoma infestans* in Argentina, Brazil, Chile, Paraguay, southern Peru and Uruguay; *Rhodnius prolixus* in Colombia, El Salvador, Guatemala, Honduras, southern Mexico, Nicaragua and Venezuela; *Triatoma dimidiate* in Belize, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, northern Peru and Venezuela;

Panstrongylus megistus in Argentina, Brazil, Paraguay, Uruguay; and *Triatoma brasiliensis* in north-eastern Brazil (WHO, 2003; Bern *et al.,* 2011).

Disease

In the Americas, *T. cruzi* infection is most commonly acquired through contact with faeces of an infected triatomine bug (vector-borne transmission) that can enter the human body through a bite wound, intact conjunctiva or other mucous membranes. Infection can also occur from: mother-to-baby (congenital), contaminated blood products (transfusions), transplanted organs from infected donors, laboratory accidents, food or drink contaminated with vector faeces (oral transmission) or consumption of raw meat from infected mammalian sylvatic hosts (Nóbrega *et al*., 2009; Dias, Amato Neto and Luna, 2011; Toso, Vial and Galanti, 2011; PAHO, 2009).

The acute phase of infection usually lasts around two months immediately after infection and is characterized by a variety of clinical manifestations and parasites that may be found in the blood. Most cases have no or few symptoms, but there may be a skin chancre (chagoma) or unilateral purplish orbital oedema (Romaña's sign) with local lymphadenopathy and fever over several weeks. More general symptoms include: headache, myalgia, dyspnoea, oedema in inferior extremities or face, abdominal pain, cough, hepatomegaly, rash, painful nodules, splenomegaly, generalized oedema, diarrhoea, multiple lymphadenopathy, myocarditis and, more rarely, meningoencephalitis

Following the acute phase, most infected people enter into a prolonged asymptomatic form of the disease (called 'chronic indeterminate') during which few or no parasites are found in blood, but with positive anti-*T. cruzi* serology. However, 10–40% will go on over the next decades to develop cardiac or digestive manifestations, or both. Cardiac sequelae include: conduction disorders, arrhythmia, cardiomyopathy, heart failure, cardiac aneurysm and secondary thromboembolism. Digestive lesions include megaoesophagus and megacolon (WHO, 2003; Bern *et al.,* 2011).

Chagas disease by oral transmission

Following advances in the control of vectors and transmission of Chagas disease via blood transfusion in the endemic regions of America, alternative mechanisms of transmission have become more important, and several outbreaks reported in Brazil, Colombia and Venezuela have occurred due to transmission of *T. cruzi* through an oral route and have been attributed to contaminated fruit, palm wine or sugar cane juice (Nóbrega *et al*., 2009; Alarcón de Noya *et al*., 2010; Dias, Amato Neto and Luna, 2011; Toso, Vial and Galanti, 2011; PAHO, 2009).

The clinical presentation of Chagas disease contracted through oral transmission is different from that observed in vector-borne infection, with more severe acute morbidity and higher mortality. After an incubation period of 5 to 22 days post-ingestion, the disease is expressed with acute manifestations of fever, gastric irritation, abdominal pain, vomiting, jaundice and bloody diarrhoea. As a result, in many cases patients develop severe myocarditis and meningeal irritation. Lethality can reach a relatively high level (up to 35.2%, with an average rate of 7.1%) (Alarcón de Noya *et al*., 2010; PAHO, 2009; Bern *et al.,* 2011).

Trade relevance

The food-borne transmission route for *T. cruzi* is a new, emerging hazard, and the extent of the possible trade impact has not been fully assessed.

The precise stage of food handling at which contamination occurs is unknown, although various foods, such as fruit juice, sugar cane and açaí palm, are involved, possibly contaminated with infected triatomine faeces during processing. Oral transmission of Chagas disease is always dependent on infected vectors or reservoirs as *T. cruzi* does not multiply in food, therefore the disease is relevant in countries with vector-borne transmission and, additionally, outbreaks contracted through oral transmission have been detected. The adoption of good food hygiene measures, as well as proper cooking of wild meat from endemic areas minimizes the risk of transmission. In the case of prepared foods produced in areas with triatomine bugs, high standards of proper cooking or pasteurization become essential. Pasteurization of açaí pulp is being adopted for the product exported to other regions of the Amazon in Brazil and abroad (Dias, Amato Neto and Luna, 2011; PAHO, 2009).

Impact on economically vulnerable populations

Food-borne transmission of *T. cruzi* may occur more often than is currently recognized. Most outbreaks are small, often affecting family groups in rural areas, and unusually in urban populations of South America (Nóbrega *et al*., 2009; Alarcón de Noya *et al*., 2010; Dias, Amato Neto and Luna, 2011; Toso, Vial and Galanti, 2011). This form of transmission is considered an emerging threat to public health; the negative socio-economic impact is due to the high morbidity and mortality in the community affected by outbreaks.

References

Alarcón de Noya, B., Díaz-Bello, Z., Colmenares, C., Ruiz-Guevara, R., Mauriello, L., Zavala-Jaspe, R., Suarez, J.A., Abate, T., Naranjo, L., Paiva, M., Rivas, L., Castro, J., Márques, J., Mendoza, I., Acquatella, H., Torres, J. & Noya, O. 2010. Large

urban outbreak of orally acquired acute Chagas disease at a school in Caracas, Venezuela. *Journal of Infectious Diseases,* 201(9): 1308–1315.

Bern, C., Kjos, S., Yabsley, M.J. & Montgomery, S.P. 2011. *Trypanosoma cruzi* and Chagas' Disease in the United States. *Clinical Microbiology Reviews*, 24(4): 655–681.

Dias, J.C., Amato Neto V. & Luna, E.J. 2011. [Alternative transmission mechanisms of *Trypanosoma cruzi* in Brazil and proposals for their prevention] [Article in Portuguese]. *Revista da Sociedad Brasileira de Medicina Tropical*, 44(3): 375–379.

Nóbrega, A.A., Garcia, M.H., Tatto, E., Obara, M.T., Costa, E., Sobel, J. & Araujo, W.N. 2009. Oral transmission of Chagas disease by consumption of açaí palm fruit, Brazil. *Emerging Infectious Diseases*, 15(4): 653–655.

PAHO (Pan-American Health Organization). 2009. Guía para vigilancia, prevención, control y manejo clínico de la enfermedad de Chagas aguda transmitida por alimentos. [In Spanish] – Rio de Janeiro: PANAFTOSA-VP/OPAS/OMS, 2009. 92 p. (*Serie de Manuales Técnicos*, 12). Doc. PAHO/HSD/CD/539.09. Available at http://bvs.panalimentos.org/local/File/Guia_Enfermedad_Chagas_2009esp.pdf Accessed 2013-06-23.

PAHO/WHO. 2012. Fact sheet. [Estimación cuantitativa de la enfermedad de Chagas en las Américas] [In Spanish]. Doc. OPS/HDM/CD/425.06. Available at http://new.paho.org/hq/index.php?option=com_content&view=article&id=5856&Itemid=4196&lang=es Accessed 2013-06-23.

Toso M., A., Vial F., U. & Galanti, N. 2011. Oral transmission of Chagas' disease. *Revista Medica de Chile*, 139(2): 258–266.

WHO (World Health Organization). 2003. Control of Chagas disease: second report of the WHO Expert Committee. Prepared by WHO Expert Committee on the Control of Chagas Disease. OMS *Serie de informes técnicos*, no. 905. 117 p. Available at http://apps.who.int/iris/bitstream/10665/42738/1/WHO_TRS_905_spa.pdf Accessed 2013-06-23.

WHO. 2007. Reporte del Grupo de trabajo científico sobre la enfermedad de Chagas, Buenos Aires, Argentina, 17–20 April 2005. Edited by F. Guhl and G. Lasdinz. WHO Doc. TDR/GTC/09. Available at http://whqlibdoc.who.int/hq/2007/TDR_SWG_09_spa.pdf Accessed 2013-06-23.

WHO. 2010. Enfermedad de Chagas: control y eliminación: Informe de la Secretaría A63/17 22 de abril de 2010. Paper prepared for the 63rd World Health Assembly. Geneva, Switzerland. 5 p. Available at http://apps.who.int/iris/bitstream/10665/4877/1/A63_17-sp.pdf Accessed 2013-06-23.

A7.25 GLOSSARY OF PARASITOLOGICAL TERMS

assemblage – the preferred term for a *Giardia duodenalis* genotype

bradyzoite – the slowly multiplying life cycle stage of some coccidian parasites (e.g. *Toxoplasma gondii*); found inside tissue cysts in host cells

cestode – tapeworm (Phylum Platyhelminthes, Class Cestoda); all are parasitic (e.g. *Diphyllobothrium* spp., *Echinococcus* spp., *Taenia* spp.)

coccidian – member of a group of protozoan parasites (Phylum Apicomplexa) that inhabit cells lining the host's intestinal tract (e.g. *Cryptosporidium* spp., *Cyclospora cayetanensis*, *Toxoplasma gondii*)

cyst – environmental life cycle stage of some protozoan parasites, containing trophozoites (e.g. *Entamoeba histolytica*, *Giardia duodenalis*,); may also refer to tissue cysts of *Toxoplasma gondii*, sarcocysts of *Sarcocystis* spp., or hydatid cysts of *Echinococcus* spp.

cysticercus (pl. cysticerci) – the infectious larval stage of some tapeworms (e.g. *Taenia* spp.)

DALY (or DALYs) – Disability-Adjusted Life Year; a measure of disease burden calculated by adding YLL and YLD

definitive host – the final host in the life cycle of a parasite and in which sexual reproduction occurs, resulting in the production of the infectious environmental stage (e.g. eggs, cysts or oocysts)

encyst (encystment or encystation) – the formation of an environmentally-resistant cyst around some protozoan parasites prior to their shedding with the host's faeces (e.g. *Giardia duodenalis*); a result of physiological and biochemical triggers within the host's digestive tract; also, the formation of a cyst around helminth larvae at the beginning of the dormant tissue phase of the life cycle (e.g. *Taenia* spp., *Trichinella* spp.)

excyst (excystment or excystation) – release of motile, infective life cycle stages of protozoan parasites following ingestion of cysts or oocysts by a host

genotype – a genetically distinct group of organisms within a species

genus – a taxonomic group of organisms with similar attributes consisting of one or more species; typically written in italics followed by the species name

helminth – worms belonging to four phyla: Nematoda (roundworms), Platyhelminths (flatworms e.g. cestodes and trematodes), Acanthocephala (spiny-headed worms) and Nemathophora (hairworms)

hexocanth – *see:* oncosphere

hydatid cyst – fluid-filled cyst containing larvae (protoscoleces) of the tapeworm, *Echinococcus* spp.; they develop in liver, lungs, brain and other organs of the intermediate host

incubation period – the period of time between exposure to a parasite and the first symptoms

intermediate host – a host in the life cycle of a parasite in which some specific developmental stage is reached, short of the sexually mature stage; the parasite is subsequently transmitted to the next intermediate host, or to the definitive host, through predation, accidental ingestion or free-living larvae

Loeffler's syndrome – a disease in which eosinophils accumulate in the lung in response to a parasitic infection (e.g. *Ascaris lumbricoides*)

metacercariae (sing. metacercaria) – encysted infectious larval stage of trematodes; found in the tissues of intermediate hosts (e.g. *Clonorchis sinensis*) or attached to aquatic vegetation (e.g. *Fasciola hepatica*)

merozoite – non-motile life cycle stage of coccidian parasites; produced during the asexual cycle in cells lining the host's intestinal tract

metacestode – the larval stage of a tapeworm found in an intermediate host (e.g. cysticercus, hydatid cyst)

nematode – roundworm (Phylum Nematoda); includes parasitic species (e.g. Anisakidae, *Ascaris* spp., *Toxocara* spp., *Trichinella* spp.)

OLM – ocular larval migrans

oncosphere – the embryo of some tapeworms (e.g. *Echinococcus* spp., *Taenia* spp.) which has six hooklets and is surrounded by a membrane and contained within an egg; also referred to as a hexacanth

oocyst – the infectious environmental stage of coccidian parasites, produced through the sexual stage of the life cycle

paratenic host – a host not necessary for the development of a parasite but which may facilitate the completion of its life cycle and its dispersion in the environment. In contrast to its development in a secondary host, a parasite in a paratenic host does not undergo any changes into the following stages of its development.

plerocercoid – a larval stage of some cestodes with aquatic life cycles (e.g. *Diphyllobothrium* spp.); found in tissues of the second intermediate host

procercoid – a larval stage of some cestodes with aquatic life cycles (e.g. *Diphyllobothrium* spp.); found in the first intermediate host

proglottids – the "segments" of tapeworms; mature proglottids contain both male and female reproductive organs, while gravid proglottids consist of uteri filled with eggs

protoscolex (pl. protoscoleces) – juvenile scolex of some tapeworms (e.g. *Echinococcus* spp.,*Taenia* spp.) which bud from the inner lining of the cyst

protozoan – single-celled eukaryotic organism; this group includes parasitic species (e.g. *Cryptosporidium* spp., *Cyclospora cayetanensis*, *Giardia duodenalis*, *Toxoplasma gondii*)

redia – a digenean trematode (fluke) in the larval stage developed from a sporocyst in the main intermediate host, and in turn forming a number of cercariae

scolex (pl. scoleces) – the "head" or anterior end of tapeworms; equipped with hold-fast structures such as suckers, grooves or hooks, or a combination

species (sing. sp., pl. spp.) – a taxonomic group of organisms within a genus which is distinct from other species based on morphological, biological, and molecular characteristics; the genus and species make up the "scientific name" (Latin binomial) of an organism, and are typically written in italics

sporocyst – structures containing sporozoites found within mature oocysts of some coccidian parasites; also, a cyst which contains the rediae larvae of some trematode parasites

sporozoite – motile, infective life cycle stage of coccidian parasites; released from mature oocysts upon ingestion by a host; may be contained within sporocysts

sylvatic – referring to diseases affecting and/or cycling through wild animals; distinguished from domestic or synanthropic cycles

synanthropic – referring to diseases or pathogens whose life cycles are ecologically associated with humans and domestic animals; distinguished from sylvatic cycles

tachyzoite – motile life cycle stage of some coccidian parasites (e.g. *Toxoplasma gondii*); undergo rapid multiplication in the host before developing into bradyzoites and forming tissue cysts

tissue cyst – cluster of *Toxoplasma gondii* bradyzoites surrounded by a cyst wall within cells of the host's organs and tissues

trematode – fluke (Phylum Platyhelminthes, Class Trematoda); all are parasitic (e.g. *Fasciola* spp., Heterophyidae, Opisthorchiidae, *Paragonimus* spp.)

trophozoite – the motile, asexually multiplying stage in the life cycle of many protozoan parasites; present in host cells or attached to cells lining the intestine

viscera – the internal organs of the body; particularly in the thoracic and abdominal cavities

VLM – visceral larval migrans

YLL – a metric describing the Years of Life Lost in a population due to different factors, including infectious diseases

YLD – a metric describing the Years Lost due to Disability in a population due to various factors, including infectious diseases

zoonosis (noun.) – a disease naturally transmitted from one species of animal to another (including those transmitted through a vector), especially to humans

zoonotic (adj.) – designating, causing or involving a zoonosis; transmitted from animals to humans