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JOURNAL TITLE: Trans R Soc Trop Med Hyg

VOLUME/EDITION: 110/1

PUBLICATION DATE: January 2016

PUBLISHER: Oxford University Press

DOI: 10.1093/trstmh/trv112

Editorial

Food-borne trematodes: a diverse and challenging group of neglected parasites.

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Keywords: Food-borne trematodes, life cycles, taxonomy, epidemiology, pathology

Parasites and their intermediate and animal definitive hosts do not know or have any borders, particularly borders defined by politics or history. Although some parasitic diseases such as malaria, and more recently also schistosomiasis, based on their pathogenicity, distribution and the number of humans infected, have received much attention, other groups undoubtedly deserve more attention than they have previously been given. Food-borne trematodes comprise a highly diverse group of taxa with complex life cycles involving snail (first) intermediate hosts and other, mainly vertebrate species as second intermediate and/or definitive hosts. The individual food-borne trematode species often occur sporadically over large areas with specific hot spots in which human infection is common, with high levels of morbidity and/or mortality. For instance, *Fasciola hepatica* has a wide distribution in Europe, the Middle East, Asia, South America and parts of Africa, with foci of high prevalence occurring, for example, in the southwest of France and, in particular, in the Alti Plano of Bolivia.[1] Human infection with small liver flukes is also patchy, although taken together the three major species, *Clonorchis sinensis*, *Opisthorchis* *felineus* and *O. viverrini*, range from Southeast Asia, north to Korea and eastern Russia and across Siberia into Europe.[2] *C. sinensis* is predominantly an East Asian species with high prevalences in parts of China (Lai this issue) and reaching northern Vietnam in the south (Pham and Nawa this issue). *O. viverrini* is most prevalent in the northeast of Thailand where it is the major risk factor for developing cholangiocarcinoma, as is *C. sinensis* within its area of distribution,[3,4] while human infection with *O. felineus* is prominent in eastern Siberia (Pakharukova and Mordvinov this issue). For many species of food-borne trematode, there is the threat of emergence in new areas due, in part, to human movement, the changing distributions of intermediate hosts related to globalization processes and climate change, and the immense increases in aquaculture with the use of susceptible fish species.[5,6]

The number of people at risk of infection with food-borne trematodes is immense and increasing for some species, with recent estimates incorporating approximately a seventh of the human population, intestinal flukes not included,[7] while over 56 million individuals, mostly from the poorer socioeconomic groups, are estimated to be infected.[8] The latter value is a considerable underestimate for at least some species.[9] These neglected parasites cause a wide range of different pathologies that can have devastating consequences for individuals and communities.[8,10] Furthermore, zoonotic cycles can have profound implications both in terms of their medical and veterinary importance, but also their transmission ecology, evolution and successful control.[2]

It is of great significance that two out of the three metazoa classified as carcinogens belong to the food-borne trematode group (*C. sinensis* and *O. viverrini* are class 1 carcinogens), with the third, *Schistosoma haematobium*, being a water-borne trematode.[11] In the northeast of Thailand, it is estimated that 8 million individuals are infected with *O. viverrini* with between 10,000 and 20,000 deaths every year caused by cholangiocarcinoma.[4] As most of the deaths occur in individuals older than 40 years,[12] mortality usually impacts whole families often with the loss of a breadwinner causing socio-economic problems in addition to bereavement.

This special issue combines a series of reviews on current research directions, as well as presenting original research and new research methodologies. It starts with a commentary by Ponce de Leon and Nadler on the importance of recognizing cryptic species, common within the food-borne trematodes, particularly the genera *Opisthorchis* and *Paragonimus*. David Blair and colleagues provide a brief review of the genetic variation in lung flukes, feeding into the initial commentary on cryptic species and the need for taxonomic clarity before the initiation of research: know the species you are working with! They point out that only a limited number of species within the genus *Paragonimus* have been studied in some detail while diversity, particularly in Africa and the Americas, remains largely unknown. Next, Pham and Nawa deal with *C. sinensis* and *O. viverrini* in Vietnam. In the past, this has been a vexing problem with no clear dividing line being drawn between the distributions of the two species and no definite data on potential areas of sympatry. Not only has this problem been clarified, but the authors also show that there may have been confusion in the identification of *Clonorchis* and *Opisthorchis*. Other trematode species, both pathogenic and, apparently, non-pathogenic for humans, with very similar egg morphology to the two carcinogenic species, also occur in zoonotic cycles in Vietnam. As the diagnosis of human infection is commonly based on the identification of eggs in fecal samples, confusion seems likely to have occurred, something that should be considered elsewhere, for example, when the possibility of hybrids between trematode species occurs.[13] This paper is also particularly valuable in summarizing information only available in Vietnamese.

The importance of *C. sinensis* in China, where 15 million people are estimated to be infected, is discussed in the paper by Lai and colleagues. As with other food-borne trematode species, the Chinese liver fluke is probably under diagnosed as infection is often either asymptomatic or very mild. The real problem comes if cholangiocarcinoma develops. As the authors point out, a great deal of epidemiological and clinical work is still required to elucidate the relationship between *C. sinensis* and this cancer. The authors also provide up to date information on the genome, diversity, transcription, the proteome as well as diagnosis, treatment, prevention and control.

Next, Pakharukova and Mordvinov review information on the potential role of *O. felineus* in causing cholangiocarcinoma in humans in Russia. Although this species is suspected of causing this cancer,[14] this paper provides considerable new evidence that this is a fact, and it will, hopefully, lead to a much increased research effort in this area.

Toledo and Estaban provide an update on human echinostomiasis, one of the least studied groups of human parasitic trematodes, although they are widely distributed particularly in the Old World topics, but also in occasionally in colder East Asia, the Middle East and Europe.[7] This is a group of species, which, although of growing public health importance, is only now undergoing substantial taxonomic revision.[15]

The first research paper by Kolporat et al. continues with the theme of the commentary. *O. viverrini* s.l. is known to consist of a number of genetically defined taxa, each of which is confined to a specific wetland system.[16] This paper provides further information on two members of this species complex, one from the Lao PDR and one from Thailand. Significant differences are found in metacercarial burden and activity in a common cyprinid host species. This indicates that substantial geographic variation also exists with respect to parasitism in the second intermediate host and adds to other biological differences found for adult worms.[17]

Fasciola gigantica and *F. hepatica* are two closely related species differing in distribution, and, in particular, in size (*F. gigantica*, as the name suggests, is the larger of the two species), otherwise they show substantial genetic similarities. Of the two species, considerably less is known about *F. gigantica*, although its potential as a significant pathogen is increasingly recognized, particularly in endemic areas in Asia and Africa. Here Valero et al. compare, for the first time, the pathophysiology of these two species in sheep hosts. This long-term experiment, covering 24 weeks, shows that size is a major factor determining the degree of pathogenicity.

The following two papers are methodological. The first by Tantrawatpan et al. shows that the taurocyamine kinase gene can be used to elucidate the genetic variation in and the phylogenetics of *Paragonimus* spp. A particularly fascinating aspect of this study is the variability found in triploid *P. westermani*, suggesting multiple origins for this phenomenon. The paper by Saijuntha et al. provides a new method for determining the taxonomic group, potentially to species level, of lung, small intestinal and liver flukes using eggs in feces. As such, it provides a valuable additional tool to overcome the pervasive difficulty of diagnosing the species of trematode infecting humans based on egg identification in fecal samples alone and as a consequence provides more accurate epidemiological information (discussed by Pham and Nawa, this issue).

Understanding the complex population biology, transmission ecology, evolution and pathology of multi-host parasites is one of the major challenges of biomedical sciences for the 21st century and the food borne trematodes are perhaps the most neglected of all the neglected tropical parasites. The papers in this issue highlight two major aspects of the current research situation with respect to food-borne trematodes: that they are of very considerable public health and veterinary importance, and, in spite of the growing list of publications dealing with them, that a great deal of work, including basic taxonomy, epidemiology, diagnosis, clinical management and pathology, remains to be done

Author's contributions: TNP, PS, RHA and JPW all contributed to organizing this special issue and to writing the editorial. All authors read and approved the final manuscript. TNP is the guarantor of the paper.

Funding: None declared.

Competing interests: None declared.

Ethical approval: Not required.

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