CHAPTER FOUR

Parasites in Food: From a Neglected Position to an Emerging Issue

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Contents

Abstract

Foodborne parasites have long been a neglected group of pathogens, as they often have insidious, chronic effects, rather than being acute diseases, and they are often associated with impoverished or marginalized populations. In addition, due to the long incubation period for most foodborne parasites, source attribution is often difficult, if not

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impossible. However, global trends have enabled foodborne parasites to emerge in different populations in new locations, transmitted through different food types, and sometimes with unexpected symptoms. This emergence of foodborne parasites has brought them into focus. In this chapter, six foodborne parasites are used as examples on emergence: *Echinococcus multilocularis* is spreading to new locations; *Cryptosporidium* spp. are beginning to be associated not only with water, but also with salads; *Trypanosoma cruzi* is being manifest with acute disease due to foodborne transmission, particularly transmitted with juices; *Trichinella* spp. have become less of a burden regarding transmission via pork in many countries, but now game animals are becoming a concern; anisakiasis is becoming a global problem as the world develops a taste for sushi, and similarly for opisthorchiasis, which is increasingly being associated with cholangiocarcinoma.

However, the emergence of these foodborne parasites provides an incentive for increased efforts being made toward control. In this chapter, having described how the parasites are emerging from their neglected position, the focus turns toward control. In addition to considering control measures that may be applied to the specific parasites, an overview is provided of some of the organized collaborations, projects, and consortia, as well as some of their outputs, that have in focus the control of these emerging and important pathogens.

1. INTRODUCTION

Parasites have long been the neglected group of pathogens (compared with viruses and bacteria), and this continues to be their position today. There are several reasons that parasites are neglected, including that many, but not all, parasitic infections do not manifest as acute diseases, but rather have a chronic, more insidious impact on their hosts. Another reason that parasites are neglected is that they are often associated with poverty, with populations that are most exposed to parasitic infections being those living in areas where the basic infrastructure elements of water supply, sanitation, housing, and transport are lacking or inadequate. Such populations cannot afford costly diagnostics or treatments, and thus the financial incentive for the biomedical and pharmaceutical industries to invest in improved approaches to combating these diseases is low compared with the incentives traditionally associated with the noninfectious diseases of wealthier populations, such as obesity and cardiac diseases. Indeed, Pedrique et al. (2013) noted in a systematic assessment of drugs and vaccines for neglected diseases that only 4% (and only 1% of all approved new chemical entities) were indicated for neglected diseases, despite these diseases accounting for around 11% of the global disease burden.

As the data of Pedrique et al. (2013) demonstrate, even today, parasites are relatively neglected; on the World Health Organization (WHO) list of neglected tropical diseases (including those proposed during the 10th Meeting of the Strategic and Technical Advisory Group for Neglected Tropical Diseases in 2017, and added according to the procedures; WHO, 2017), of the 20 diseases, or groups of diseases listed, 12 (60%) are parasitic. It is also worth noting that among these parasitic diseases listed, five (42%) have the potential to be transmitted by food.

The Drugs for Neglected Diseases initiative (DNDi) has also produced a list of diseases that they believe to be neglected. In the DNDi list, among the eight diseases or groups of diseases listed, five (approximately 62%) are parasitic diseases, although the emphasis in this list is more on vectorborne parasitoses.

However, although many parasites, including foodborne parasites, remain neglected, several are also considered to be emerging threats. As there are several different types of disease emergence, for a disease to be defined as emerging is not necessarily obvious (Moutou & Pastoret, 2015). For example, an emerging disease may be one that has never been identified previously, such as Middle East respiratory syndrome (MERS) that was first identified in Saudi Arabia in 2012, and found to be due to infection with a specific novel coronavirus (MERS-CoV). However, the term “emerging disease” could also refer to the emergence of a particular disease in a geographic region where it has not previously been identified, and/or with symptoms with which the disease has not previously been associated, such as the emergence of Zika virus infections associated with microcephaly in Brazil in 2015. In addition, for diseases of animals in particular, the association of a disease with a new species, possibly in a new geographical region and/or with a new clinical spectrum, can also be considered as disease emergence; for example, the emergence of the prion disease, chronic wasting disease, in reindeer and moose in Norway in 2016. However, a disease does not necessarily have to be entirely new to a species or region in order to be considered emerging; an unexpected increase in disease incidence in an area or species where it has previously been diagnosed may also result in the disease being considered to be emerging. However, this may not necessarily indicate a real increase, but may simply reflect an improvement in our knowledge or awareness of a particular disease, and/or an increase in the sensitivity of diagnostic tools. For foodborne parasites, being considered as an emerging issue generally does not reflect new organisms being discovered (although with increasingly sophisticated tools we may now separate into individual species or subspecies parasites that were previously grouped together), but the recognition of spread and establishment of these pathogens in populations where they were previously not considered to be a problem.

As with other pathogens, the emergence of the foodborne parasites is often associated with human activity (Moutou & Pastoret, 2015), either directly or indirectly. Thus, climate change, globalization, alterations in legislation, population growth and movement, including urbanization, cultural changes, and many other factors may all result in specific pathogens, including foodborne parasites, emerging, or reemerging, in unexpected ways; it is well recognized that many current emerging infectious diseases, not just foodborne parasites, are associated with human modification of the environment (Pearce-Duvet, 2006). The commonality is that all these factors result in humans having greater exposure to a previously unfamiliar pathogen, or its natural host, or generally promote dissemination to humans from the environment or other hosts (Morse, 1995). With regard to food, the complicated trade routes, the changes in our dietary habits, healthy-eating trends, in which minimally processed, "organic" foods are considered preferable or linked to virtuosity by the consumer, and how particular sectors of the food industry may be associated with distinct population groups, are all factors that may tip a pathogen toward becoming emerging in a specific area.

In the following pages, further details are provided on six selected foodborne parasites (one cestode—*Echinococcus multilocularis*, two protozoa—*Cryptosporidium* spp. and *Trypanosoma cruzi*, two nematodes—*Trichinella* spp. and anisakids, and one trematode—*Opisthorchis* spp.), and how the factors listed above, acting in concert or alone, have moved the position of those parasites from being neglected to being recognized as emerging or reemerging issues; a summary is provided per parasite in Table 1. These selected parasites are all very different from each other not only in terms of taxonomy but also in terms of pathology, symptoms, and lifecycle. Yet there are some commonalities; the zoonotic potential (that the parasites are not only infectious to humans, but that some or all species of the group of hosts may also infect particular other animals) is also important, especially for those for which the transmission route to humans is by consumption of an animal that has already been infected itself.

The relevant factors regarding emergence or reemergence have already altered the spread and distribution of various pathogens, and will also affect their epidemiology in the future as ecosystems continue to evolve, and new technologies enable us to identify and characterize these pathogens.

Table 1 Parasites in Food: From a Neglected Position to an Emerging Issue

	Description of Emergence or Reemergence	**Relevant Factors for Emergence or Reemergence**
Cestodes		
Echinococcus multilocularis	Increasing prevalence in some areas and expansion into new areas	Definitive host populations spreading and increasing—in Europe, rabies vaccination programs have promoted the growth of the fox population, and in North America, the range of coyotes and foxes has expanded, and dogs are imported from endemic areas
Protozoa		
Cryptosporidium	Considered largely hand-to-mouth or waterborne, foodborne outbreaks are becoming increasingly recognized	Globalization of the food supply; use of organic fertilizers Improved diagnostics and detection methods
Trypanosoma cruzi	Largely considered directly vectorborne and affecting mostly impoverished rural populations, in some areas foodborne transmission has become more important and may affect all sectors of society. In addition, foodborne transmission may result in greater disease severity	Environmental changes such as urbanization, habitat fragmentation, and deforestation
Nematodes		
Trichinella spp.	Although trichinosis transmitted through infected pork has been reduced through intervention measures, transmission from game meat is becoming more important; infections may occur in countries where physicians are not familiar with trichinosis, and thus diagnosis and treatment could be delayed	Increased consumption and use of game meat, particularly associated with wild boar due to their rising populations in many countries. Illegal import of wild game/bushmeat may be a particular concern for exposing consumers in countries where physicians are not familiar with the infection

Continued

Table 1 Parasites in Food: From a Neglected Position to an Emerging Issue—cont'd

	Description of Emergence or Reemergence	**Relevant Factors for Emergence or Reemergence**
Anisakidae	Previously limited to countries where consumption of raw seafood is part of traditional culture, cases of anisakiasis are now increasing in other areas of the world; in addition, even if the larvae are inactivated there remains the potential for an allergenic response in some individuals and more serious effects of infection have been postulated	Increased consumption of seafood, particularly seafood consumed raw or very lightly cooked (spread of this dietary preference globally); increased prevalence of natural definitive hosts (sea mammals—partly due to protective conservation measures) may result in greater prevalence in intermediate hosts; improved diagnostics in humans, but potentially reduced skill for detection in fish and confusion over operating procedures and management plans
Trematodes		
Opisthorchis spp.	Infections have been previously limited to endemic areas where the lifecycles of the two species occur, and where consumption of raw freshwater fish are part of the culinary traditions, but cases of opisthorchiasis are now being diagnosed in other parts of the world; in addition, further research is unravelling the link between opisthorchiasis and cholangiocarcinoma (CCA)	Increased consumption of fish, and, in some areas, increased consumption of raw or inadequately cooked fish which is necessary for transmission; although establishment of the lifecycle in nonendemic areas is unlikely, human migration and tourism mean that infected people may live in places where the parasite is not endemic, and thus are less likely to be diagnosed due to lack of knowledge among diagnosticians—lack of diagnosis and treatment increases the risk of CCA developing; the increasing aquaculture market is also considered to be a probable route for the parasite to travel outside its endemic area

Change and adaptation to change are ongoing processes and mean that we should try to stay aware of the current state of the events such that we can address not only the situation today, but also the trends in the future. With this in mind, this chapter also provides a section on mitigation approaches that should be of both relevance now, and also to safeguard future public health regarding these foodborne parasites. As well as describing parasite-specific practical interventions, the chapter concludes with drawing attention to initiatives, recent, ongoing, and recently established, which indicate how foodborne parasites, both in general and the specific parasites under discussion, are being taken seriously be several groups globally. Tackling these issues from a One Health perspective, such that human infections, animal health, and the environment are all considered to have roles, should enable us to ensure that the impacts associated with foodborne parasites, as we know them now decrease and maybe disappear entirely.

2. SPECIFIC EXAMPLE PARASITES: THE TRANSITION FROM NEGLECTED POSITION TO EMERGING ISSUE

2.1 *Echinococcus multilocularis*: Becoming More Globalized

This cestode parasite does not have humans as part of its usual lifecycle, which normally involves only canids, particularly foxes, as the definitive host, and small mammals, particularly rodents, as the intermediate host. However, humans can become infected by ingesting eggs excreted in the feces of an infected canid and become an aberrant intermediate host. Although clinical signs and symptoms of alveolar echinococcosis (AE) may take decades to appear, they are severe, with proliferation of the larval stage of the parasite, particularly within the liver, resulting in a range of symptoms similar to those associated with liver cancer, possibly spreading to other organs. Without treatment, the disease is likely to be fatal within a decade. Echinococcosis is listed on the WHO list of neglected tropical diseases (WHO, 2017), due to its association with severe morbidity and mortality in the hotspot areas where human cases occur (particularly western China, Tibet, eastern Russia, and the Near East) and also because the populations affected are often poor, pastoral communities, who may be remote from the general population in the region; thus, the disease is frequently of low priority in the region's healthcare budget. Furthermore, due to the requirement for relatively expensive equipment for detecting the disease (imaging equipment such as CT scan), the infection may easily go undiagnosed in such populations; even if diagnosed, the treatment required is long-term, which is difficult to follow-up in isolated, marginalized communities (Craig et al., 2007).

Although human infection with *E. multilocularis* is rare in most European countries and definitive evidence for its foodborne transmission is lacking, due to the severity of its symptoms, this parasite has nevertheless been considered to be among the most important foodborne parasites in Europe (Bouwknegt, Devleesschauwer, Graham, Robertson, & van der Giessen, 2018). Indeed, although targeted interventions have resulted in a significant decrease in the prevalence of human infection with *Echinococcus granulosus* (causing cystic echinococcosis (CE)) in several regions that used to be highly endemic, the same has not been achieved for *E. multilocularis* (Craig, Hegglin, Lightowlers, Torgerson, & Wang, 2017). This is presumably because the domestic dog-livestock cycle associated with *E. granulosus* is relatively easier to interrupt (by worming dogs, preventing dogs from scavenging domestic animal remains at abattoirs and in the fields, and efforts at meat inspection), than the predominantly sylvatic *E. multilocularis* cycle (foxes–rodents). Not only is the prevalence of *E. multilocularis* apparently not decreasing, but the distribution of the parasite seems to be spreading in some areas of northern Europe and it seems to be emerging, becoming identified in some areas previously not considered particularly associated with the parasite, in other regions of the world (Conraths & Deplazes, 2015; Davidson, Romig, Jenkins, Tryland, & Robertson, 2012; Gottstein et al., 2015; Vuitton et al., 2015). For example, a case-finding study noted an increase in the prevalence of human AE in Switzerland over a 50-year period from 1956 to 2005, which could not be explained by improved diagnosis; the authors suggested that this change in prevalence may be associated with a rising fox population, which, in turn, is associated with a successful antirabies vaccination program (Schweiger et al., 2007). In North America, canine infections with *E. multilocularis* seem to be extending beyond their "traditional" limits of the Arctic and north-central North America, with a few cases being identified in dogs in Ontario (Trotz-Williams et al., 2017) and a relatively high prevalence being found in urban coyotes in Calgary and Edmonton (Catalano et al., 2012); this indicates the potential for an elevated threat to human health in these regions of Canada, and an unprecedented cluster of human cases was diagnosed in Alberta between 2013 and 2017. The reasons for the occurrence of *E. multilocularis* in new regions of Canada has been considered to be not only due to the range of wild hosts (coyotes, foxes) being extended, but also the import of dogs from endemic areas, including Europe, may be partly responsible for this apparent spread (Trotz-Williams et al., 2017). Indeed, the discovery of European haplotypes in Canadian wildlife does indicate the introduction of this parasite from Europe (Gesy & Jenkins, 2015).

Although there is no evidence that foodborne transmission of *E. multilocularis* is increasing, a recent meta-analysis demonstrates that transmission of AE due to the ingestion of food or water contaminated with eggs of the parasite can occur, but these risk factors appear not to elevate infection risk significantly (Conraths et al., 2017). It should be borne in mind that for an infection for which symptoms occur many years after infection, determining the vehicle of transmission is always difficult. However, it would seem probable that with increased environmental contamination, due to greater prevalence of infected definitive hosts, then the likelihood that food would be contaminated is also greater, and that other infection routes and vehicles will also be affected.

2.2 *Cryptosporidium* spp.: Transmission Emerging From Water to Salad and Other Fresh Produce

This protozoan parasite, causing diarrhea and other abdominal symptoms in the infected human host, was first described in mice over a century ago. However, its importance as a human pathogen was not recognized until around 70–80 years later when the HIV pandemic brought sharply into focus the importance of this parasite as causing severe, opportunistic infections in the immunocompromised. Almost simultaneously came the realization that the transmission stage, the oocyst, was resistant to most standard drinking water treatment technologies in use at that time, thus resulting in large waterborne outbreaks, involving hundreds, even thousands, of individuals. At this point in time, from around 1980 to 2000, *Cryptosporidium* certainly moved from being a parasite so neglected that its significance as a disease-causing agent of humans and domestic animals was unrecognized, to being an important pathogen, emerging globally, and with an impact not only in countries with poor infrastructure, but also in the wealthy countries of Europe, Australasia, and North America. The severity of the disease in some populations is exacerbated by the limitations in available treatment, a problem that continues to this day.

Although some foodborne outbreaks were identified in these earlier years of recognition of *Cryptosporidium*, these tended to be predominantly small-scale local outbreaks, frequently associated with milk and related dairy products, or with apple cider in which the apples had been contaminated prior to the drink being made. Indeed, in the 10 years from 1993 to 2003 just 10 foodborne outbreaks were recorded, with fewer than 450 cases in total (see table 1 in Robertson & Chalmers, 2013). However, in the 10 years from 2005 to 2015 the number of foodborne outbreaks recorded has increased by 50% (15 outbreaks listed; see table 2 in Ryan, Hijjawi, & Xiao, 2018), with over 1800 cases recorded, an increase of over 400% (Ryan et al., 2018). Thus, although *Cryptosporidium* had already become an emerging issue 20 years ago, more recently it seems to be reemerging as a foodborne pathogen. Interestingly, also, the predominant food transmission vehicles recorded seem to have changed, shifting from dairy products and apple cider, which were the main transmission vehicles during the first decade (1993–2003), to over 45% of the outbreaks and more than 90% of the cases being associated with salad ingredients or garnish in more recent times. These later outbreaks also seem to affect larger numbers of people; of the nonsalad/garnish-associated outbreaks the mean number of people affected per outbreak was around 30 (ranging from 4 with raw meat to 74 with the vehicle of infection not identified), whereas for those outbreaks associated with salad ingredients, the mean number of people infected was around 200 (ranging from 18 to 648). The reason for this reemergence of *Cryptosporidium* as a foodborne pathogen, particularly associated with salad vegetables, has not been closely investigated but potential factors could include a general rise in the per capita consumption of salad, the increase in popularity of prewashed read-to-eat (RTE) salad vegetables, the rise in international trade in salad ingredients, particularly with transport from warmer countries to colder countries during the winter months, more intensive farming decreasing the gap between fresh produce and animals, and improved awareness, diagnostics, and trace back during outbreaks, enabling not only cryptosporidiosis cases and outbreaks to be identified, but the implicated product also. Although greater awareness of cryptosporidiosis and improvements in diagnostic sensitivity undoubtedly play a role in more outbreaks being detected, for the particular transmission vehicle, the second factor listed here may be of particular relevance. Bagged, prewashed RTE salad vegetables were introduced in the United States in the mid-1990s, and soon became a popular consumer choice, with the number of consumers continuing to rise steadily (in United States 223.95 million in 2011, 232.91 million in 2015; https://www.statista.com). Similar trends are occurring elsewhere in the world. Although surveys of RTE salads in UK indicate that the majority are of acceptable microbiological quality (Little & Gillespie, 2008), and similar data have been obtained in Italy (De Giusti et al., 2010), such studies tend not to consider parasites. One problem with the bulk washing of salad prior to bagging is that point-source contamination can be spread throughout a large batch, and the sanitizers used for salad washwater are usually aimed at reducing bacterial contamination (on the produce itself, but, more importantly, within the washwater; Gil, Selma, López-Gálvez, & Allende, 2009) and are not necessarily effective at killing hardy *Cryptosporidium* oocysts. Thus, in this way, given the distribution of RTE salad, there is the potential for many people to become exposed to a contamination that, initially at least, may have been limited in spread. Indeed, the largest foodborne outbreak of cryptosporidiosis is associated with precut mixed salad leaves obtained from a particular supermarket chain, with leaves from growers in UK, Spain, Italy, and France (Ryan et al., 2018). This indicates also the complexity in traceback when an outbreak occurs, and is probably particularly difficult for products with a short-shelf life (such that the food is rapidly consumed or discarded) and an infectious agent, such as *Cryptosporidium*, with an incubation period that exceeds or matches the shelf-life of the implicated product.

2.3 *Trypanosoma cruzi*: Foodborne Transmission Becoming More Common Than Vectorborne and Results in More Severe Symptoms

Chagas disease, caused by infection with the protozoan parasite *T. cruzi*, is listed by the World Health Organization as a neglected tropical disease (WHO, 2017) and has also been described as one of the "social diseases" of poverty, along with malnutrition, diarrhea, tuberculosis, and other parasitic diseases (Storino, 2000). Chagas disease may be fatal, and around 12,000 people die annually from this infection (de Noya, Gonzalez, & Robertson, 2015). The disease develops in two distinct stages, in which an acute stage, which occurs shortly after infection, is followed by a chronic stage that usually takes several years to develop; the latter stage is most commonly associated with the clinical pathology. Cell death in the target tissues results in clinical manifestations due to the damage to the affected organs, often the digestive system, nervous system, or the heart. The disease has long been associated with less affluent socioeconomic groups in specific rural areas of South America as the usual vectors, triatomines, which thrive in ecotopes such as palm trees, piles of rocks, hollow trees, and mammal burrows, are also well adapted to living in the sort of human homes that are particularly associated with rural poverty, being poorly constructed or made of adobe (mud) bricks, not plastered internally, and with thatched roofs. In such locations, the triatomines can shelter and reproduce, emerging at night to feed on human hosts, and, if infected with trypanosomes, may then infect the host by defecating into the bite wound (de Noya et al., 2015). Although initiatives directed against vectors and improvements in housing have decreased vectorborne transmission through the skin in recent years, oral (foodborne) transmission appears to be on the rise (de Noya et al., 2015). Of the many foodborne cases reported in the literature, a high proportion are associated with fruit juice, with contamination via triatomines (either being ground up in the juice preparation, or defecating into the juice). There are several important differences between the two transmission routes, including foodborne infection more often occurring as an outbreak, that not only triatomines with fast reflex defecation are involved in the lifecycle for foodborne transmission, that the parasite load can be very high (if one or more whole insects are ground into the vehicle of infection), and, importantly in the context of the current discussion, rather than being particularly associated with poor people living in rural areas in nonimproved housing, that large numbers of people of any social status may be exposed (de Noya et al., 2015). This latter point may be particularly exemplified by the outbreak in Caracas in 2007, in which infection was confirmed in 103 people, of whom 75% were symptomatic and over 20% required hospitalization, and one child died (Alarcón de Noya et al., 2010). What was particularly noticeable about this outbreak was not only more obvious and severe clinical signs than expected in the exposed people, but that the population affected was predominantly urban and middleclass, a demographic group not normally associated with Chagas disease. The authors suggested that environmental changes had altered the behavior and ecology of the infection reservoirs, resulting in the urbanization and domiciliation of lifecycle. Indeed, oral transmission is now considered to be the most important route of infection for Chagas disease in Venezuela and the Brazilian Amazon (Silva-Dos-Santos et al., 2017), and environmental changes such as deforestation, habitat fragmentation, urbanization, etc., are again considered to be the reason for the emergence of this infection (Nava, Shimabukuro, Chmura, & Luz, 2017).

Although Chagas disease is generally considered a serious disease, regardless of transmission route, a further concern with foodborne transmission is that disease severity seems to be greater, particularly with prolonged fever in the initial phases of infection (de Noya et al., 2015). The reasons for the greater disease severity with oral transmission have not been fully elucidated, but experiments comparing oral and intraperitoneal (i.p.) infection in mice, using the same strain and dose of parasite have shown that with oral transmission, as well as transmission being more successful, there is also a higher maximum peak of parasitemia and parasite loads in different tissues are greater during acute infection than in mice infected via the i.p. route (Margioto Teston, de Abreu, Abegg, Gomes, & de Ornelas Toledo, 2017).

The various foodborne outbreaks recorded, along with the higher clinical burden of disease (de Noya et al., 2015), have brought further attention to this parasite, with calls to policy makers and stakeholders to focus attention on control of transmission of this parasite via the foodborne route (Robertson, Devleesschauwer, Alarcón de Noya, Noya González, & Torgerson, 2016), and to use integrated surveillance systems and effective outreach programs to mitigate or control transmission of this parasite (Nava et al., 2017). Indeed, with this background, Chagas disease is now sometimes considered a worldwide problem, and to address source tracking for foodborne transmission, qPCR has been recently evaluated as a methodology for confirming implicated food commodities in outbreaks (de Souza Godoi et al., 2017; Mattos et al., 2017).

2.4 *Trichinella* spp.: Game Animals Replace Undercooked Pork as the Major Vehicle of Infection in Some Countries

Human trichinosis, in which people are infected by consumption of larvae of the nematode *Trichinella* in the undercooked meat of an infected animal, has long been recognized as an important foodborne parasitosis. In many countries of the world, including throughout Europe, testing of pork at the slaughterhouse level, using a recommended methodology or equivalent, is compulsory unless the pig production system has been certified as *Trichinella*-free due to meeting a particular standard of controlled housing (European Commission, 2015). The symptoms of trichinosis depend on the stage of infection, with abdominal symptoms (diarrhea, vomiting, abdominal pain) associated with invasion of the intestine, followed by fever, inflammation, swelling, being associated with migration of the new larvae about a week after initial infection, and then rash and myalgia, possibly with heart, lung, or CNS involvement, associated with the subsequent encystation of these larvae into the tissue. Meat control and enclosed pig farming mean that in Europe, human infections with *Trichinella spiralis*, the species closely associated with domestic pork, occur relatively infrequently apart from in locations where infrastructure insufficiencies, including socioeconomic problems, lack of veterinary controls, and inadequate education, may result in infected pork being included in traditional cured, dried, or smoked products (see, for example, Cacciò, Chalmers, Dorny, & Robertson, 2018). Thus, although considerable budget is spent on control of this parasite in many countries, the global burden of disease (measured in disability adjusted life years, DALYs) is, compared to that of many of other foodborne parasitic diseases, relatively how (Devleesschauwer et al., 2015). However, although pork may no longer present the biggest risk for trichinosis, other animal species may act as hosts for *Trichinella* spp., and nonpork meat sources may represent the emergence or reemergence of this infection and human outbreaks of trichinosis (Rostami, Gamble, Khazan, & Bruschi, 2017). As these outbreaks are most likely to be small, family-size outbreaks, they are unlikely to receive as much media attention, or even scientific interest as those associated with pork. Although the European legislation does, indeed, address testing for *Trichinella* in animals other than pigs (listed are horses, wild boar, bears, walruses, crocodiles, and birds, and other carnivorous mammals (including marine mammals) are also mentioned in general; European Commission, 2015), the fact that many of these animals, probably with the exception of horses, are often not slaughtered through a legislated system, but maybe hunted by individuals, means that meat from these animals is more likely to evade being tested, although this is not always the case. Testing of meat for *Trichinella* larvae is particularly likely to be ignored if the animals have been hunted illegally. Furthermore, some countries outside Europe do not necessarily legislate for testing such animals. For example, it has been noted that in China there is currently no mandatory testing for *Trichinella* larvae in meats other than pork, despite a range of less usual animal meats (wild animals, raw meat, and under-cooked foods such as dumplings or scalded dog meat) being considered as delicacies by some consumers, and, indeed, may be consumed quite widely (Bai, Hu, Liu, Tang, & Liu, 2017). Indeed, review papers from China indicate that dog and game meat may be of increasing significance as sources of trichinosis infections in people, although pork still remains the most usual infection vehicle at present (Cui, Wang, & Xu, 2011; Wang, Cui, & Xu, 2006). Dogs, which are known scavengers, are particularly likely to be infected with *Trichinella*, and outbreaks of trichinosis associated with consumption of dog meat have been reported, particularly in China (Rostami et al., 2017). It is worth noting that over 10% of outbreaks of trichinosis reported from China in the period 2000–03 were associated with consumption of infected dog meat (Wang et al., 2006).

Nevertheless, in general, wild boar, horse, and bear are relatively common nonpork meat sources of trichinosis, whereas although infections from consumption of meat from dog, turtle, jackal, cougar, and walrus have occurred, they are more unusual, presumably because these are less usual meat sources (Rostami et al., 2017). An overview comparison of sources of meat types associated with trichinosis cases and outbreaks divided by region or country (Murrell & Pozio, 2011) indicated that of 27 geographic areas listed, domestic pigs were most associated with trichinosis for 11 of them, but for 13 of these regions wild game was the equivalent or predominant source, with all cases associated with wild game in seven of these regions (Ethiopia, Canada, Iran, Lebanon, Greece, Israel, South Korea).

From the available data, it is clear that the wild boar populations globally are experiencing an unprecedented demographic explosion that has been documented in a range of countries including in Europe, USA, and Australia (Ruiz-Fons, 2017). The expanding populations of wild boar may increase the likelihood of meat from these animals being consumed, either as a part of hunting bags at the individual level or supplied to shops and other establishments. It is perhaps worth noting that a major outbreak of trichinosis in Belgium in November 2014 was associated with consumption of wild boar imported into Belgium from Spain and used at three different restaurants (Messiaen et al., 2016). The reason for how this heavily infected wild boar meat evaded detection in the import and supply chain is not clear.

Hunters may also be particularly exposed to *Trichinella* if, rather than bringing the meat home for preparation, they attempt to cook it while out in the field; one example of this was a small outbreak that occurred in Alaska in 2014, when a group of hunters attempted to cook bear meat from the bear they had killed over an open fire (reported in Rostami et al., 2017). As previously mentioned, when animals are hunted illegally then it is highly unlikely that the meat will undergo the relevant veterinary controls. For example, a small outbreak occurred in southern Italy in 2016 that was associated with illegally hunted wild boars in a national park (Turiac et al., 2017), and another larger outbreak occurred in Serbia during winter 2016–17, with 114 people diagnosed with trichinosis (*T. britovi*), associated with consumption of wild boar that had not been through veterinary controls, although it was not noted whether the hunting was legal or not (Cacciò et al., 2018).

Tourists traveling to exotic destinations and participating in safari-type experiences are a further group that are more often associated with trichinosis associated with unusual meat, that has frequently been prepared by smoking or barbecuing or grilling on an open fire (e.g., Dupouy-Camet, Lecam, Talabani, & Ancelle, 2009). Indeed, it has been speculated (Robertson, Sprong, Ortega, van der Giessen, & Fayer, 2014) that in such situations, local people may be less likely to expose themselves to infected meat as their culture is not to eat meat "rare," but that tourists may be unaware of the potential dangers of meat in a different setting than their own home countries and cultures, and thus do not alter their preferences accordingly. An example provided in the review paper of Robertson et al. (2014) is an outbreak of trichinosis, acquired in the Arctic (Nunavut, Canada) but diagnosed in France, which was associated with consumption of grizzly bear meat by five travelers. The meat not consumed by the travelers was consumed locally, but well cooked, and resulted in no suspected cases, but the travelers consumed the meat either raw or pan-fried (Houzé et al., 2009).

Thus, whereas postmortem control of meat and controlled swine rearing has been effective in interrupting the domestic cycle of trichinosis in many countries, the disease is nevertheless reemerging in specific demographic groups, with game meat of different sorts now becoming the predominant source of infection, at least in Europe and North America. In a review from 2015 of *Trichinella* imported with live animals and meat (Pozio, 2015), it was noted that at that time point there was not a large problem with cases of trichinosis due to imported wild animal meat. However, that wild boar and bear meat have been introduced illegally to Europe with personal baggage, and that tons of bushmeat from Africa are also apparently imported illegally, clearly suggests that a risk of imported parasites exists; one specific concern with cases of trichinosis derived from such imported meat is that if cases of infection occur in countries where physicians are not familiar with the disease, then diagnosis, and thus treatment, may be delayed (Pozio, 2015).

2.5 Anisakiasis—And the Global Spread of Sushi

Consumption of raw or undercooked marine fish has long been known to be associated with infection by various nematodes in the family Anisakidae, the causative agents of anisakiasis, in which humans are aberrant hosts. The species of particular importance to human health are those in the genera, *Anisakis* and *Pseudoterranova*, although not limited to these genera, with the species *Anisakis simplex* and *Pseudoterranova decipiens* of greatest relevance.

In the regular lifecycle of species in this family, marine mammals are the definitive hosts and the intermediate hosts include marine crustaceans followed by various species of marine fish or cephalopods. When humans become infected, by consuming undercooked seafood containing the infective larvae, the immune response to the larvae burrowing into the wall of the digestive tract is usually the main cause of the pathology, for which severe abdominal pain is the most obvious manifestation. Two forms of anisakiasis are recognized depending on where larval invasion occurs, intestinal, which is more common in Europe, and gastric, which predominates in Japan. Intestinal anisakiasis, in particular, is often misdiagnosed, and many patients require surgery due to perforation or occlusion of the bowel.

In addition, some people may be allergic to antigens associated with the larvae, which may also be in the surrounding flesh of the fish, and acute allergic manifestations may occur in the consumer, even if the larvae are dead. Furthermore, some work has indicated that *Anisakis* infection could be a risk factor for the development of some cancers associated with the gastrointestinal tract (Garcia-Perez et al., 2015), due not only to the inflammatory reaction elicited during infection, but also neoplastic alterations (Speciale et al., 2017).

Anisakiasis was previously considered to be restricted only to those cultures or areas where consumption of raw fish was considered to be a regular part of the diet; namely, coastal areas of South America where ceviche is consumed, the Netherlands where raw herring are eaten, Spain where raw anchovies are consumed, and Japan, the land of sushi and sashimi, from where most cases have been diagnosed. Due to the restricted geographical locations, global awareness of this foodborne parasitosis has previously been likewise limited. However, a review from 2005 describes the reported increase in prevalence of anisakiasis in the previous two decades as "dramatic" (Chai, Murrell, & Lymbery, 2005), and a recent case report describes anisakiasis as "a growing disease in Western countries" (Carmo, Marques, Bispo, & Serra, 2017). Furthermore, another case report, from Portugal, where although seafood is part of the traditional diet, raw seafood is not, describes anisakiasis as "an emerging cosmopolitan zoonosis" (Baptista-Fernandes et al., 2017).

Although this increase, which is considered to be still continuing, probably partially reflects improvements in diagnostic techniques, particularly endoscopy, another very relevant parameter is alteration in dietary preferences. Although meat consumption per capita is greater than that of seafood and is increasing, between 1961 and 2013, the rise in consumption was almost twice that for aquatic animals than for meat (FAOSTAT, http://www.fao.org/faostat/en/#compare). The various meat-related food scares and scandals in recent decades, such as mad cow disease in the 1990s and horsemeat food fraud in 2013, may be partially responsible for pushing consumers to explore alternative protein sources than meat. The consumer demand is not only rising or seafood, but, in particular, the demand for raw or lightly cooked fish is also increasing. As explained in the prize-winning documentary from 2011, *Sushi: The Global Catch* (Director, Mark Hall), within a relatively short period of time, sushi has expanded being from a particularly Japanese dish for special occasions, to a global phenomenon that can be found for sale in supermarkets, restaurants—in petrol stations and at football games—all over Europe, North America, and Australasia; and not only through Europe and North America, but also wider afield in Africa and Asia—during filming of *Sushi: The Global Catch* the first sushi restaurant in Rwanda opened. But consumption of raw fish involves not only sushi and sashimi; several other raw fish dishes are also increasing in popularity, including, but not limited to, carpaccio, ceviche, crudo, gravlax, koi pla, poke, and tartare. With such dishes becoming more common worldwide, the potential for exposure to Anisakid larvae is also becoming a more global phenomenon, representing an emerging parasitic disease in regions where consumption of raw fish was previously unknown or unusual, although it is also considered to be an emerging disease in countries where raw fish are a traditional dish (for example, "boquerones en vinagre" (anchovies in vinegar) in some regions of Spain; Bao et al., 2017). Given that some surveys have indicated that the prevalence of infection in anchovies is affected by where they are caught, and that the likelihood of fish being infected in a particular region is also closely affected by the presence of the parasite definitive host in that region, there is certainly a strong possibility for human exposure to vary with time, not only according to human consumption of raw fish, but also associated to where fish are caught, and the presence of marine mammals in that area (Rello, Adroher, Benítez, & Valero, 2009). Although the relationship between the population size of the definitive hosts of a parasite, and the parasite population size in intermediate hosts is complex, it has been speculated that as coastal marine cetacean populations have recovered in size due to implementation of protective conservation strategies (Magera, Mills Flemming, Kaschner, Christensen, & Lotze, 2013), so has the likelihood that fish will be infected with anisakid larvae (Chai et al., 2005). Indeed, in addition, in the Baltic sea an increased occurrence of the anisakid worms *P. decipiens* and *Contracaecum osculatum* has been associated with a rising gray seal population in the area (Zuo, Kania, Mehrdana, Marana, & Buchmann, 2018). Finally, alterations in the fishery supply chain, with control today no longer being the task of veterinary inspectors, but maybe more likely to be the job of the food business operator, has also been suggested to be a reason why infected fish may not be removed from the chain due to training in the detection of the larvae in fish being insufficient (D'amico et al., 2014). Indeed, the same authors suggest that concerns about transmission of this foodborne pathogen in raw fish have resulted in a complex legal framework regarding management of the product chain that, rather than protecting the consumer, has given rise to confusion and a wide range of differences in operating procedures and management plans (D'amico et al., 2014).

2.6 *Opisthorchis* spp.: Tourism, Travel, and More Raw Fish

Members of the Opisthorchiidae family are considered to be neglected tropical diseases by WHO, being within the category of foodborne trematodiases (WHO, 2017). As with all trematodes, these parasites have indirect lifecycles, with mollusks acting as one of the intermediate hosts. Among the Opisthorchiidae family are three important genera with respect to public health, *Opisthorchis, Clonorchis*, and *Metorchis*, although information about the third of these, *Metorchis*, is very limited. Although the lifecycles of all three of these genera of parasites are very similar, for the purposes of this chapter the focus is on *Opisthorchis*. Within this genus, two species are of relevance, *Opisthorchis viverreni* and *Opisthorchis felineus*. The definitive hosts of these parasites are fish-eating mammals including humans; the main reservoir hosts for *O. viverreni* are pigs, rodents, dogs, and cats, and for *O. felineus* are cats, canids, mustelids. In humans, after consumption of the metacercariae (encysted in the skin or flesh of the second intermediate host, various freshwater fish in the cyprinid family), the excysted juveniles move from the duodenum to the biliary ducts and take up residence there (also in the liver, gall bladder, and, for *O. felineus*, pancreatic ducts). Eggs are passed in the feces, and if they are ingested by the first intermediate host, an appropriate freshwater snail, particularly those in the family Bithyniidae, they hatch and then undergo several stages of asexual reproduction, resulting ultimately in the release of free-swimming cercariae. These actively seek their second intermediate host, which they penetrate, encysting to form the metacercariae, either in the muscles or below the scales. It is this stage that is infective to the definitive hosts, including humans. That other fish-eating mammals also act as definitive hosts means that control of the lifecycle is complicated, as the lifecycle can be maintained even when steps are taken to prevent human feces contaminating freshwater where the fish and snails reside.

Although many infections with either species of *Opisthorchis* can be asymptomatic or presenting as only mild symptoms, such as dyspepsia, abdominal discomfort, malaise, indigestion, diarrhea, they can also have more serious clinical presentation, such as hepatomegaly and liver cirrhosis, cholecystitis, and malnutrition. However, the most serious outcome of infection, and which is associated with chronic high worm burdens, is bile duct cancer (cholangiocarcinoma; CCA). The etiology behind the development of CCA in infected people is likely to be multifactorial, being associated with chronic inflammation resulting from a combination of mechanical damage, parasite secretions, and immunopathology (Sripa et al., 2007). It should be noted that although reports of associations between CCA tend to be more concerned with *O. viverrini* infection than O. *felineus*, investigations using an experimental hamster model indicate that actually *O. felineus* is likely to produce greater pathogenesis than *O. viverrini* (Lvova et al., 2012), and that in this model *O. felineus* has carcinogenic potential in terms of development of bile duct cancer (Maksimova et al., 2017), and development of precancerous lesions (Gouveia et al., 2017). Nevertheless, although some studies also clearly indicate an epidemiological association (Pakharukova & Mordvinov, 2016), a study investigating associations between *O. felineus* infection and CCA in the Russian Federation does not provide an unequivocal answer (Fedorova et al., 2017); although the incidence of liver and intrahepatic bile duct cancers (code C22 in ICD-10) was significantly higher in regions with high *O. felineus* infection, compared with low incidence regions, in another region with high C22 cancer incidence, new cases of the infection had not been reported. As the authors point out, however, CCA usually develops a decade or more after *Opisthorchis* infection, and the study is also limited by the lack of distinction between liver and bile duct cancers (Fedorova et al., 2017).

An important difference between the two parasites is their geographical distribution. Whereas, *O. viverrini* is mainly found in South East Asia (Cambodia, Lao PDR, Thailand, Vietnam) where over 10 million people are considered to be harboring the infection, *O. felineus* has a more northern and western distribution, occurring in Belorussia, Kazakhstan, Russia, Ukraine, and various foci in Europe, with between 1 and 2 million people considered to be infected (Keiser & Utzinger, 2009); for both species together, the median number of DALYs in 2010 was around 200,000 (Torgerson et al., 2015).

The reasons for both these species of parasites being generally considered neglected are various, but among them is their association often with conditions of poverty and that the symptoms are often not obvious, and morbidity may be subtle (Fürst, Keiser, & Utzinger, 2012). In addition, the most serious public health consequence of infection, CCA, may take years to develop; although infection can be relatively readily diagnosed (standard formal-ether sedimentation and microscopy or ELISA either for coproantigens or antibodies) and cheaply treated with prazinquantel, the lack of pathognomic symptoms means that CCA-affected people may not be detected until the end stages of the disease; the prognosis without early diagnosis and intervention is very poor (Hughes et al., 2017).

As with anisakiasis, transmission of the *Opisthorchis* spp. is dependent on consumption of inadequately cooked fish, although in this case freshwater fish rather than marine. Thus, the regions with which opistorchiasis cases are originally associated, are those with a particular tradition for raw freshwater fish dishes. However, for the reasons previously outlined regarding dietary habits for anisakiasis (increased consumption of fish in general, and particularly a rising increase in lightly cooked or raw fish), opistorchiasis has moved from becoming a wide-spread, but neglected, foodborne parasitic disease to an emerging issue. Tourists to Southeast Asia and Thai laborers have apparently been regularly reported to carry *O. viverrini* beyond the normal distribution of infection (Andrews, Sithithaworn, & Petney, 2008), and it has also been noted that, due to the lack of diagnostic symptoms and the prolonged duration of infection, infected persons may remain undiagnosed for a long time. Indeed, as tourism to SE Asia has risen markedly (for example, the number of tourists to Thailand has risen from 11.6 million in 2004 to 24.81 million tourists in 2014, to over 32 million in 2016), the likelihood of visitors to the area becoming infected and bringing their infections back to their own country with them has also risen. The increasing movement of people from endemic countries, for employment reasons as well as tourism or visiting family who have already moved abroad, means that patients with *Opisthorchis* infections will be living far beyond the endemic regions, and this infection is becoming a global problem, far exceeding being a medical problem associated only with limited regions (Maksimova et al., 2017). Although this transport is unlikely to result in establishment of the lifecycle elsewhere (as both intermediate hosts would be required, along with contamination of the aquatic environment with the trematode eggs from the feces of the infected person), it may well be very detrimental to the health of the infected person, due to lack of diagnosis or treatment. However, as also pointed out by Andrews et al. (2008), the potential for spread of O. *viverrini* beyond SE Asia is even greater when considering the fish export/import market. Asia is the world's largest producer of freshwater aquaculture products, with production of finfish in inland aquaculture well over 40 million tonnes in 2014, compared with under 0.5 million tonnes in Europe (FAO, 2016). Indeed, carp, which are cyprinids, produced by aquaculture in Asia, are responsible for over 50% of the global finfish aquaculture production (Penman, Gupta, & Dey, 2005) and are also used in sushi and thus eaten raw.

Although SE Asia, the endemic area for O. *viverrini,* has the most sizeable inland aquaculture, one case reported in the literature regarding acquisition of opisthorchiasis from imported fish is concerned with O. *felineus* that was transmitted to a family after eating illegally imported smoked carp, imported from Siberia (Yossepowitch et al., 2004). In addition to this outbreak, several outbreaks of opisthorchiasis have been reported from Italy in more recent years; of eight outbreaks reported between 2003 and 2011, together resulting in over 200 confirmed infections, all involved consumption of raw tench (*Tinca tinca*) that had been caught in lakes in central Italy (Pozio, Armignacco, Ferri, & Gomez Morales, 2013). It has been noted that the occurrence of these outbreaks in Italy since 2003 may reflect changes in fish consumption habits (Armignacco et al., 2008); in particular, the authors noted that tench has previously not been used much, due to low commercial value, and also that in Italy it is traditional that fish are well cooked, with raw fish only becoming popular in recent years. In addition, some of the outbreaks demonstrated particular features of importance. For example, in the outbreak from 2007 that resulted in infection in 20 individuals, the fish had been frozen for 3 days at −10°C, before being cut into fillets and marinated in vinegar and wine for 24 h before consumption (Armignacco et al., 2008). Thus, it is clear that the metacercariae of O. *felineus* not only survive smoking (Yossepowitch et al., 2004), but also freezing and marinating. A larger outbreak that occurred during 2011 and involved around 80 infected individuals was partially due to the restaurant using tench rather than whitefish due to cost and availability factors, thus food fraud issues may be of relevance (Cacciò et al., 2018). In addition, it seems likely that among the people exposed were several tourists (of the infected people traced in this outbreak two were from Austria and seven from the Netherlands); not only might tourists be more likely to be unable to recognize the taste of different locally caught fish, but also (especially for asymptomatic infections) it is possible that the people infected may not be diagnosed, particularly if they do not become linked to an outbreak. Living with chronic or cryptic infections may mean that they are at risk of later development of CCA (Cacciò et al., 2018).

3. INTERVENTIONS

3.1 General Comments

For each of the parasites, improvements in diagnostics and treatment are likely to improve the clinical situation at the individual patient level, and this is particularly so for those parasites for which lack of identification may result in devastating long-term or chronic diseases, such as AE due to infection with *E. multilocularis*, Chagas disease for *T. cruzi*, various prolonged gastrointestinal problems with anisakiasis, or CCA for *Opisthorchis* spp. Indeed, even for cryptosporidiosis, the potential for long-term sequelae has been reported (Osman et al., 2017; Rehn et al., 2015; Stiff, Davies, Mason, Hutchings, & Chalmers, 2017); although for most people infected it is more likely to manifest as an acute, but short-lived, self-limiting episode of diarrhea. However, for most of the parasites described here, such improvements are unlikely to have a significant direct impact on transmission at the community or population level, particularly for *E. multilocularis* and *Anisakis* spp., for which humans are a dead-end host, and therefore further transmission will not occur.

Among the other interventions that could be considered, some are parasite-specific, whereas some are more general and can be broadly divided into two groups: interrupting the lifecycle, and preventing foodborne transmission. Both these groups include interventions that are focused upon specific measures and more general, often educational, efforts.

Interventions that may reduce foodborne transmission are considered according to the specific selected parasites under consideration are raised and discussed in the following sections. However, it should be noted that in order to determine whether the interventions suggested are worthwhile implementing, a cost-benefit analysis (or, if possible, a social cost-benefit analysis) should be conducted to determine whether the "cost" involved in the intervention provides an acceptable saving in DALYs and/or economically. It should also be noted that not all the parasites listed here are solely foodborne (other transmission routes exist for some parasites, notably, *E. multilocularis, Cryptosporidium* spp., and *T. cruzi*) thus interventions that may reduce foodborne transmission need not necessarily completely prevent the transmission cycle.

3.2 Parasite-Specific Interventions: *E. multilocularis*

As already described, foodborne transmission of *E. multilocularis* results from contamination of food that is eaten without heat treatment, usually fresh produce, with *Echinococcus* eggs. Thus, any intervention that reduces environmental contamination with *E. multilocularis* eggs will reduce the likelihood of contamination of food. Canids are the definitive hosts of this parasite, so regular worming of dogs and keeping the stray dog population under control are important strategies. In areas that are endemic for the parasite and where dogs are an important definitive host, such strategies of limiting dog populations and the prevalence of *Echinococcus* infection in dogs are likely to reduce environmental contamination from these definitive hosts (Hegglin & Deplazes, 2013; Ito, Romig, & Takahashi, 2003). In countries where the parasite currently is not found, mandatory worming of dogs at the border may protect not only potential contamination of food (such as berries) from the particular infected dog but also introduction and establishment of the parasite; however, it is important to note that compulsory dog treatment may not keep an area free of this parasite, even with 100% treatment compliance, due to the sylvatic lifecycle. In areas where the lifecycle is established, then control of the parasite by eliminating wildlife hosts entirely (foxes, voles) is not feasible or appropriate, and treating foxes by setting out bait that includes suitable antihelminthic treatment (praziquantel) has been discussed vigorously. Indeed, König et al. (2008) demonstrated that in less than a year of intensive baiting, the prevalence of *E. multilocularis* in foxes in some regions could be reduced to close to zero. However, even after such a significant decrease, to ensure that elimination is achieved, this intensive baiting needs to be continued (Hegglin & Deplazes, 2008). Furthermore, it is important to be aware that not only foxes will be enticed by bait, and thus if this strategy is to be pursued then it is important that the removal of bait by other animals is considered; removal of bait by wild boars has been suggested to have a significant impact on whether this strategy is effective or not (Antolova, Miterpakova, Reiterova, & Dubinsky, 2006). Cost-effectiveness or cost-benefit studies, which also take into account ecological parameters, are of clear importance here (Janko & König, 2011), and factors such as available financial resources, priority setting of political decision-makers, and public attitudes are also of relevance (Hegglin & Deplazes, 2013).

3.3 Parasite-Specific Interventions: *Cryptosporidium* spp.

Any interventions that reduce the potential for contamination of food with matter derived from feces, particularly human feces or feces of young ruminants such as calves and lambs, are likely to be effective at reducing the risk of contamination of food with oocysts of *Cryptosporidium*. However, with such a generalized pathway, with many different host species, it is difficult to select parasite-specific interventions to reduce foodborne cryptosporidiosis. Use of a HACCP approach in any food industry that may be relevant for transmission of this parasite may assist in pinpointing where contamination could occur and places where interventions may be of most value. Relevant interventions are thus based around general hygiene principles, ensuring that irrigation water is free from contamination with animal feces or sewage effluent, and ensuring proper hygiene among food handlers, including that persons who have diarrheal disease, or have recently suffered from diarrheal disease, do not handle foods. Pasteurization of milk is a good control measure for dairy products, not just for *Cryptosporidium,* and may also be relevant for fruit juices. Given the potential for spread of *Cryptosporidium* oocysts throughout a batch during commercial washing of fresh produce in the production of RTE salads, specific attention should be focused upon the washwater; given the high biological oxygen demand of this water, disinfection is not easy. Indeed, the washing process, that is intended to make the produce cleaner and safer, may, in fact, do the opposite.

3.4 Parasite-Specific Interventions: *T. cruzi*

As already described, foodborne transmission of *T. cruzi* results from contamination of food, or more frequently beverages (fruit juice), with trypomastigotes from the triatomine vectors, or, less commonly, from reservoir hosts such as opossums. Reducing the likelihood that triatomines and reservoir hosts can gain access to food such as fruit juices, such as by storing food and beverages covered, or keeping them in a refrigerator in endemic areas are obvious approaches to reducing the likelihood of contamination. In consideration of prophylactic and control measures for foodborne Chagas diseases (Robertson and Noya 2015), the authors not only consider prevention of how food can become contaminated, using a HACCP approach to consider the weakest points in the food chain, from production to consumption, but, due to the inextricable link of this illness with both poverty and the vector reduviid bug, also discuss vector control in general. Within buildings where high-risk food products may be prepared, stored, or served, two approaches are both worthy of consideration; these are residual spraying of insecticides and also improving housing infrastructure, including plastering of walls, use of concrete flooring and roofs of suitable materials, and also using screens on windows and doors.

Educational tools are also considered of importance, and the use of mandatory rules to prevent food contamination, particularly in places such as canteens and restaurants, is also recommended. The authors also note how blenders, used in the preparation of fruit juices, should be considered as high-risk equipment regarding the potential for contamination, particularly by nymph stages of the triatomines. These stages, which are very small, may fall into the blender, but, due to the smooth sides, be unable to climb out again, and, as nymph stages do not possess wings, are also unable to fly out (Robertson & Noya, 2015). Thus, keeping blenders in a sealed unit, such as a cupboard, when not in use, and rinsing them before use in the preparation of juices or other blended products are simple approaches toward limiting contamination.

3.5 Parasite-specific interventions: *Trichinella* spp. in game animals

In western Europe, at least, the transmission of *Trichinella spiralis* in the domestic pork industry is negligible. This is largely due to strict controls and biosafety in pork husbandry, and thus the majority of pigs raised for slaughter do not have the opportunity to ingest any meat containing viable *Trichinella* larvae. These controls are backed up by the mandatory testing of slaughter pigs for *Trichinella* larvae by an approved method. It is clear that in order to control *Trichinella* transmission on the basis of the sylvatic cycle, that is not via pork but through consumption of game animals, education of hunters and game meat consumers is key. It has been noted that investment of funds into relevant stakeholders, such as hunters, should be a priority for public health services concerned with control of this foodborne parasite (Pozio, 2014). Although hunters should also have the opportunity to have their "bag" tested, how this would be paid for is unclear, and hunters themselves may be unwilling to take on this additional expense. Given that such testing may be difficult to implement, the importance of adequate cooking should be emphasized. In addition, and as noted by Turiac et al. (2017), it is necessary continually raising the awareness on the epidemiological and clinical features of this zoonosis among healthcare personnel for an immediately suspicion of the disease.

3.6 Parasite-Specific Interventions: Anisakidae

Despite the various reasons for anisakiasis being considered an emerging/reemerging parasitic disease (e.g., Zanelli et al., 2017), it is clear that proactive risk management and consumer protection are on the agenda.

In Europe, the European Food Safety Authority (EFSA) conducted a risk assessment regarding parasites in fishery products, with particular emphasis on *Anisakis* (EFSA, 2010). In particular, EFSA considered the potential for allergic reactions, evaluated alternative treatments for killing viable parasites in fishery products and assessed their effectiveness in comparison with freezing, and discussed whether criteria could be set regarding fish that may not present a health hazard regarding the presence of parasites when eaten raw or cold smoked (EFSA, 2010). EFSA concluded that freezing or heat treatments were the most effective methods for killing the larvae, with heating at >60°C for at least 1 min, and freezing either at −35°C for at least 15 h, at −20°C for not less than 24 h, or at −15°C for at least 96 h. As noted by Bao et al. (2017), their QRA simulation clearly shows that should an education campaign results in an *X*% increase in the number of anchovy meals that are frozen, then the incidence of anisakiasis in the population will also reduce by *X*%. However, Bao et al. (2017) also note that although consumers may be aware that freezing prevents transmission of this parasite, most do not actually do so—indicating the need to target this consumer group, and to determine why they do not do this, particularly in those regions where the disease incidence is highest.

Marinating and cold smoking were acknowledged as not providing a sufficient level of safety, with no sea fishing grounds considered to be known to be free of *A. simplex*. However, the risk from aquaculture salmon, farmed in floating cages or onshore tanks, and fed on compound feed, was considered to be negligible (EFSA, 2010) and has been latterly supported by a large-scale study of farmed Norwegian salmon (Levsen & Maage, 2016). A risk assessment focusing specifically on the likelihood of farmed salmon being sold containing viable anisakid larvae also supports this finding (Crotta, Ferrari, & Guitian, 2016).

A further consideration regarding management of anisakiasis has been delivered through considering "horizon scanning," which resulted in a proposal for collaborative software to provide multilevel management of parasites (not limited to anisakids) in seafood (Llarena-Reino, Abollo, Regueira, Rodríguez, & Pascual, 2015). Professional training was considered to be a key driver. It should also be noted that the presence of anisakid larvae in imported fish has resulted in several notifications to the European Rapid Alert System for Food and Feed (RASFF), with over 91% of parasitic infestations in the RASFF database from 2012 due to import of fish in which anisakid larvae were detected (Robertson et al., 2014). More recently, data from 2017 (1st January until 31st December) show a similar awareness of this parasite, as from 41 parasite infestation reports in RASFF, 35 (ca. 85%)

mention *Anisakis* specifically, whereas others not included among the 35 could be anisakid larvae (e.g., parasitic infestation of fish mentioned, but the parasite not specified).

3.7 Parasite-Specific Interventions: *Opisthorchis* spp.

A cross-sectional study in Thailand found that prioritization of the parasite *Opisthorchis viverrini* by village-level health centers had an impact on risk of infection (Ong et al., 2016). Although, interestingly, behavior regarding consumption of raw fish did not have a significant impact on risk of infection, the authors emphasize the need for a holistic approach in considering control measures for this pathogen, particularly consideration of those factors that constitute the broader pathogenic landscape (Ong et al., 2016). At the same time, other authors seem to consider that interventions directed toward lifecycle interruption for this parasite are destined to fail, citing failure to alter eating practices and the relatively high prevalence of infection in reservoir hosts, such as dogs and cats (Hughes et al., 2017). These authors instead suggest that identification of biomarkers that can be used as indicators of the carcinogenic pathway being activated may be more relevant, enabling detection of the most serious sequelae of this infection, CCA, and thus enabling medical interventions to have a higher likelihood of being successful (Hughes et al., 2017). Various biomarkers have already been suggested, including overexpression of proteins orosmucoid 2 and kinesin 18A (Rucksaken et al., 2012), annexin A1 (Hongsrichan et al., 2014), and various other dysregulated proteins (Khoontawad et al., 2017). Other suggested markers, include, for example, a carbohydrate antigen associated with CCA, on which particular epitopes may be recognized using monoclonal antibody-based techniques (Sawanyawisuth et al., 2012). With regards to *O. felineus*, which has a different geographical distribution, the emphasis remains predominantly on control at the fish level; a landmark paper following the outbreaks in Italy summarized the treatments that could be used to inactivate the metacercariae in fish, with particular reference to the fact that one outbreak had occurred despite the fish being frozen at −10°C (Pozio et al., 2013). Other control mechanisms suggested at the local level are to try to reduce infection of dogs and cats that are otherwise maintaining the lifecycle, by educating fishermen not to discard unwanted catch on the lakeshore where they can be eaten by these animals, and for restaurants also to ensure disposal of fish leftovers or waste such that they are not accessible to dogs and cats (Pozio et al., 2013).

3.8 Current and New Efforts Toward Research and Control

For all foodborne parasites, realization of the problem associated with them is probably the fundamental initial step that enables the implementation of other preventative initiatives. In this respect, the transition from being a neglected subject to an emerging or reemerging problem is actually of assistance, as people are more engaged when they realize that a particular issue is of direct concern to themselves, rather than merely to a group of people who may live very far away and whose problems may seem to be of little global or wider relevance. Although foodborne parasites have previously been a focus of only a very limited group of research scientists, doctors, and veterinarians, various broader interest networks indicate that foodborne parasites are climbing up the agenda and capturing attention from a wider audience. Below an overview is provided of both some general foodborne parasite initiatives and also some parasite-specific initiatives; key points are summarized in Table 2.

For example, WHO and FAO have made some concerted efforts in recent years to compare different foodborne parasites with risk-ranking exercises and also establishing the actual burden due to foodborne parasites (see, for example, FAO/WHO, 2014; Hald et al., 2016; Havelaar et al., 2015; Kirk et al., 2015; Robertson et al., 2014; Torgerson et al., 2015). Although the information published from the work by the WHO Foodborne Disease Burden Epidemiology Reference Group (FERG) did not focus on foodborne parasites alone, their inclusion at all, and the accompanying recognition of the relevance of foodborne parasites (e.g., *Taenia solium* being one of the major causes of deaths due to foodborne diseases) brought this pathogen group into greater focus. Some selectivity of the parasites included was, however, noticed—for example, the exclusion of *T. cruzi* on the basis of its regional occurrence (Robertson et al., 2016).

The increased focus on foodborne parasites in general in more recent times is also reflected in specific actions like the establishment of the Food and Environmental Parasitology Network (FEPN) in Canada in 2009 (see http://www.fepn.net/), with the intention of identifying and communicating risks and research, facilitating discussion and collaboration, developing and validating methods, generating data, and providing advice, the International Association for Food and Waterborne Parasitology (IAFWP) in 2015 (see https://www.iafwp.org/), with the mission to promote and facilitate research and collaboration on this subject with the overall intention of reducing the global burden of parasites transmitted by food or water, along with the companion journal (Food and Waterborne Parasitology Journal,

Table 2 Parasites in Food: From a Neglected Position to an Emerging Issue

	Initiatives Established	**Relevant Links or References**
Foodborne parasites in general	Food and Environmental Parasitology network (FEPN) in Canada; International Association for Food and Waterborne Parasitology (IAFWP), with associated journal; COST Action, FA1408, A European Network for Foodborne Parasites (Euro-FBP); OIE (World Organization for Animal Health) Collaborating Centers for foodborne parasites: Food-Borne Parasites from the Asia-Pacific Region, Food-Borne Zoonotic Parasites, and Food-Borne Zoonotic Parasites from the European Region; European Food Safety Authority (EFSA) Opinion on Foodborne Parasites	http://www.fepn.net; https://www.iafwp.org/; https://www.journals.elsevier.com/food-and-waterborne-parasitology; https://www.euro-fbp.org/; http://www.cost.eu/COST_Actions/fa/FA1408; http://www.oie.int/en/our-scientific-expertise/collaborating-centres/annual-reports; http://www.efsa.europa.eu/en/events/event/171206
Specific foodborne parasites		
Cestodes		
Echinococcus multilocularis	EFSA Opinion on *Echinococcus multilocularis*; EMIA consortium project (*Echinococcus multilocularis* infection in animals)	European Food Safety Authority (2015) and Oksanen et al., 2016
Protozoa		
Cryptosporidium	ACCORD (ACcelerator for CryptOsporidium Research & Drug Development to Reduce Child Mortality); US CDC CryptoNet	Shoultz, de Hostos, & Choy, 2016; https://www.cdc.gov/parasites/crypto/pdf/cryptonet_fact_sheet508c.pdf

Trypanosoma cruzi	WHO Program on Control of Chagas Disease; The International Federation of Associations of People Affected by Chagas Disease (FINDECHAGAS)	http://www.who.int/chagas/en/; http://www.findechagas.com
Nematodes		
Trichinella spp.	CDC Trichinellosis Information for Hunters; U.K. Food Standards Agency *Trichinella* testing of wild boar carcasses; testing of hunting dog sera	https://www.cdc.gov/parasites/trichinellosis/hunters.html; https://www.food.gov.uk/sites/default/files/multimedia/pdfs/trichinellatestingwildboar.pdf; Gómez-Morales et al. (2016)
Anisakidae	EFSA Opinion on parasites in fishery products; Parasite risk assessment with integrated tools in EU fish production value chains (PARASITE); Scanisakis, for UV-based detection of Anisakids	European Food Safety Authority (2010); http://parasite-project.eu/project; Levsen et al., 2018; https://cordis.europa.eu/result/rcn/189395_en.html
Trematodes		
Opisthorchis spp.	Lawa Model, uses an EcoHealth/One Health tactic; Cholangiocarcinoma Screening and Care Program (CASCAP); Tomsk OPIsthorchiasis Consortium (TOPIC)	Sripa et al., 2015; http://www.who.int/neglected_diseases/news/fbti_thailand_uses_integrated_ecosystems_health_approach/en/; Khuntikeo, Loilome, Thinkhamrop, Chamadol, & Yongvanit, 2016; Ogorodova et al., 2015

published by Elsevier; see https://www.journals.elsevier.com/food-and-waterborne-parasitology), and, in Europe, the COST Action, FA1408, A European Network for Foodborne Parasites (Euro-FBP), an EU-funded networking project running between 2015 and 2019 (see https://www.euro-fbp.org/ and http://www.cost.eu/COST_Actions/fa/FA1408), with the ultimate goal of decreasing the impact on human health from foodborne parasites through establishing a risk-based control program containing robust and appropriate protective strategies. In addition, there are three OIE (World Organization for Animal Health) Collaborating Centers for foodborne parasites: Food-Borne Parasites from the Asia-Pacific Region (based in Changchun, China), Food-Borne Zoonotic Parasites (based in Saskatchewan, Canada), and Food-Borne Zoonotic Parasites from the European Region (based in Maisons-Alfort Cedex, France). The remits of these three centers are similar, although within a regional focus; in their annual reports from 2016 (http://www.oie.int/en/our-scientific-expertise/collaborating-centres/annual-reports/) all three Centers mention in particular *Trichinella* and *Toxoplasma* activities, the Canadian Center also mentions *Taenia saginata* in cattle (Cysticercus bovis), *Cyclospora*, and *Giardia*, the Chinese Center also mentions *T. solium* (Cysticercus) in pigs, *Clonorchis sinensis*, and *Cryptosporidium*, and the European Center also mentions *Cryptosporidium* and *Alaria alata* (which is not currently considered to be zoonotic). Thus, of the six foodborne parasites in focus in this chapter, only two (*Trichinella* and *Cryptosporidium*) were of focus for the OIE Foodborne Parasite Collaborating Centers in 2016, indicating, perhaps, that even these Centers need to expand their considerations.

Also within Europe, the EFSA has taken on the task of considering and evaluating the public health risks associated with three specific foodborne parasites (*Cryptosporidium*, *Echinococcus*, and *Toxoplasma*), with the opinion document due in October 2018 (see http://www.efsa.europa.eu/en/events/event/171206).

As noted, in addition to these parasite-wide initiatives, there have also been some more parasite-specific initiatives. With regard to the six parasites considered here and their foodborne transmission, *E. multilocularis* is part of the ongoing EFSA opinion, but it is a measure perhaps of the potential severity of this infection that EFSA already published an opinion on this parasite in 2015 (European Food Safety Authority, 2015) and, in addition, funded a consortium project between 2012 and 2015 known as EMIA (*E. multilocularis* infection in animals), which included six European consortium partners, and five external experts.

Cryptosporidium is also part of the ongoing EFSA opinion, but also has been very much in focus with respect to the Euro-FBP COST Action (e.g., Cacciò et al., 2018; Chalmers & Cacciò, 2016). As *Cryptosporidium* is largely considered to be a waterborne, rather than foodborne, pathogen, much of the emphasis still remains on the water mode of transmission, or, more particularly directed toward effective drug development, with initiatives such as ACCORD (ACcelerator for CryptOsporidium Research & Drug Development to Reduce Child Mortality) that are intended to develop effective treatments for cryptosporidiosis (Shoultz et al., 2016), and is now associated with PATH—Program for Appropriate Technology in Health (http://sites.path.org/drugdevelopment/projects/edd/accord/). Furthermore, the US Center for Disease Control and Prevention (CDC) has launched an initiative called CryptoNet (https://www.cdc.gov/parasites/crypto/pdf/cryptonet_fact_sheet508c.pdf), the purpose of which is to facilitate systematic collection and molecular characterization of *Cryptosporidium* isolates, thereby providing better understanding of cryptosporidiosis epidemiology in United States, which, among other objectives, intends to improve detection and investigation of foodborne outbreaks.

For *T. cruzi,* the WHO Programme on Control of Chagas Disease (http://www.who.int/chagas/en/) has enabled various subregional initiatives through the Pan American Health Organization (PAHO), which, although not specifically concerned with foodborne transmission, as vector control and development of treatment has been in focus for many years, has enabled strong collaboration to develop. This was exemplified using a Partnership Assessment Tool (Salerno, Salvatella, Issa, & Anzola, 2015). The International Federation of Associations of People Affected by Chagas Disease (FINDECHAGAS) is another patient-centric, multicountry group that was created in Brazil in 2009 with the main goal being to improve social policies, especially in health, with actions that are targeted toward prevention, diagnosis, treatment, and social and psychological protection for carriers and their families (http://www.findechagas.com). Thus, although the main focus is not foodborne transmission, this is obviously also a relevant element.

With education considered a key intervention to reduce transmission of *Trichinella* via game animals, targeted initiatives have been developed. For example, the U.S. Center for Disease Control and Prevention has a web page specifically aimed at hunters (Trichinellosis Information for Hunters; https://www.cdc.gov/parasites/trichinellosis/hunters.html) that explains not only why hunters should be aware of this infection, but also how animals with trichinellosis may appear and how to prevent infection. Similarly, the

U.K. Food Standards Agency has published a leaflet to provide guidance to hunters regarding *Trichinella* testing of wild boar carcasses, including information on the infection itself, samples that should be taken for testing, and a form to accompany samples sent in for analysis (Food Standards Agency, 2010; see https://www.food.gov.uk/sites/default/files/multimedia/pdfs/trichinellatestingwildboar.pdf). Various other countries have similar information for hunters, usually in national languages. Obviously, it would be useful for hunters to know the likelihood of animals that they hunt being infected, and, given that testing of wildlife is impractical, work by Gómez-Morales et al. (2016) has suggested that one approach to obtain such data would be by testing the sera of hunting dogs in defined locations, such that they act as sentinels for circulation of this infection among the wildlife. As a test, Gómez-Morales et al. (2016) analyzed sera in hunting dogs from hunting dogs from 23 districts in a particular region of Italy where there is extensive hunting of wild boar, and an outbreak due to consumption of wild boar meat has been recorded; results indicated that serological testing of hunting dogs could provide an indication on the circulation of *Trichinella* spp. in the wildlife in a specific region during a particular timeframe. As the authors note, however, as both hunters and their dogs may travel between districts, this information must also be taken into account.

In addition to the EFSA opinion on parasites in fishery products (EFSA, 2010), that had a particular emphasis on anisakiasis, an EU-funded project "Parasite risk assessment with integrated tools in EU fish production value chains (PARASITE), Grant Agreement (GA) no. 312068; http://parasite-project.eu/project" which ended in 2016 had particular focus on Anisakids, with objectives (in work packages) focusing on exposure assessment, DNA bar-coding, determination of allergenic capacity, improved detection, investigation of interventions that could inactivate the parasites and reduce allergenic capacity, and quantitative risk analysis. The project has resulted in the development of a graphical exposure risk profile, which includes those fish species or their products, which are considered to be of greatest risk as a source of anisakiasis within Europe (Levsen et al., 2018). As well as other outcomes of this project (see https://cordis.europa.eu/result/rcn/189395_en.html), the project resulted in the development of an automatic device, Scanisakis, for UV-based detection of the zoonotic species within the genera *Anisakis*, *Pseudoterranova*, and *Contracaecum*. In addition, the project developed a device for determining the viability of anisakid larvae, being able to distinguish between live and dead larvae on the basis of various selected viability features and was tested for use on frozen, marinated, and salted products.

Of the six parasites considered in this chapter, *Opistorchis* spp. is, perhaps, the one that remains more neglected than emerging, despite perhaps being the one that currently exerts the greatest public health burden, in terms of the severity and prevalence of infection on a global scale. Nevertheless, there are initiatives in place that seek to tackle this parasite. One approach, now known as the Lawa Model, uses an EcoHealth/One Health tactic; first introduced into the Lawa Lake area in Khon Kaen province, Thailand, where *O. viverrini* is endemic, the program used a combination of anthelminthic treatment, intensive health education, and ecosystem monitoring, all with community participation (Sripa et al., 2015). The results were so positive that the Lawa Model has been hailed as a flagship approach by the World Health Organization (see http://www.who.int/neglected_diseases/news/fbti_thailand_uses_integrated_ecosystems_health_approach/en/) and has been recommended by WHO as an approach worth implementing in other areas and countries. Another approach that has also been initiated in Thailand is the Cholangiocarcinoma Screening and Care Program (CASCAP), which is primarily to instigate long-term screening of population at risk of *O. viverrini* infection and CCA (of whom approximately 20 million are in Thailand, where this initiative is located) such that precancerous changes to the biliary tract and liver are identified in addition to early stage CCA that can be successfully treated (Khuntikeo et al., 2016). Despite being targeted at the clinical level, CASCAP also seeks to address research needs (particularly regarding diagnostics and treatment), to address the socioeconomic aspects of CCA at the community level with the intention of developing policies to address the impact, and to review the efficacy of current control and prevention programs, including education, in order to develop measures for control of *O. viverrini* infections and CCA. Hughes et al. (2017) note that longer-term public education schemes, such as that organized by CASCAP, should be commenced and enlarged such that communities are provided with education about the dangers associated with raw, partially cooked, or fermented fish. The hope is that, over time, attitudes toward consumption of raw fish will modify, even in communities where it is an important part of the local culture. Another initiative concerned with control of opisthorchiasis includes both species (and *C. sinensis*) and is based around a group of professionals who have formed a consortium called TOPIC (Tomsk OPIsthorchiasis Consortium) who wish to raise awareness, strengthen integrated control, and conduct research in order to combat these parasites; the Lawa Model is proposed to be followed by TOPIC also (Ogorodova et al., 2015).

4. CONCLUSION

Pathogens that are neglected because their effects are limited to particular populations or particular locations are, in our increasingly mobile and globalized world, ripe to emerge—they will evolve to adopt new transmission routes, invade new hosts, use new vehicles of infection, and produce new pathologies. As many parasitic infections have been neglected, it is no surprise to see that many are now emerging, appearing in unexpected hosts, in new locations, using different transmission vehicles, or resulting in a different spectrum of symptoms. In this chapter, just six foodborne parasites are used as examples, but others could also have been selected. In recognizing these emerging foodborne parasites and rising to combat them in their new situations, we do ourselves the additional favor of also having the opportunity of addressing pathogens that, although neglected, have been a significant burden, both in terms of health and socioeconomy, often in impoverished or otherwise marginalized communities.

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