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Emerging helminth zoonoses

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Abstract

As our ability to recognise and diagnose human disease caused by helminth parasites has improved, so our understanding of the epidemiology and clinical manifestations of these diseases has improved. Humans can develop patent infection with a wide range of helminth parasites, whose natural host is another vertebrate. Rather than focusing on a comprehensive review of zoonotic helminth infections, this review describes in detail examples of zoonotic helminth infections that have newly appeared in human populations, or have existed but are increasing in incidence or geographic range. Examples include intestinal capillariasis, anisakidosis, eosinophilic enteritis, oesophagostomiasis and gnathostomiasis. Potential reasons for the emergence of these infections, including changes in social, dietary or cultural mores, environmental changes, and the improved recognition of heretofore neglected infections often coupled with an improved ability to diagnose infection are discussed. © 2000 Published by Elsevier Science Ltd. on behalf of the Australian Society for Parasitology Inc.

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1. Introduction

The high degree of co-adaptation observed between *Homo sapiens* and our helminths is unremarkable given that we have evolved with them. The selection pressure on both ourselves and our parasites has generally meant that the pathology induced by such parasitism is limited. Likewise our parasites frequently have a very limited host range; indeed establishing mature infection in an animal model can be a significant achievement [1]. However, a number of examples of important zoonotic helminth infections of humans are well recognised. These include infections where other species, especially primates are equally permissive hosts, (e.g. *Loa loa*), and infections where another mammal is required for completion of the lifecycle, (e.g. echinococcosis and cysticercosis).

It is certain that throughout history, humans have been exposed to helminth parasites of other species. Given the host-specificity of most parasites, the outcome of this encounter is most often aborted infection. However, in some circumstances a zoonotic helminth is able to establish itself, and when this does occur, the consequent pathology may be more severe (see below).

A number of factors have led to the emergence of 'new' zoonotic parasitic helminth infections. These include: (i) changes in social, dietary or cultural mores which have led to the increased opportunity for exposure, (ii) environmental changes and (iii) the improved recognition of heretofore neglected infections, often coupled with an improved ability to diagnose infection. With respect to the latter, the ability to utilise molecular techniques to establish the species of pathogen responsible has led to significant advances in recognition of previously unrecognised zoonotic helminth infection [2].

Rather than focussing on an exhaustive review of the extensive literature of single case reports, or reviewing small series of zoonotic helminth infection, this review will highlight instances where a case can be made for the status of the zoonotic helminth infection as a genuine new or emerging infection. Those infections where there is a large body of case reports, but no clear case for increasing incidence will not be discussed at length in this review. A selected list of such parasitic zoonotic helminth infections is presented in Table 1. Zoonotic helminth infections discussed elsewhere in this special issue of the journal, (e.g. alveolar echinococcosis) which would otherwise qualify for consideration will not be further discussed. For the purpose of this review, emerging zoonotic helminth infections will be defined as those infections that have

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Table 1
Important helminth zoonoses of humans

Infection	Organism	Natural definitive hosts or major host reservoirs	Intermediate host(s)	Distribution
Anisakiasis	*Pseudoterranova, Phocanema, Contracaecum*	Porpoise, whale, seal, walrus, sea lion	Herring, cod, salmon, mackerel	World-wide
Capillariasis, hepatic	*Capillaria hepatica*	Rats		World-wide
Capillariasis, intestinal	*C. philippinensis*	Fish-eating water-birds	*Eleotris melanosoma* (birut), *Hypseleotris bipartita* (bagsit), *Ambassis miops* (bagsan)	Philippines, Thailand
Cercarial dermatitis	*Trichobilharzia* spp., *Gigantobilharzia* spp., *Austrobilharzia* spp., *S. douthiti*, *S. spindale*	Birds (black swans, silver ducks, silver gulls), rodents, water-buffalo	Snails	World-wide
Clonorchiasis	*Clonorchris sinensis*	Dog, pig, cat, mouse, camel	Snails, carp	Asain Pacific
Coenurosis	*Taenia multiceps*, *T. crassiceps*, *T. serialis*	Dogs	Herbivores	Africa, North America, Western Europe
Cutaneous larva migrans	*Ancylostoma caninum*, *A. brasiliense*	Dogs, cats	None	World-wide
Cysticercosis	*Taenia solium*	Pigs	Humans	World-wide
Dicrocoeliasis	*Dicrocoelium hospes*, *D. dendriticum*	Herbivorous animals	Snails, ants	World-wide
Dipylidiasis	*Dipylidium caninum*	Dog, cat	Fleas, lice	Europe
Dirofilariasis, pulmonary	*Dirofiliaria immitis*	Dog, cat, fox, wolf, coyote, sea lion	Mosquitoes	Japan, Australia, United States
Dirofilariasis, subcutaneous	*D. tenuis* (*Dirofiliaria conjuncitvae*)	Raccoon	Mosquitoes	United States
	D. repens, *D. striata*	Dogs, cats	Mosquitoes	Europe, Africa, Asia
Echinococcosis	*Echinococcus granulosus*	Carnivores (esp. dogs, foxes, wolves, dingoes)	Herbivores (esp. sheep)	South America, Mediterranean, Central Asia, Australia, New Zealand
	E. multilocularis	Foxes	Rodents	Northern Hemisphere
	E. vogeli	Bush dog, paca	Rodents	South America
Echinostomiasis	*Echinostoma* spp.	Mollusks, fish, crustaceans, amphibians, rats, pigs	Freshwater snails	Philippines, China, Thailand, Korea, Russia
Eosinophilic enteritis	*Ancylostoma caninum*	Dogs	None	Australia
Fascioliasis	*Fasciola hepatica*	Sheep, cattle (herbivores)	Snails, aquatic vegetation	World-wide
	F. gigantica	Sheep, cattle (herbivores)	Snails, aquatic vegetation	Africa, South America
Fasciolopsiasis	Fasciolopsis buski	Pig	Snails, aquatic vegetation	China
Gastrodisciasis	*Gastrodiscoides hominis*	Herbivores (esp. pigs)	Freshwater snails, aquatic plants	Bangladesh, Thailand, Malaysia, Philippines, Indonesia
Gnathostomiasis	*Gnathostoma spinigerum*	Dogs, cats	Freshwater fish, frogs, reptiles, birds; Copepod (*Cyclops*)	Asia
	G. hispidum, *G. doloresi*, *G. nipponicum*	Pigs, ichthyophagous birds, carnivorous fish, frogs and rodents	〃	Japan, China, Malaysia, Philippines

Table 1 (*continued*)

Infection	Organism	Natural definitive hosts or major host reservoirs	Intermediate host(s)	Distribution
	G. binucleatum	Dogs, cats	〃	Mexico, Ecuador
	G. turgidum	Possums	〃	USA, Latin America
	G. procyonis	Raccoons	〃	USA, Mexico
	G. americanum, *G. robustum*, *G. brasiliense*, *G. gracile*	Large felines	〃	Brazil
Heterophyiasis	*Heterophyes heterophyes*	Fish-eating mammals	Freshwater fish, snails	Asian Pacific, Egypt, Iran, Turkey, Tunisia
Hymenolepis dimunata infection	*Hymenolepis dimunata*	Rodents	Rat fleas, cockroaches	World-wide
Lagochilascariasis	*Lagochilascaris minor*	Opossum	Rodents	South America
Metagonimiasis	*Metagonimus yokogawai*	Dogs, cats, pigs, pelicans	Freshwater fish, snails	Asian Pacific
Nanophyetiasis	*Nanophyetus salmincola*	Coyotes, wolves	Freshwater fish, mollusks	Siberia, US Pacific North-west
Oesophagostomiasis	*Oesophagostomum* spp.	Non-human primates	None	Africa, Philippines, China, Brazil
Opisthorchiasis	*Opishthorchis felineus*	Dog, cat, pig	Freshwater fish, snails	Eastern Europe, Russia, India
	O. viverrini	Civet cat, dog	Freshwater fish, snails	Thailand
Paragonimiasis	*Paragonimus* spp.	Wild and domestic felines	Freshwater snails, crabs	Asian Pacific
Pentastomiasis	*Armillifer* spp.	Snakes	Mammels	Africa, Asian Pacific
	Linguatula spp.	Dogs, foxes, wolves	Rodents, herbivores	World-wide
Schistosomiasis	*Schistosoma mattheei*	Sheep, cattle, horses, antelope	Snails	Southern Africa
Sparganosis	*Spirometra* spp.	Dogs, cats	Copepod (*Cyclops*); amphibians, reptiles, mammels	Western Hemisphere, South-east Asia
Strongyloidiasis	*Strongyloides fulleborni*	Primates	None	Equatorial Africa, Papua New Guinea
Toxocariasis	*Toxocara canis*	Dogs	None	World-wide
	Toxocara cati	Cats	None	World-wide
Trichinosis	*T. spiralis*	Swine, rats	Carrion	World-wide
	T. nativa	Bears, foxes	Carrion	Arctic
	T. nelsoni	Hyenas, large felines	Carrion	Equatorial Africa
	T. britovi	Dogs	Carrion	Temperate climates
	T. pseudospiralis	Birds, mammals	Carrion	World-wide
Trichostrongyliasis	*Trichostrongylus orientalis*, *T. colubriformis*	Cattle, sheep, donkeys, deer, rabbits	None	Middle East and Asia

newly appeared in a population or have existed but are rapidly increasing in incidence or geographic range [3].

2. Capillariasis

Zoonotic infections due to nematodes of the genus *Capillaria* has recently risen in prominence. Although more than 250 species of *Capillaria* have been identified, only three are known to infect humans: *Capillaria philippinensis*, *Capillaria hepatica*, and *Capillaria aerophilia*. Of the three, *C. philippinensis* is the only species of significance, and potentially an emerging zoonotic helminth.

C. philippinensis infection was first described in rural communities in the Philippines in 1965 [4], and soon after in Thailand [5]. However, the geographic extent of infection has continued to widen, with cases since recorded in Indonesia, Japan, Taiwan, India, Iran, and Egypt [6–10]. A number of case reports have documented importation of infection into Europe from endemic areas [7,11,12]. Of interest, examination of human stool samples from prehistoric settlements in France [13] suggests that the infection may have been endemic in humans at that time. The parasite is enzootic in fish-eating birds. Humans become infected by eating uncooked small fresh water fish. The fish contract infection from the faeces of infected birds, or from faecal contamination of water by infected humans. The role of other fish-eating mammals in transmission of the infection is not well defined.

In contrast to the related Trichurid parasites *Trichinella* and *Trichuris*, and to all important intestinal helminth infections of humans other than *Strongyloides*, the parasite is able to replicate within a single human host and thus reach large numbers in the small intestine. In untreated infection, the parasite load rises to high level and leads to progressive small bowel dysfunction, marked by diarrhoea, abdominal pain, malabsorption and weight loss. Infection is frequently fatal in the absence of appropriate anthelmintic chemotherapy.

Diagnosis relies on the identification of parasite eggs in the stool of infected patients. Eggs are peanut-shaped with flattened bipolar plugs; striations are present on the shell. The eggs can be confused with *Trichuris trichuria* eggs by the inexperienced observer. Eggs may be excreted intermittently; thus multiple stool examinations may be necessary to confirm the diagnosis.

Albendazole, given in a dose of 200 mg twice daily for 10 days is the preferred treatment. Mebendazole, in a dose of 100 mg twice daily is an acceptable alternative, but needs to be given for 20 days, and relapses are more frequent with this drug [8].

While reports of infection do not appear to be rising in frequency, this zoonotic nematode parasite has nevertheless emerged in the past 20 years.

3. Anisakidosis

Consumption of raw fish including mackerel, Pacific salmon, cod or herring carrying in their viscera or muscle the larval form of anisakid parasites results in anisakidosis. While three genera of the anisakid family, *Pseudoterranove* (*Phocanema*, *Terranova*, *Porrocaecum*), *Contracaecum* and *Anisakis* can cause the syndrome, the former two do not frequently cause symptoms, and are diagnosed only by identification of the parasites in vomitus or stool. The greatest experience of anisakidosis is in Japan, where the consumption of raw fish has been a standard cultural practice for centuries. More than 97% of cases manifest as acute gastric anisakidosis, where 2–5 h after ingestion the patient experiences severe epigastric pain. A diagnosis is readily made by upper gastrointestinal endoscopy, where the worm is visualised either adherent to or within the mucosa. Endoscopic removal of the larva is curative. Rarely the parasite may lodge in other locations, anywhere from the pharynx [14], the oesophagus [15], or the small or large intestine [16]. Even more rarely, the parasite may penetrate the gut and lodge in the peritoneal cavity [17].

In recent years it has been recognised that the manifestations of infection with Anisakid parasites may be dominated by an allergic response [18]. Sensitisation may occur to both live parasites, or to parasitised food in which worms have been killed by cooking or pasteurisation. Sensitisation may result in urticaria, angioedema or anaphylaxis after eating infected seafood [19]. Indeed, this syndrome may be responsible for a significant proportion of cases of so-called idiopathic eosinophilic gastroenteritis [20]. In addition, the local allergic response may result in significant pathology, including intestinal obstruction, and mesenteric adenitis mimicking the symptoms of appendicitis.

Reports of anisakadosis have risen sharply from the first description of human infection in 1960 [21], to 1995 when the annual incidence was reported to exceed 2000 cases in Japan alone [22]. Two factors have been cited to explain the rise of anisakidosis as an emerging parasitic disease, one dietary, and the other environmental. The amount of raw fish consumed in Western countries, principally in Asian food such as sushi has increased dramatically in recent years. This has led to the recognition of infection in ethnic groups who otherwise would not have been exposed. As noted in other settings, the skill and vigilance of those preparing the animal for consumption has a marked impact on the danger of eating the food. It has been suggested that sushi prepared by a professional chef is much less likely to be infected with anisakid parasites than the same food prepared at home by an inexperienced cook [23]. An alternate explanation has been proposed to explain the rise in infection, particularly in countries where consumption of raw fish is the rule, principally Japan. As anisakid worms are the ascarid parasites of marine mammals, (dolphins, whales, seals and sea lions), the

recovery in the population of these species following the regulation of hunting may have resulted in a concomitant increase in the level of contamination of fish [22].

4. Eosinophilic enteritis *(Ancylostoma caninum)*

Hookworms are common parasites of dogs and are capable of producing the larva migrans syndromes in humans. Cutaneous larva migrans is characterised by progressive linear eruptive lesions due to the prolonged subcutaneous migration of zoonotic hookworm larvae. In the US, this condition is mainly due to *Ancylostoma braziliensis*, a parasite that is common in both dogs and cats. A more recent addition to the spectrum of zoonotic hookworm infection is eosinophilic enteritis caused by *Ancylostoma caninum*, first reported in Townsville, Australia [24].

Until recently, segmental eosinophilic inflammation of the gastrointestinal tract has been uncommonly identified. Indeed, before 1979, only about 100 cases had been reported. In 1988 33 cases were reported from Queensland [25], and an additional 60 cases were reported in 1990 [24]. In two of the patients, a juvenile adult *A. caninum* was identified, suggesting that this helminth is the aetiological agent of eosinophilic enteritis [26]. Subsequently, when enzyme-linked immunosorbent assay (ELISA) and Western blot study using ES antigens from adult *A. caninum* was undertaken on 233 persons with either eosinophilic enteritis or abdominal pain (with and without eosinophilia), all 233 clinical cases tested positive by Western blot, compared with 10% of controls [27]. Of note, the level of dog ownership in the study groups was high, ranging from 71 to 100%.

A survey in Brisbane, Australia indicates that feral dogs are the likely source of infection through contamination of public areas, and that transmission may occur year round with a seasonal peak in summer [28]. When faecal samples were examined during both summer and winter from both domesticated and euthanised refuge dogs, hookworm eggs were found in the stools of nine of the 54 (17%) domesticated dogs but only during summer. In contrast, eggs were found in the stools of 115 of 401 pounds dogs (29%) during both seasons. Among the feral dogs, eggs were found more commonly in summer than winter (38 vs. 22%) and less commonly in dogs over 3 years of age. The seasonal variation was attributed to changes in transmission, correlating with variations in temperature and humidity. The substantial reservoir of infection in this sample of Brisbane dogs indicated a high risk of infection to humans. In addition, the identification of hookworm eggs in both summer and winter suggests a continuous risk of infection to humans in this region, but with an increase during the summer months when the exposure of humans with exposed skin to contaminated soil is more likely.

While the Australian data suggest a recent local epidemic of *A. caninum*-induced eosinophilic enteritis, it is clear that this syndrome had gone unrecognised for some time, with at least two cases having gone undiagnosed for a period of several years [29]. The number of infected individuals may expand greatly in the future as a result of two factors, namely the increased awareness of the entity, and the high prevalence of dog ownership.

The Australian data indicate that occult human infection with *A. caninum* is common among dog owners in an urban environment where human hookworm infection has largely disappeared. What remains unanswered, however, is the extent of this problem outside northeastern Australia. Many of the infected patients studied exhibited mild, nonspecific symptoms or no symptoms at all, suggesting that the infection is often subclinical and hence may be more widespread than previously believed. Furthermore, since *A. caninum* has an almost worldwide distribution, it would be expected that *A. caninum*-induced eosinophilic enteritis infection should not be limited to Australia. As of this writing only isolated case reports exist of enteric human infection due to *A. caninum* in South America, the Philippines, Israel and the US [26,30].

A number of factors may help explain the apparent dearth of cases outside Australia. The diagnosis is notoriously difficult to establish, due in part to the lack of a widely available serologic test, the absence of eggs in the stools of infected individuals, and the technical difficulty in identifying the parasites within the intestinal lumen by colonoscopy. Colonoscopic detection is particularly difficult for two reasons. First, the infection is typically caused by a single, immature adult worm that is difficult to visualise. Second, in most biopsy-proven cases inflammation is confined to the ileum 15 cm or more proximal to the ileocaecal junction, a site beyond the reach of colonoscopes currently in routine use. Furthermore, the worm is easily overlooked in surgical specimens, despite examination by experienced surgical pathologists and curious medical students [29].

The expense and invasive nature of colonoscopy, the procedure required to establish the diagnosis of eosinophilic enteritis, indicates a clear need for the development of a serodiagnostic test available for routine use. In addition to facilitating clinical diagnosis, it would also enable study of seroprevalence, and if warranted a comprehensive strategy for surveillance and control. While some progress has been made [26], the performance of the ELISA using ES antigens from adult *A. caninum* has yet to attain satisfactory levels. A recently described Western blot for detection of IgG4 antibodies to an immunodominant ES antigen (Ac68) from the parasite has demonstrated improved sensitivity and specificity, 75 and 100%, respectively [31]. However, further work needs to be done to improve the sensitivity of the test, and its limited availability restricts its wider use.

In one of the reports from Townsville, use of an anthelmintic drug appeared effective [27]. Patients were empirically treated with mebendazole when the clinical features were observed to be consistent with *A. caninum* infection,

and symptoms had not resolved spontaneously. All patients eventually recovered, regardless of the use of anthelmintic therapy, but recurrent episodes were common. Although not specifically reported, one would assume that albendazole would be equally efficacious.

Dog ownership appears to be a substantial risk factor for the development of *A. caninum*-induced eosinophilic enteritis. The percentage of dog ownership in the Australian studies was high, ranging from 71 to 100% [27]. While the prevalence of dog ownership varies throughout the world, most of the world's population shares its environment with *A. caninum*-infected dogs. Thus, exposure to canine hookworms is likely to be widespread. In the US an estimated 53 million dogs are distributed among 31 million households [32]. This number is not expected to decline for the foreseeable future [33]. While the incidence of eosinophilic enteritis due to *A. caninum* is unknown in the US, one would assume a significant portion of these animals are infected given the cosmopolitan distribution of the parasite. Risk factors associated with the high incidence of this infection in Australia (warm summer climate, large dog population, frequent watering of lawns and gardens) are common elsewhere, including the US.

An effective surveillance and control program would necessitate attention to potentially infected dogs. However, pups and kittens are frequently not brought to veterinarians until they are at least 6 weeks old, by which time exposure to environments with extensive contamination with hookworm eggs may have already occurred. An education campaign to highlight the risk to humans would be a logical component of any control program.

5. Oesophagostomiasis

Human infection with the nematode parasite *Oesophagostoma bifurcum*, was until recently considered a rare zoonosis. The parasite is a member of the hookworm family of strongylid parasites, and is a common intestinal nematode of primates [34]. The first reports of infection in humans date back to 1905 [35], but in 1991 Polderman et al. [36], reported that the parasite was commonly found in humans in Northern Togo and Ghana. Recent estimates indicate that in these areas over 230 000 individuals carry infection [37].

As the eggs of the parasite are morphologically indistinguishable from human hookworm, to prove that this was indeed a new infection it was necessary to recover adult worms from infected subjects and to confirm that they were morphologically distinct from *Ancylostoma* and *Necator* [36]. Polderman et al. [36] in addition undertook coproculture of eggs recovered from the stool of infected patients and demonstrated that the parasite larvae were morphologically distinct from human hookworm larvae.

The relationship of human infection to the parasite life-cycle present in monkeys remains to be fully defined. It is likely that human-human transmission is occurring in the endemic areas [37]. Further, in some locations no monkeys are present, thus suggesting that the parasite may not be an obligate zoonotic infection [36].

The most prominent clinical manifestation of infection is the so-called 'Dapaong tumour', named after the capital of Togo's northernmost province. It is caused by the development of an inflammatory mass around juvenile worms, either within the colonic wall or in the abdominal cavity. Adhesions to the abdominal wall then develop. The presence of pain is variable, and secondary complications such as colonic obstruction may occur. Much more frequently infection is asymptomatic. However, ultrasound examination frequently demonstrates hundreds of small nodules within the wall of the large intestine that is thickened and oedematous [38]. Rare manifestations include ectopic disease in the omentum, liver or skin [39].

As infection is responsive to albendazole, the morphological diagnosis of the presence of 'hookworm' eggs in stool would be sufficient indication for therapy with this drug, which will cure both infections.

6. Gnathostomiasis

Gnathostomiasis is a foodborne zoonotic disease caused by several species of the nematode *Gnathostoma*. Most reported infections in humans are due to the species G*nathostoma spinigerum*; however, the life cycle is identical among all species of *Gnathostoma*. Adult parasites are found in the stomach wall of animals that consume raw fish. When egg-containing faeces from these animals are deposited in fresh water, free-swimming first-stage larvae are formed, which are then ingested by the small crustacean *Cyclops*. Freshwater fish feed on the minute water fleas, liberating the infective larvae which then develop into L3 in the fish muscle tissue. Consumption of infected fish results in the development of the adult parasites, thus completing the cycle. Although feral cats and dogs are the most commonly identified definitive hosts, adult parasites have also been identified in tigers, leopards, lions, minks, opossums, otters, and raccoons. Humans usually acquire the infection after ingesting raw or undercooked fish. However, other animals such as frogs, snakes, chickens, snails, and pigs can serve as intermediate hosts. Thus, ingestion of undercooked fish is not the only means of acquiring infection. The parasite fails to reach maturity in the human host. Curiously, on the infrequent occasions when the parasite has been recovered, it has almost always been identified as an immature male.

Within 24–48 h of ingestion of *Gnathostoma* spp., patients may develop non-specific signs and symptoms such as malaise, fever, urticaria, anorexia, nausea, vomiting, diarrhoea, and epigastric pain. Eosinophilia (usually $>50\%$) develops in association with larval penetration of the gastric or intestinal wall [40]. The worm migrates through the skin

and subcutaneous tissues, causing intermittent swelling that is often painful or pruritic. Patients with clinical gnathostomiasis most commonly present with symptoms due to subcutaneous migration of the worm. This occurs 3–4 weeks after ingestion but may be delayed until months or years later. Although the parasite tends to remain in the subcutaneous tissues, resulting in cutaneous gnathostomiasis, the worm can migrate to deeper tissues, resulting in visceral disease. Gnathostomiasis has been reported to involve the pulmonary, ocular, genitourinary, gastrointestinal, auditory, and central nervous systems, occasionally with fatal consequences [40].

Since it was first discovered in the stomach wall of a tiger that died in the London Zoological Gardens in 1836 [41], various species of *Gnathostoma* have been identified throughout the world [42]. However, most endemic foci have been identified in Asia [43]. Until recently, most cases of human gnathostomiasis were reported from Thailand and Japan, and infections identified in western countries were limited to travellers to the Far East. However, over the last 30 years, the geographic range of the disease has been extended to countries along the Pacific coast of the Americas; notably Argentina, Peru, Ecuador and Mexico [44–46], where it is now recognised as an emerging public health problem.

The first case of clinical gnathostomiasis was reported in Mexico in 1970 [46]. Since then, the number of patients in Mexico diagnosed with this disease has dramatically increased [47]. A 1989 report described increasing numbers of patients with eosinophilia and cutaneous findings consistent with gnathostomiasis observed in the towns along the Papaloapan river basin in the Gulf of Mexico [47]. Larvae of *Gnathostoma* spp. were recovered from some of the patients, indicating that gnathostomiasis was the likely cause. Many of the cases occurred in areas near the Presidente Miguel Aleman dam. Ecological and social changes resulting from the construction of the dam were implicated as contributing factors in the increasing incidence of this helminthic zoonosis, which had previously only been rarely reported outside Asia. The construction of the dam was followed by the importation of tilapia fishes in 1964, and their subsequent cultivation in the dammed waters of the area. Similarly, the construction of the dam coincided with the rise in popularity of eating raw freshwater fish in the form of ceviche or callos. Unfortunately, by the time that the scope of the infection was discovered, tilapia fishes (presumably infected with *Gnathostoma* larvae) had already been shipped from the Temazcal Fish Culture Center to many other aquiculture centres throughout the country, providing the substrate for a potentially explosive outbreak of gnathostomiasis.

A more intensive investigation identified over 1000 cases in six coastal states bordering either the Pacific or the Gulf of Mexico and involving some tourist areas, (e.g. Acapulco [48]). Three of the identified foci were centred on the Presidente Miguel Aleman Dam and Papaloapan River basin in the Gulf of Mexico. Almost all the patients had eaten undercooked fish, particularly tilapia.

Following the identification of these large and widely distributed endemic foci, an attempt to identify the source of infection in freshwater fish was undertaken near Culiacan, the capital of Sinaloa, a state on the north Pacific coast of Mexico. Although an earlier study in the area had resulted in the identification of fish infected with *Gnathostoma* larvae [48], this effort was unsuccessful, perhaps due to the relatively small number of fish examined ($<0.001\%$ of the estimated annual production [49]). Nevertheless, larvae were found in four different species of fish-eating birds trapped in the area. Clinical gnathostomiasis was identified in 300 people from this area over a 3-year period, an incidence much greater than had been previously reported in Asia [40].

The appearance of the disease in Culiacan was reported to coincide with the custom of eating raw freshwater fish in the form of ceviche or callos, a custom that had begun 20 years earlier, shortly after the construction of three nearby dams and the formation of lakes that produce 700–900 ton of freshwater fish annually. Cases of gnathostomiasis in Mexico reported from Oaxaca, Veracruz, Nayarit, Guerrero, and Tamaulipas were also associated with the development of aquiculture in freshwater bodies formed by newly constructed dams [48,49]. Freshwater fish were apparently introduced into Sinaloa from other lakes in Mexico, including Temascal, which had been shown to be endemic for gnathostomiasis [47]. Since no cases of gnathostomiasis had been reported in Mexico before 1970, mass production and commercial distribution of tilapia has been implicated as the most likely explanation for the findings.

Although previous reports had identified *G. spinigerum* as the aetiologic agent of gnathostomiasis in Mexico, recent evidence suggests that cases identified as being due to *G. spinigerum* are, in fact, due to *Gnathostoma binucleatum* [50]. At least two other *Gnathostoma* species appear to be unique to Mexico and have been implicated in human infection [50].

Although Mexico and countries in Asia have to date reported the largest number of cases of gnathostomiasis, endemic foci have been identified on nearly every continent [42]. Therefore, one would expect that human infections may occur globally, but have not been recognized or reported. Indirect evidence supporting this hypothesis can be found in a recent report where gnathostomiasis was identified in three travellers who had recently returned from Southeast Tanzania [51], an area of the world where *Gnathostoma* spp. had not previously been reported. The infection was confirmed parasitologically in one person, and serologically in all three persons. All three individuals had consumed undercooked fish caught in a local river. At this time it is impossible to determine with any degree of certainty whether this report represents an isolated event, or whether the disease is more widespread but remains undetected or unreported.

As with many helminthic zoonoses, serologic testing is not widely available. Currently, testing is available only through the Hospital for Tropical Diseases, Mahidol University in Bangkok, Thailand [52–54]. Attempts at immunodiagnosis in Mexico have been impeded by the paucity of adult or larval antigen [49]. This is largely due to the fact that the definitive and intermediate (paratenic) hosts for this infection have yet to be identified in Mexico. An ELISA was developed using crude somatic extract of adult *Gnathostoma doloresi* worms found in Japan. Despite this geographic discrepancy, the test exhibited a sensitivity and specificity of 93 and 98.7%, respectively.

Definitive cure of gnathostomiasis can be achieved by extraction of the infective larvae from the subcutaneous tissues. In the past, attempts to extract the larvae were rarely successful. However, with the introduction of albendazole, patients can be cured medically [55]. The drug is safe and well tolerated, although abnormal liver function tests have been reported with therapy [56]. In addition, albendazole appears to stimulate the outward migration of the worm [57], facilitating definitive parasitologic diagnosis, speciation, and cure.

Most cases of gnathostomiasis have involved women. Possible explanations for this include the traditional role many women play throughout the world in preparing food. It has been postulated that they become infected when they sample the food while preparing it. However, the disease is also commonly acquired through the consumption of traditional or fashionable dishes consisting of undercooked fish. Given the apparent global distribution of this parasite, eradication appears unlikely. Rather, control of gnathostomiasis will only be achieved through intensive education campaigns to raise public awareness of this food-borne helminthic zoonosis.

7. Discussion

Our review of the reason for emergence of the five zoonotic helminth infections described above, indicate that the reasons for change in incidence can be grouped into five categories: (i) changes in dietary practice (capillariasis, anisakidosis, and gnathostomiasis), (ii) changes in notification consequent to increased awareness of infection (all five infections), (iii) changes in environmental conditions/ecology (anisakidosis and gnathostomiasis) and (iv) changes in human behaviour (eosinophilic enteritis and gnathostomiasis). Not discussed in this review is the relative decline in the incidence of many zoonotic helminth infections, (e.g. cystic echinococcosis). Reasons for the decline in these infections are also likely to be multifactorial. The explanations for the decline in some infections may be the same as those leading to the rise in others, (e.g. changes in dietary practice or environmental change). For example, over the last century, the percentage of persons in most industrialised countries who are in contact with livestock animals has greatly decreased. However, the number of pet-owning households is likely to have increased over the same period.

Several important helminth and protozoal zoonoses (including eosinophilic enteritis) are associated with typical companion animals such as cats and dogs. In the US, there are an estimated 53 million dogs distributed among 31 million households [32]. Nearly 60% of all households own either a dog or a cat. The overall increase in the number of pet-owning households has been accompanied by some substantial shifts in the types of pets owned. There has been an increase in the share of households that own less traditional pets, such as birds, fish, ferrets, rabbits, and reptiles [33]. It is estimated that 20.6 million households contain over 98 million additional kinds of companion animals (birds; horses; fish; rodents, including ferrets, rabbits, hamsters, guinea pigs, and gerbils; and reptiles, such as turtles, snakes, lizards) [32]. These data suggest that the incidence of helminthic zoonoses acquired from companion animals may similarly increase.

Most cases of zoonotic helminth infection are preventable by simple measures such as careful personal hygiene, attention to food preparation, eliminating intestinal parasites from pets, and not allowing children to play in potentially contaminated environments. Unfortunately, at least in the US, few people are aware of the health hazards associated with pets, or the potential for zoonotic helminth infection from food preparation [23].

Surveys of families of patients with larva migrans and of pet owners in general reveal a remarkable ignorance of potential zoonoses [58]. Veterinarians could be effective in educating the pet-owning public, particularly since most owners of companion animals use veterinary services. Among veterinarians, small-animal practitioners encounter zoonoses more frequently. In a survey by Harvey et al. [59] approximately one-third of American veterinarians either never discuss potential hazards with clients or do so only when asked. In a recent survey [60], most physicians were uncomfortable discussing zoonoses with their patients. Furthermore, when asked, physicians indicated that veterinarians should play an equal or greater role in advising patients about zoonotic diseases. In particular, they suggested that veterinarians should be involved not only in controlling zoonotic disease pathogens in animals, but also in providing information for patients and physicians. However, the survey demonstrated an unsatisfactory level of communication between physicians and veterinarians about zoonotic disease issues. Additionally, patients themselves do not appear to view veterinarians as a source of zoonotic disease information.

Education programs about human disease due to zoonotic infections associated with household pets or poorly prepared or cooked food could be instituted in a variety of ways, but an effective campaign should ideally combine both passive, (e.g. small signs in exam rooms or zoonotic disease

brochures in reception areas) and active measures, (e.g. public service advertisements in the mass media).

The control of infection associated with environmental change, or changes in dietary practice driven by food shortages will be more difficult, as the resources required would likely be significant.

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