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Fish-borne nematodiases in South America: neglected emerging diseases

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Abstract

Fish-borne zoonotic nematodes may infect humans when fish or squid are ingested raw or inadequately cooked. Human infections may have serious consequences, including the unexpected deaths of infected people. This kind of disease is poorly known in general, and the characteristics of such infections in South American countries as a whole have never been assessed. In this paper the present status of fish-borne nematodiases in humans in South American countries is characterized. Potentially zoonotic nematode species are very common in both freshwater and marine fish in South America. Reports of human infections have only been found in some countries, and their incidence (especially with anisakids and *Gnathostoma* spp.) varies from country to country. Apparently they are more abundant in countries with strong traditions of eating raw fish, and are more frequent on the western coast of South America. So far fish-borne nematodes have been reported in Argentina, Brazil, Chile, Colombia, Ecuador and Peru. In recent years, cases of human infection have appeared in probably underestimated numbers. People need to be clearly informed about risky feeding habits, and physicians need to learn more about zoonotic diseases.

Introduction

Human infections with fish-borne nematodes have been reported worldwide and some are considered to be emerging diseases (Cross, 1992; Stephen *et al.*, 2003; Butt *et al.*, 2004; Nawa & Nakamura-Uchiyama, 2004; Murrell & Fried, 2007; Herman & Chiodini, 2009). Fish-borne nematodiases are acquired by the consumption of live, raw, smoked, lightly cooked or marinated fish and/or squid and may be caused by infections with *Anisakis* spp., *Pseudoterranova* spp., *Gnathostoma* spp., *Capillaria philippinensis* (which is considered to be *Calodium philippinensis* by some authors) and, more rarely, with *Hysterothylacium aduncum*, *Contracaecum* spp., *Eustrongylides* spp. and *Dioctophyme renale* (Cross, 1992; Yagi *et al.*, 1996; Barriga *et al.*, 1999; Cabrera *et al.*, 2003; Ignatovic *et al.*, 2003; Shamsi & Butcher, 2011; Eberhard & Ruiz-Tiben, 2014; Cornaglia *et al.*, 2016). In an exceptional case, infection with *Angiostrongylus cantonensis* after ingestion of raw fish was reported in France by Thobois *et al.* (1996). Sometimes those infections may be highly pathogenic and can even cause the deaths of infected people (Cross, 1992). In South America there are reports of infection with *Anisakis* spp., *Pseudoterranova* spp., *D. renale* (just one case reported) and *Gnathostoma* spp. Most of these cases were reported from Peru, Chile and Ecuador, i.e. countries where people have a strong tradition of eating raw or undercooked fish, as in the form of the traditional recipe called ‘ceviche’. In some other countries there are also reports of a few cases, but in most of them there are no reports of human infections. Serious concerns about this problem have been reviewed in countries such as Peru (Barriga *et al.*, 1999; Cabrera & Trillo-Altamirano, 2004), Ecuador (Lazo, 2004), Chile (Jofré *et al.*, 2008; Tuemmers *et al.*, 2014) and Brazil (Okamura *et al.*, 1999; Lima dos Santos, 2010; Knoff *et al.*, 2013b; Eiras *et al.*, 2016a). However, a general overview of human infections with fish-borne nematodes in all the South American countries in total has never been produced. We present an overview of fish-borne nematodiases in South America, focusing on the characterization of the fish-borne zoonotic nematodiases in each country, and discussing the relative incidence of infection and diversity of parasite species in different South American countries, along with the causes of infection and the measures taken to control human infections with fish-borne nematodes.

Materials and methods

Fish-borne nematodiasis cases reported in the literature were gathered by an extensive Internet electronic search using appropriate keywords, e.g. nematode, human infections, emerging

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diseases, neglected diseases, anisakiasis, gnathostomiasis, capillariasis, sushi, sashimi, ceviche, traveller diseases, *Gnathostoma*, *Pseudoterranova*, *Anisakis*, *Capillaria*, etc., as well as various combinations of these keywords with all the South American countries. The Internet search engines PubMed, Medline, Google and Google Scholar were used as much as possible and the reference of every paper was checked in order to identify useful and reliable publications. We believe that nearly all the reported cases in South America have been tracked.

Considering several *Gnathostoma* species responsible for human diseases, we only refer to the specific names of specimens which were identified by morphological or molecular means, because serological methods alone are insufficient to differentiate the causative pathogens at the species level (Nopparatana *et al.*, 1991; Ishiwata *et al.*, 2003). Therefore, when the species identification is only based on serological methods, the cases are referred to as *Gnathostoma* sp. in table 1 and the corresponding presumptive species identified by serology are indicated in brackets.

Sometimes fish-borne nematodiasis cases have been reported among travellers returning from different South American countries. In those cases, the country of infection is considered to be the country where the infection was presumably acquired in South America and not necessarily the travellers' place of residence.

Results

The number of cases of infection, parasite species, country and references are indicated in table 1. In total, there are reports of 49 cases of anisakidiasis, 1 case of dioctophymiasis and 93 cases of gnathostomiasis in South America. Anisakid infections are predominant in Chile and Peru, whereas gnathostomiasis is predominant in Peru, followed by Brazil and Ecuador.

Discussion

In South America there are 13 countries, among which only two, Bolivia and Paraguay, have no coastlines. The distribution of human infections with fish-borne nematodes per country revealed that there are no reports of infection in several countries (Bolivia, French Guiana, Guyana, Paraguay, Suriname, Uruguay and Venezuela), i.e, just over half of the South American countries. This fact does not necessarily mean that infections do not occur in those countries. Several researchers pointed out that, due to the reasons discussed further on, human infections are probably underestimated. Concerning the specific cases of Bolivia and Paraguay, the occurrence of infections with marine parasites is rather unlikely because they do not have a coastline, and therefore eating sea fish is not as common as in other countries. Furthermore, feeding habits in Paraguay do not include the eating of raw fish (Canese, 1998), such behaviour being essential to prevent infection.

Some of the cases listed in table 1 refer to infections in returned travellers who became infected in South America and whose infections were detected after returning to their native countries. These were the cases of 'anisakiasis' from Chile to Belgium (Verhame & Ramboer, 1988); *Gnathostoma* sp. (*G. binucleatum*?) from Brazil or Colombia to Belgium (Theunissen *et al.*, 2016), from Peru to Brazil (Dani *et al.*, 2009), from Peru to Switzerland (Chappuis *et al.*, 2001) and from Peru to Germany (Bommer, 2004); and *Gnasthostoma* sp. from Colombia to Argentina (Orduna *et al.*, 2013), from Brazil to France (Cornaglia *et al.*, 2016) and to Japan (Nawa, unpublished data, in Nawa & Nakamura-Uchiyama, 2004), from Ecuador to Peru and from 'Caribbe' to Peru (Villar de Cipriani, 2003). Similarly, infections acquired abroad and detected in South American countries were not considered, as in the case of a patient who was infected with *Gnathostoma* sp. in the United States but the infection was detected in Colombia (Jurado *et al.*, 2015).

As can be seen in table 1, the human infections are mostly due to anisakids (*Anisakis* spp. and *Pseudoterranova* spp.) and *Gnathostoma* spp. Besides these three genera, one case of infection with *D. renale* was reported in Brazil (Lisboa, 1945). A case of intestinal capillariasis, presumably acquired in Colombia and detected in Spain (Dronda *et al.*, 1993), was not considered because of the uncertainity of infection in Colombia. In this case the reported patient had a history of frequent travel to other countries in South and Central America. Other fish-borne zoonotic nematode species (*Eustrongylides* spp., *Contracaecum* spp., *H. aduncum* and, more rarely, *A. cantonensis*) have not been reported to date.

Besides the data indicated in table 1, there are several other sources of information about the occurrence of these diseases. Weitzel *et al.* (2015) reported that about 30 cases of pseudoterranoviasis have been reported in Chile. Likewise, Ollague (1985) reported an epidemic of gnathostomiasis (about 200 registered cases) in Guayaquil, Ecuador, and Lazo (2004) reported that in the year 1990 the cases of human gnathostomiasis in Ecuador exceeded 2000. Therefore, if those cases are taken into account besides the cases reported in table 1, the approximate distribution of fish-borne nematodiases cases in total by country is: 1 case in Colombia, 3 in Argentina, 9 in Brazil, 59 in Peru, about 64 in Chile and over 2233 in Ecuador. In one case there are doubts about the country of infection (Brazil or Colombia – Theunissen *et al.*, 2016), and another case was referred to as occurring in the 'Caribe' (Villar de Cipriani, 2003). Most probably these figures do not correspond to the real situation. According to a number of researchers (Barriga *et al.*, 1999; Okamura *et al.*, 1999; Cabrera *et al.*, 2003; Cabrera & Trillo-Altamirano, 2004; Jofré *et al.*, 2008; Cardia & Bresciani, 2012; Eiras *et al.*, 2016a), fish-borne nematodiases are generally underestimated in South American countries, partially because physicians apparently have little experience and lack the training for diagnosis/treatment of fish-borne diseases. This is also considered to be case in other countries such as Australia (Shamsi, 2014) and some European countries, as can be seen in a report from Belgium (Verhame & Ramboer, 1988).

In terms of the distribution of anisakid infections, except for three cases in Brazil and two in Argentina, all cases were reported in just two countries, Chile and Peru. This is likely due to the consumption of 'ceviche', the traditional raw fish dish, which is commonly consumed in those countries, but is not so common in the countries of the east coast of South America. Another important concern is the possible importance of consumption of raw fish prepared according to traditional Japanese dishes, such as 'sushi' and 'sashimi'. Eiras *et al.* (2016a) discussed this problem in Brazil in detail, showing that the number of 'Japanese' restaurants has increased exponentially in the past few years. We have no such detailed data concerning the other South American countries but some authors are concerned about the possible importance of these restaurants for the propagation of fish-borne nematodiases in humans (Adams *et al.*, 1994; Mercado *et al.*, 2001; Cabrera & Trillo-Altamirano, 2004; Jofré *et al.*, 2008; Florencia *et al.*, 2011; Torres-Frenzel & Torres, 2014). No doubt

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Table 1. Human cases of fish-borne nematodiases in South American countries. Parasites are listed in alphabetical order, secondly by alphabetical order of the country and, for the same country, by chronological order of description.

Parasite	Country	Number of cases	Reference
Anisakiasis[a]	Argentina	1	Florencia *et al.* (2011)
Anisakiasis	Chile	1	Verhamme & Ramboer (1988)
Anisakidosis	Brazil	2	Takahashi *et al.* (1998)
Anisakis physeteris?	Peru	2	Cabrera & Suárez-Ognio (2002)
Anisakis simplex	Peru	1	Cabrera & Trillo-Altamirano (2004)
Anisakis simplex	Peru	1	Pers. comm. from R. Martinéz to Cabrera & Trillo-Altamirano (2004)
Anisakis / Contracaecum?	Argentina	1	Menghi *et al.* (2011)
Anisakis sp.? *Pseudoterranova* sp.?	Chile	1	Torres *et al.* (2000)
Anisakis sp.	Brazil	1	Rosa da Cruz *et al.* (2010)
Anisakis sp.	Chile	1	Castillo *et al.* (2003)
Anisakis sp.	Peru	1	Barriga *et al.* (1999)
Dioctophyme renale	Brazil	1	Lisboa (1945)
Gnathostoma binucleatum	Brazil? Colombia?	1	Theunisson *et al.* (2016)
Gnathostoma spinigerum	Peru	1	Chappuis *et al.* (2001)
G. spinigerum	Peru	1	Bommer (2004)
Gnathostoma sp. (*G. doloresi* ?)	Ecuador	14	Mimori *et al.* (1987)
Gnathostoma sp. (*G. spinigerum* ?)	Brazil	1	Vargas *et al.* (2012)
Gnathostoma sp.	Argentina	1	Kaminsky *et al.* (1989)
Gnathostoma sp.	Brazil	1	Nawa, unpublished data, in Nawa & Nakamura-Uchiyama (2004)
Gnathostoma sp.?	Brazil	1	Eiras *et al.* (2015)
Gnathostoma sp.	Brazil	1	Chaves *et al.* (2016)
Gnathostoma sp.	Brazil	1	Cornaglia *et al.* (2016)
Gnathostoma sp.	"Caribe"	1	Villar de Cipriani (2003)
Gnathostoma sp.?	Colombia	1	Zuluaga *et al.* (1988)
Gnathostoma sp. [b]	Colombia	1	Orduna *et al.* (2013)
Gnathostoma sp.	Ecuador	15	Ollague *et al.* (1984)
Gnathostoma sp.	Ecuador or Peru	1	Costa *et al.* (2001)
Gnathostoma sp.	Ecuador	1	Villar de Cipriani (2003)
Gnathostoma sp.	Ecuador	3	Lazo (2004)
Gnathostoma sp.	Peru	1	Rodríguez *et al.* (2000)
Gnathostoma sp.	Peru	10	Costa *et al.* (2001)
Gnathostoma sp.	Peru	9	Villar de Cipriani (2003)
Gnathostoma sp.	Peru	1	Bravo & Mohanna (2008)
Gnathostoma sp.	Peru	1	Dani *et al.* (2009)
Gnathostoma sp.	Peru	18	Álvarez *et al.* (2011)
Gnathostoma sp.	Peru	6	Laga *et al.* (2013)
Phocanema sp. (= *Pseudoterranova*)	Chile	1	Sapunar *et al.* (1976), quoted from Jofré *et al.* (2008)
Pseudoterranova cattani	Chile	4	Weitzel *et al.* (2015)
P. decipiens	Chile	1	Mercado *et al.* (1997)
P. decipiens	Chile	7	Mercado *et al.* (2001)

(*Continued*)

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Table 1. (*Continued.*)

Parasite	Country	Number of cases	Reference
P. decipiens	Chile	1	Jofré *et al.* (2008)
P. decipiens	Peru	2	Tantalean & Huiza (1993)
P. decipiens	Peru	1	Cabrera *et al.* (2003)
P. decipiens	Peru	1	Cabrera & Trillo-Altamirano (2004)
P. decipiens?[c]	Peru	1	Cabrera & Trillo-Altamirano (2004)
Pseudoterranova sp.	Chile	1	Mercado *et al.* (2006)
Pseudoterranova sp.	Chile	15	Torres *et al.* (2007)
Terranova sp. or *Phocanema* sp.[d] (= *Pseudoterranova*)	Chile	1	Canese (1998)

[a]The worms were not observed. The diagnosis was highly probable but based only on symptomatology.
[b]This case was reported without immunodiagnosis and the validity of the description was questioned by Joob & Wiwanitki (2014). The same case was commented on by Rodrigues-Morales *et al.* (2014). See replies by Orduna *et al.* (2014a, b).
[c]Described as *Toxocara* sp. by Beltrán and co-workers (Beltrán, 2000; Beltrán *et al.*, 2001) – quoted from Cabrera & Trillo-Altamirano (2004).
[d]This case was described in Paraguay. The patient arrived in Paraguay from Chile the day after eating 'ceviche', and did not eat raw fish in Paraguay. Therefore, we consider that the infection was acquired in Chile and diagnosed in Paraguay.

this problem deserves the attention of sanitary authorities and researchers to clarify its impact on public health. At the moment, based on the available data, it can be presumed that human infections on the west coast of South America are mainly due to the consumption of 'ceviche', whereas those on the east coast are due principally to 'Japanese' or similar restaurants.

According to Mercado *et al.* (2006) the majority of fish-borne nematodiases in Chile, a country with a high incidence rate, are due to infection with *Pseudoterranova* spp., the most frequent nematode in the muscles of marine fish in this country. The emergence of anisakidosis due to *A. physeteris* was probably related to the El Niño along the Peruvian coast in 1997–98 (Cabrera & Suárez-Ognio, 2002). During El Niño, due to the decrease in numbers of fish from colder waters, there was an increase in the catch of *Coryphaena hippurus* (common dolphinfish, also known as Mahi-mahi), which is often infected with species of Anisakidae and is commonly used to prepare 'ceviche' (Cabrera & Suárez-Ognio, 2002). El Niño and its biological consequences, therefore, affect the prevalence of species of Anisakidae in fish, and the availability of fish species to fishermen may be an important factor for the mechanisms of human infections with fish-borne nematodes (Cabrera & Suárez-Ognio, 2002). This question deserves further research.

Concerning infection with *Gnathostoma* spp., most of the cases occurred in Peru (Álvarez *et al.*, 2011) and especially in Ecuador (Lazo, 2004; Nawa *et al.*, 2015), where gnathostomiasis is considered to be an endemic disease. The absence of gnathostomiasis in Chile is puzzling. Assuming that the infections are acquired by consuming 'ceviche', it seems that freshwater fish, which are the intermediate/paratenic hosts for *Gnathostoma* spp., are not commonly used to prepare this dish in Chile.

Several species of *Gnathostoma* are assumed to cause human infections in South America. In addition to the well-known *G. binucleatum* as the causative pathogen (Theunissen *et al.*, 2016), *G. spinigerum* is also referred to as a human pathogen in the Americas (Chappuis *et al.*, 2001; Bommer, 2004; Vargas *et al.*, 2012). However, according to recent molecular studies by Almeyda-Artigas *et al.* (2000) and Léon-Règagnon *et al.* (2002), the *Gnathostoma* species involved in human infections in Mexico and Ecuador are all *G. binucleatum*, with the suggestion that *G. spinigerum* does not exist in the Americas. At times, *G. doloresi* has also been wrongly considered as a human pathogen in South America, because Mimori *et al.* (1987) used crude somatic extract antigen of *G. doloresi* for immunodiagnosis of gnathostomiasis in Ecuador. At present, therefore, all gnathostomiasis cases in the South American countries are attributed to *G. binucleatum*.

An important question directly related to human infections concerns the number and specific diversity of fish species infected with potentially zoonotic nematodes. In a recent survey, Eiras *et al.* (2016b) listed the parasites of 685 different marine fish species from South America and found that 185 species were infected with potentially zoonotic nematodes. Earlier, Eiras *et al.* (2010) listed the parasites of freshwater fish from Brazil and showed that 74 fish species were infected with various species of zoonotic nematodes. Furthermore, some of the most commercially important fish species often present high values of prevalence and intensity of infection (Felizardo *et al.*, 2009; Knoff *et al.*, 2013a; Mattos *et al.*, 2014; Rodrigues *et al.*, 2015). Therefore, the potential of those fish species for causing human infections is high.

An important factor is that physicians in general do not have sufficient knowledge about this problem in South American countries, as stated above, and some authors think that the number of real cases is much higher than reported. Furthermore, Alvarez *et al.* (2011) reported that the number of gnathostomiasis cases in Peru has increased significantly in recent years, Tuemmers *et al.* (2014) reported that, in Chile, health problems from 'sushi' consumption more than doubled during 4 months of 2013 compared to the same period in 2012, and Torres *et al.* (2000) mentioned the increase of anisakiasis in Chile. Thus, the need to inform people about the risks of eating raw fish is obvious.

Some procedures may be adopted to reduce the risk of human contamination. First, the ingestion of fish after being cooked adequately (60°C for at least 10 min) is a certain way of preventing infection. If fish are to be consumed raw, the most efficient ways of preventing infections are those advised by the US Food and Drug Administration (FDA): storing the fish at a temperature of −20°C or lower for 7 days (total time), or at −35°C or lower for 15 h. These procedures may need some modification according to the size of the fish, fish species, target parasites, etc. (US Food and Drug Administration, 2011).

Any attempt to reduce, or even to eliminate, human infections with fish-borne nematodes has to take into account a number of important measures integrating three factors: changing feeding behaviour, providing clear information to people and increasing the knowledge of physicians. We should realize that winning such a 'battle' is not easy, especially in countries where eating raw fish dishes is an old and highly conservative tradition. The successful example of The Netherlands, where human infection due to the strong tradition of eating raw herring ('maatjes') was practically eliminated by compulsory freezing of the fish (Verhamme & Ramboer, 1988), demonstrates that it is possible to eliminate such infections.

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