

THE IMPACT OF FISH PARASITES ON HUMAN HEALTH (REVIEW ARTICLE)

By

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Abstract

One of the most important problems faced by world at the present time is food deficiency. Today the third world is facing protein deficiency as one of the major global challenges. In Egypt, the continuous population explosion requires more food production to meet the consequent increasing demands. However, there are many zoonotic fish parasites not only in Egypt but worldwide.

Key words: Egypt, Fish, zoonotic heminthes, Review

Introduction

Fishes are considered to compensate the continuous lack of such element due to its comparatively low price (El-Tantawy and El-Sherbiny, 2010). Fishes were used even in prehistoric ages and were supposed to be beneficial to long life and intelligence (Hamilton, 1971). Fish as food products have a very high nutritive value approximating that of red meat. Its protein is readily available (at a level of 96%) which stems from a low content of collagen and elastin. It is worth mentioning that as little as 100 g ration of fish provides a human with 1/3 to 1/2 of the daily requirement for animal protein. Fish constitutes an important and indispensable component of the human diet due to the content of polyunsaturated fatty acids (PUFA), the so-called "Omega-3 acids". They are necessary for the comprehensive development and functioning of the brain as well as senses of sight and hearing. A study conducted in Netherlands reported that eating a pound of fish a week could reduce the coronary heart diseases in man. Some fish, specially cold water species such as cod, salmon, mackerel and sardines, contain some oils that are not found in other food and have major effects on body chemistry, which reduces the tendency of blood to clot and helps in lowering cholesterol level in the blood. The medical value of fish oil cannot

be ignored keeping in mind the use of cod and sharks among patients suffering with vitamin A and D deficiency (Uradzinski *et al*, 2007)

Among the animals, fishes are the most important hosts for maintenance of parasites mainly helminthes. Most of fishes have parasites and they not only serve as hosts of different parasites but also serve as carrier of many larval parasitic forms that mature and may cause serious diseases in many vertebrates including man. With the increasing interests in aquaculture, parasitic infestations are becoming threats for fish health management. It is therefore an essential area for proper attention to be given by the scientists for sustainable aquaculture production (Chandra, 2006).

Humans suffer from numerous parasitic food-borne zoonoses, many of which are caused by helminths. The helminth zoonoses of concern in this review are those transmitted from fish, freshwater, brackish and marine. In the past, these diseases were limited for the most part to populations living in low- and middle-income countries, but the geographical limits and populations at risk are expanding and changing because of the growing international markets, improved transportation systems, and demographic changes (Chai *et al*, 2005).

WHO (1995) estimated that the number of people currently infected with fish-borne trematodes exceeds 18 million, but worldwide the number of people at risk, including those in developed countries, is more than half a billion. The recognition of the public health significance of these zoonoses, their links to poverty and cultural traditions, to intensification of agriculture, to environmental degradation, and the lack of tools for control is increasing.

Fish and parasites: Although fish are a valuable source of food, their consumption may contribute to food poisoning and infections as they contain pathogenic bacteria and/or their toxins, parasite and chemical residues (Uradzinski *et al*, 2007). Several studies and comprehensive textbooks in fish parasitology have been achieved in the last years, from these, the following can be drawn:

A- Global studies: Many protozoan parasites infect fishes (opalinids, coccidia, dactylospores, trypanosomes, Hixamida, Myxosporea, Microspora) (Azevedo *et al*, 1993; Bassey, 2011; Abowei and Ezekiel, 2011, Eli *et al*, 2012) and monogenean trematodes (Reed *et al*, 1996) but all of them were never recorded from humans. Yamaguti (1937; 1938; 1939; 1940; 1941) reported the helminth fauna of Japan. Tsai and Cross (1966) reported *Anisakis*-like larvae from the marine fishes of Taiwan. A survey on anisakidae larvae found in fishes and cephalopods caught in the Seto Inland Sea and the Japan Seawas published by Hatada (1970) while the dynamics of the nematode larvae, *Anisakis simplex* invasion in the South Western Baltic herring was studied (Grabda, 1974). Davey (1971) had given a revision of the genus *Anisakis*. In 1977, Hauck discussed the occurrence and survival of the larval nematode *Anisakis spp.* in the flesh of fresh frozen, brined and smoked pacific herring. Bhaibulaya and Siwaraksa (1979) reported *Anisakis* larvae from the marine fishes of the Gulf of Thailand. In 1983, Bagrov described morphological variability of larvae of *Ani-*

sakis spp. Petter *et al.* (1985) studied teleost fishes from the Bay of Kotor (Yugoslavia) for parasitic nematodes and they found several species of adult or larval nematodes of the genus *Anisakis*. Smith and Wootten (1987) reviewed many and varied aspects of the extensive world literature on *Anisakis*. Wootten (1978) studied the occurrence of larval Anisakids in small gadoids from Scottish waters and noted increased infection rate with increasing age and length of fish.

Hristovski and Jardas (1991) discussed endohelminths of fishes from the mid-Dalmation region of the Adriatic Sea. Naidenova and Morvinova (1997) studied the helminth fauna of Mediterranean Sea fishes. Diamant *et al.* (1999) reported several species of digeneans from the rabbit fish, *Siganus rivulatus*, and Dzikowski *et al.* (2003) reported that multi-annual changes in the parasite communities of the same species. Scholz (1999) studied some parasites in cultured and feral fish. He only selected a few parasites of each major group of fish parasites, i.e. protozoans, myxosporeans, helminths and parasitic crustaceans. Stewart and Bernier (1999) studied the common parasites, diseases and injuries of fresh water fishes in the Northwest Territories and Nunavut. Hoffman (1999) gave brief descriptions of North American freshwater fish and their parasites. Salgado-Maldonado *et al.* (2005) reviewed the helminth parasites in freshwater fish from the Papaloapan river basin, Mexico. They presented a checklist for these helminthes based on the previously published records and original data.

Chandra (2006) reviewed a parasitological investigation and research in Bangladesh. Considerable works mainly on systematic, nature of infestation and pathology of different groups of fish parasites had been done. A total of 290 species of parasites had been recorded from freshwater and marine fishes in Bangladesh. Two helminth parasites of zoonotic importance *Dibothriocephalus latius* and *Gnathostoma spinigerum* were also reported.

Moles (2007) summarized the published records of parasites of freshwater and marine fishes of Alaska and the surrounding seas through 2006. Of 601 species of fish believed to inhabit the waters of Alaska, parasites were listed for 89 species. Ghaffar (2014) studied the seasonal variation and histopathology of helminth parasites in the fish, *Lutjanus argentimaculatus* (Forsk, 1775) red snapper, and reviewed some of the previous works that dealt with fish parasites around the world especially in Pakistan.

Muzzall and Whelan (2011) presented a synopsis and literature review for fishes parasites of Great Lakes from 1871-2010. The synopsis was based on information from the literature (articles, theses, dissertations, reports) on the major parasite groups (protozoans, digenetic trematodes, monogeneans, aspidobothreans, cestodes, nematodes, acanthocephalans, leeches, copepods, molluscs).

B- Local and Arabian studies: Digenetic trematodes of marine fishes from the Red Sea received great attention from several workers. Nagaty and his group reported on these digeneans from 1930 until 1972 (Nagaty, 1930; 1937; 1941; 1942; 1948; 1954; 1956; 1957; Nagaty and Abdel-Aal, 1961; 1962a,b,c; 1964; 1972). Ramadan continued working on digeneans of Red Sea fishes, where he described several new species and revised the taxonomy (Ramadan, 1982; 1983; 1984; 1985; 1986; 1988; Saoud and Ramadan, 1985).

Al-Bassel (1997) studied the helminth parasites infecting some fishes from the Mediterranean Sea. He investigated 465 fish belonging to 7 families and 9 genera caught from the Libian coastal waters near Misurata. Al-Bassel (2003) surveyed the helminth parasites of fish from inland waters in the Fayoum Government, Egypt. He investigated 450 fishes belonging to 7 genera and 7 species for helminth parasites. Of these, 220 fish were found to harbour Acanthocephala (14%), cestodes (16.22%), Digenea (10.66%), Monogenea (1.77%) and nematodes (6.22%).

Alkawari *et al.* (1996) worked on the biodiversity of helminth parasites of fishes in Arabian Gulf. Parasitic fish diseases in Egypt were reported by Eissa (2002). El-Said-Hassanine (2000) reported two digenetic trematodes from some fishes in the Gulf of Aqaba. El-Labadi *et al.* (2006) recorded the intestinal digenetic trematodes of some fishes from the Gulf of Aqaba, Red Sea.

Mhaisen and Al-Nasiri (2012) reviewed the parasites of fishes at Salah Al-Deen Province, Iraq. They reported 84 parasite species; 6 ciliophorans, 21 myxozoans, 17 monogeneans, 6 trematodes, 9 cestodes, 10 nematodes, 5 acanthocephalans, 2 annelids and 8 arthropods. These were recorded from 21 fish species, among which 18 fish species belonged to the family Cyprinidae. Mhaisen *et al.* (2012) reviewed the fish parasites of Al-Furat fish farm, Babylon province, Iraq. These fishes included the common carp (*Cyprinus carpio*), the grass carp (*Ctenopharyngodonidella*) and the silver carp (*Hypophthalmichthys molitrix*) as well as the mullet (*Liza abu*). The parasitic fauna included 60 valid parasite species: 10 protozoans, 3 myxozoans, 29 monogeneans, 1 trematode, 5 cestodes, 3 nematodes, 2 acanthocephalans, 6 crustaceans and 1 mollusc. The common carp was found to harbour 56 species of parasites, the grass carp 25 species, the silver carp 25 species and the mullet six species.

Fish parasites and human health: Fish of most species are intermediate hosts of transient forms of a vast number of parasites. Muscles of fish belonging to the most valuable species are habitat of larvae, whereas parasites very often occur in their gastrointestinal tract, liver and other internal organs, as well as on their skin. The most dangerous are those which, when ingested with courses made of fish or marine invertebrates may undergo developmental stages in the internal organs or muscles of humans, thus including unpleasant influence of life threatening diseases. A risk of infection with parasites usually occurs with the consumption of live

parasite-containing flesh, liver or gonads in the form of traditional courses prepared from raw or slightly salted or marinated fish, as well as cold-smoked products, which were not frozen prior to smoking. Among the vast number of fish products, only a few are pathogenic to humans, including mainly digeneans, tapeworms and nematodes. Digeneans use fish, shell fish and crustacea as a second intermediate host and humans or other mammals feeding on fish, as the definitive host. Tapeworms parasitizing in fish occur as adult forms in the gastrointestinal tract or in the form of larvae in various tissues. The final host of larvae living in the muscles and organs of fish are most often predatory fish, birds, mammals feeding on fish, and sometimes humans. Larvae of some species of nematodes, parasitizing fish, may also be harmful to humans. The Clupeidae, Scombridae and Gadoid fish may be infested with *Anisakis simplex* larvae. The larvae, curled into flat spirals, rises primarily in the peritoneum, liver, and gonads and sometimes also in the abdominal segments of muscles (Sikorski, 2004).

Adams *et al.* (1997) reported that the most important of helminths acquired by humans from fish are the anisakid nematodes (particularly *Anisakis simplex* and *Pseudoterranova decipiens*), cestodes of the genus *Diphyllobothrium* and digenetic trematodes of the families Heterophyidae, Opisthorchiidae and Nanophyetidae. Stewart and Bernier (1999) mentioned that the effect of parasites on the value of the fish is perhaps greater than their impact on human health. Also, they added that parasites can reduce the value of fish to harvesters by damaging the skin, infesting the meat, or spoiling the flavour or condition of the fish. Barber and Poulin (2008) reported that some parasites may be responsible for acute, economically important outbreaks of disease in exploited fish populations or reduce productivity through nutritional effects; others may be responsible for chronic long-term changes in population structure. They added that infec-

tion-associated changes to host phenotype may influence the outcome of intraspecific or interspecific interactions and have important consequences for individual performance, whether measured by an ecologist in terms of evolutionary fitness or by a fisheries manager as reductions in stock biomass. Andréoletti *et al.* (2011) reported that for fishery products caught from fishing grounds in the Baltic Sea, four groups of viable parasites present possible health risks, *Anisakis simplex*, *Contracaecum osculatum*, *Pseudoterranova decipiens* and *Diphyllobothrium* spp. The incidence of transmission of disease from fish to humans is dependant upon several factors including the type of the parasite, the susceptibility of the host and environmental factors.

All of the important Fishborne zoonotic parasites (FZPs) are helminths, the majority of which are trematode. There are strong linkages of FZPs to poverty, pollution and population growth. For example, in some areas, shortage of fuel in poor homes may permit only partial cooking of raw fish. Overcrowding in endemic areas lead to deterioration of the environment and increased pollution of surface waters with sewage, night-soil, and animal excreta. Development can also create increased risks; for example, dams create reservoirs highly favourable for snail vectors, as well as fish, which are the major transmitters of fishborne trematodes.

Trematodiasis; The liver flukes: The causative agents of human infections include *Clonorchis sinensis* Looss, 1907 (in East and Southeast Asia), *Opisthorchis viverrini* Stiles and Hassall, 1896 (in Southeast Asia), *O. felineus* Blanchard, 1895 (in Russia and Eastern Europe), and *Metorchis conjunctus* Looss, 1899 (in North America). A total of 17 million people around the world are estimated to be infected with these liver flukes (WHO, 1995).

Liver flukes have long been known to cause serious disease in certain areas of the world. Cholangitis, choledocholithiasis, pancreatitis and cholangiocarcinoma are the ma-

major clinical problems, associated with the long chronic pattern of these infections. Although the extent of the problem is difficult to assess due to the lack of comprehensive epidemiological studies, particularly in Southeast Asia, there is evidence that the greatest risk factor for humans, is the consumption of raw or improperly cooked or processed fish, that is increasing in some regions, facilitated partly by population migrations and partly by commercial provision of these products (WHO, 2004).

a- *Clonorchis sinensis*: the Chinese liver fluke, is the most important species of fish-borne zoonotic parasite in East Asia (Rim, 1990a; Hong, 2003). In 1947, the estimated number of infected people worldwide was about 19 million (Stoll, 1947), but more recently it has been estimated to be about 7-10 million (Crompton, 1999). In Japan, this parasite was formerly quite prevalent, but has been successfully controlled since the 1960s (Hong, 2003).

In China, clonorchiasis is distributed in a total of 24 provinces, municipalities and autonomous regions (Chen *et al*, 1994). Guangdong Province (including Hong Kong) and Guangxi Zhuang Autonomous Region, Heilongjiang, Jilin and Liaoning provinces are the areas with most reported infections (Yu *et al*, 2003). In a nationwide survey, the prevalence of *C. sinensis* was 0.4% among almost 1.5 million people examined (Xu *et al*, 1995). In Taiwan, clonorchiasis was formerly endemic in three areas, Mei-Nung in the south, Sun-Moon Lake in the center and Miao-Li in the north (Cross, 1984), but the current status is unknown. In Vietnam, clonorchiasis has been endemic mainly in the north, especially along the Red River Delta including Haiphong and Hanoi (Rim, 1982a). In southern parts of Vietnam, *C. sinensis* is not reported, although opisthorchiasis is reported to be endemic (De *et al*, 2003). Besides, Morsy and El Maridi (1978) in Jordan reported zoonotic *C. sinensis* among Palestinian refugees in Al-Baqaa Camp. In Saudi Arabia, Al Karawi *et al*.

(1993) reported clonorchiasis in 35 patients with acute gallstone pancreatitis and/or cholangitis whom underwent endoscopic sphincterotomy and considered its endemicity there. Morsy and Al-Mathal (2011) reported *C. sinensis* in Egypt.

b- *Opisthorchis viverrini*: is a particularly serious liver fluke (Rim, 1982b; Kaewkes, 2003) and is highly prevalent in Southeast Asia including Thailand, Laos, Cambodia and South Vietnam; about 9 million people are estimated to be infected globally (Yossepowitch *et al*, 2004). In Thailand, it is widespread in the north and northeastern regions. The number of infected people in the northeastern region alone was estimated in the 1960s to be over 3.5 million (Wykoff *et al*, 1965), and this figure seems to have changed little; the estimated number of infected people is currently about 6 million (Sripa *et al*, 2003). In Laos, the Mekong River basin is the most heavily infected area (Chai *et al*, 2005). In Vietnam, several southern provinces such as Phu Yen have reported infections, with prevalences above 10% (De *et al*, 2003).

c- *Opisthorchis felineus*: was first described from a naturally infected cat and subsequently from a man in 1892 (Beaver *et al*, 1984); it is now recognized as a natural parasite of dogs, cats, foxes, and pigs in eastern and southeastern Europe and the Asiatic parts of Russia and common also in southern, central, and eastern Europe, Turkey and Siberia west of the Ob River, including Tomsk and Tyumen. In 24 regions of the Ukraine, the number of human infections reported between 1952 and 1968 was 9340 (Rim, 1982b). The global incidence in 1947 for this parasite was estimated to be about 1.1 million (Stoll, 1947); the incidence appears to have not changed significantly and is now estimated to be about 1.6 million (Yossepowitch *et al*, 2004).

d- *Metorchis conjunctus*: the Canadian liver fluke, is a parasite of carnivorous mammals in Canada and USA (MacLean *et al*, 1996). Human infections with this fluke

have occurred in Canada since 1946 (Yamaguti, 1958), particularly in aboriginal populations from Quebec to Saskatchewan, and the eastern coast of Greenland (MacLean *et al*, 1996; Behr *et al*, 1998)

Disease and public health impact: The hepatic lesions and clinical manifestations in infected people are similar for all the liver fluke infections (Rim, 1982b). Bronchial asthma and allergic lesions are encountered in early stages, along with painful enlargement of the liver, congestion of the spleen, and local eosinophilia in the wall of bile ducts in chronic and severe infections. Bile stones may form around eggs and cause cholecystitis and colicky pain. Carcinoma of the bile duct or the pancreas, with metastases into the epigastric lymph nodes, is responsible for death of some patients.

The adult worms of *C. sinensis* and *O. viverrini* are found commonly in the intrahepatic bile duct, some in the gall bladder and along the biliary tract of infected humans. The main pathogenesis in the biliary tract is mechanical, chemical, and immunological irritation by the worms (Li *et al*, 2004). This results in obstruction of the bile duct and bile stasis, periductal inflammation, and cholangitis. Histopathologically, the enlargement of the bile duct, periductal fibrosis, adenomatous hyperplasia, and cystic degeneration are the most prominent features (Lee *et al*, 1978). In mild infections, the patient is usually asymptomatic. Heavy infections, however, can cause significant symptoms causing the patient to seek medication. Jaundice, indigestion, epigastric discomfort, anorexia, general malaise, diarrhea and mild fever are common clinical symptoms. Complications such as pyogenic cholangitis, biliary calculi, cholecystitis, liver cirrhosis, pancreatitis and cholangiocarcinoma, are often associated with infection (Sripa, 2003).

Among these, cholangio-carcinoma is the most serious. It arises from metaplastic changes of biliary epithelial cells and usually occurs in the secondary intrahepatic bile ducts, where the flukes are preferentially

situated. The contributing factors promoting carcinogenesis include ingestion of carcinogen co-carcinogens, and host endogenous influences such as malnutrition, immunological defects, and genetic factors (Watanapa and Watanapa, 2002).

The histopathological changes include adenomatous hyperplasia of the biliary epithelium, thickening of the bile duct wall, periductal inflammation with eosinophils and round cells and fibrosis in the portal areas. A large number of flukes can cause obstruction of the biliary tract. Based on 70 necropsy cases in Thailand, hepatomegaly was remarkable in most chronic and severe cases of opisthorchiasis, with marked dilatation and hypertrophy of the bile ducts (Sripa, 2003).

Inflammation of the bile duct and cell infiltrations may be secondary to superimposed bacterial infections; suppurative cholangitis is frequently the end result and the infection may extend into the liver parenchyma causing hepatitis. Adenomatous and fibrous hyperplasia, seen in the bile ducts, can also occur in the pancreatic duct. Moderate infection levels with less than 100 worms of *O. viverrini* are usually asymptomatic. However, infections with hundreds or thousands of worms can cause right upper quadrant pain, diarrhea, flatulence, fatigue, dyspepsia, pain over the liver, jaundice in some patients and a moderate elevation of the body temperature (Mairiang and Mairiang, 2003).

High incidences of cholangiocarcinoma, based on both necropsy and liver biopsy data, have been reported for *O. viverrini*. For instance, in Khon Kaen, northeastern Thailand, the incidence of cholangiocarcinoma is estimated to be 129 per 100,000 males and 89 per 100,000 for females, compared with one to two per 100,000 in western countries (Vatanasapt *et al*, 1990). Jaundice usually occurs in cases with heavy infections and especially when there is carcinomatous transformation with an increased biliary obstruction.

Patients with cholangiocarcinoma may present obstructive jaundice, fever, and acute complications such as cholangitis, acalculous cholecystitis and generalized bile peritonitis. Using hamsters as an experimental animal model, it was shown that chemical-carcinogens such as dimethylnitrosamine which is present in fermented fish including 'Pla ra' plays the role of an 'initiator', and *O. viverrini* acts as a 'promoter' for the development of cholangio-carcinoma (Thamavit *et al*, 1994).

Intestinal flukes; heterophyids: These minute intestinal flukes of the family Heterophyidae are parasites of birds and mammals. A large number of species have been reported from humans, among which *Metagonimus yokogawai* and *Heterophyes heterophyes* are generally considered the most important species (Yu and Mott, 1994). The importance of these flukes is being increasingly recognized through recent studies from the Philippines (Belizario *et al*, 2001), from Thailand on *Haplorchis taichui* (Waikagul, 1991; Sukontason *et al*, 2001) and from Korea on several species including *Heterophyes nocens* and *Metagonimus* spp. (Chai and Lee, 1991; 2002). Although generally not considered of significant clinical importance relative to the liver flukes, several heterophyid species, including *Stellantchasmus falcatus*, *Haplorchis* spp., and *Procerovum* spp., can cause significant pathology, often fatal, in the heart, brain, and spinal cord of humans (Africa *et al*, 1940). The exact mechanisms of pathogenesis responsible are not clear but may be related to invasion of the circulatory system by worm eggs. Disease is usually related to worm burdens, which in some cases can be very heavy (MacLean *et al*, 1999).

a- *Metagonimus yokogawai* (Katsurada, 1912): The genus *Metagonimus* is characterized by a laterally deviated ventral sucker and absence of ventrogenital apparatus or genital sucker. Four species, namely *M. yokogawai*, *M. takahashii*, *M. minutus*, and *M. miyatai*, have been reported from hu-

mans. Human infections were also recorded from Siberia, Europe, China, and Taiwan. In Japan, prevalence has decreased since the 1970 s, except in a few foci as areas surrounding the Hamana Lake (Ito *et al*, 1991). In Russia, *M. yokogawai* is endemic in the Amur and Ussuri valleys of Khabarovsk territory, where the prevalence in ethnic minority groups varies between 20-70% (Yu and Mott, 1994). Intestinal histopathology is characterized by villous atrophy and crypt hyperplasia, with variable degrees of inflammatory reactions (Chai, 1979). In light infections, fatigue and mild gastrointestinal troubles such as epigastric pain, diarrhea and anorexia are present; while in heavy infections, abdominal cramps, malabsorption and weight loss may occur.

Other *Metagonimus* spp. infecting man: *M. takahashii* Suzuki, 1930 was reported in Japan from mice and dogs fed with metacercariae encysted in fresh water fish other than sweetfish (Chai and Lee, 2002). *M. miyatai* was first found in Japan in 1941, but its taxonomic significance was later established to be a distinct species (Saito *et al*, 1997).

b- *Heterophyes heterophyes* (v. Siebold, 1852) Stiles and Hassal, 1990. It was first found by Bilharz in 1852 in the intestine of a child in Egypt. This species is seen in Nile Delta, Middle East and Turkey. It is parasitic in humans and fish-eating birds and animals. It is characterized by having 70-80 digitate spines on the genital sucker. First intermediate host is the brackish water snail *Pirenella conica* and the second is *Mugil and Tilapia* fishes. Khalil Bey (1924, 1933) was the first Egyptian scientist who discovered *Heterophyes Heterophyes* life history in Egypt. The infection was common in northern parts of the Nile Delta especially in lakes as Idku, Maryut and Manzala (Youssef *et al.*, 1987). Kuntz and Chandler (1956) found that in the Nile Delta *H. heterophyes* infected man, dogs, cats, rodents and birds. Then after, many authors dealt with *H. heterophyes* and heterophyiasis. Nagaty and Khalil (1961) and Khalil *et al.* (1964) used Yomesan in

treating heterophyiasis. Sheir and Aboul-Enein (1970) used Niclosamide in treating heterophyiasis. Paperna *et al.* (1978) reported microsporidian infection in the cyst wall of *Heterophyes* metacercariae encysted in fish. Rifaat *et al.* (1980) in villages on the lakes of Borollos and Manzalla reported a rate of 2.4% heterophyiasis. The mean prevalence of heterophyid infections in the villages of Khuzestan, southwest Iran, was found to be 8% (2-24% in range). In post-mortem examination of carnivores in the same areas, 14.2% of jackals, 33.3% of foxes, and 2.5% of dogs were infected with *H. heterophyes* and *M. yokogawai* (Massoud *et al.*, 1981). Human infections were also reported in Japan (Kagei *et al.*, 1980) and the Republic of Korea (Chai *et al.*, 1986; Chai and Lee, 2002).

c- *Heterophyes nocens* Onji and Nishio, 1916 was first reported in Japan from experimental dogs and cats fed with metacercariae from the mullet *M. cephalus*, and it is now known to occur elsewhere in the Far East. This species is distinguished from *H. heterophyes* by the smaller number (50-62) of spines on the gonotyl. The snail and fish hosts are brackish water species (Chai and Lee, 2002). In April 1990, a highly endemic focus was discovered on a southwestern coastal island, where 42 (43%) of 98 residents examined were infected (Chai *et al.*, 1994a). Another endemic area with a prevalence of 75% was later found in a western coastal village (Chai *et al.*, 1997). Several other coastal areas and many islands have been added to the list of endemic areas (Chai *et al.*, 2004). In Japan, human *H. nocens* infections were reported from Kochi, Chiba, Yamaguchi, Chugoku and Hiroshima Prefectures. Recently, two lakeside villages of Mikkabi-cho, at the north end of Hamana Lake, Shizuoka Prefecture, were found to have prevalences of 7.5 and 10.5% (Kino *et al.*, 2002a; b).

d- *Haplorchis* spp.: The genus *Haplorchis* is characterized by the presence of only one testis and a ventro-genital-sucker complex

armed with gonotyl and chitinous spines (Yamaguti, 1958). Five species, namely *Haplorchis taichui*, *H. pumilio*, *H. yokogawai*, *H. pleurolophocerca*, and *H. vanissimus*, are responsible for human infections (Yu and Mott, 1994); the first three are the most important. *H. taichui* Chen, 1936 was first described from birds and mammals from central Taiwan (Faust and Nishigori, 1926). Human infections are now commonly found throughout Asia (Velasquez, 1982). *H. pumilio* (Looss, 1986) was originally described from birds and mammals in Egypt; it is also now known to be distributed in Asia (Yu and Mott, 1994). *H. yokogawai* (Katsuta, 1932) was described from dogs and cats fed with metacercariae from mullet in Taiwan; human infections have now been reported from many Asian countries, Australia, and Egypt (Velasquez, 1982). Haplorchid infections are known to be asymptomatic or of very mild intestinal manifestations.

The intestinal flukes-echinostomes: Trematodes of family Echinostomatidae (Poche, 1926) are intestinal parasites of birds and mammals. At least 30 genera and more than 200 species are known; about 15 species infect humans (Yamashita, 1964 and Huffman and Fried, 1990). There are 11 reported fish-borne echinostome species of which *Echinostoma hortense* and *Echinochasmus japonicus* are the most important (Yu and Mott, 1994 and Chai and Lee, 2002). Most human echinostome infections have been reported from Asia and the Western Pacific, but infections probably occur also in Africa (Yu and Mott, 1994). The disease is generally mild, but ulcerations and bleeding in the stomach or duodenum may occur, as in *E. hortense* infection (Chai *et al.*, 1994b).

a- *Echinostoma hortense* (Asada, 1926): The genus *Echinostoma* Rudolphi, 1809 is characterized by an elongated body and presence of a head collar with dorsally uninterrupted crown of spines. More than 95 species are known (Yamaguti, 1958), and seven species infect humans (Yamashita, 1964; Yu and Mott, 1994). *E. hortense* has

27 or 28 collar spines around the oral sucker, and two tandem slightly lobulated testes. It was first described from synanthropic rats in Japan, and then from humans and rodents in the Republic of Korea (Chai and Lee, 2002) and China (Yu and Mott, 1994). An infection rate of 22.4% has been reported among residents of Cheongsong-gun, Republic of Korea (Chai and Lee, 2002). In a survey in Liaoning province, northeast China, 6 out of 10 hospitalized patients with hepatitis who had eaten raw loach were found to be infected, and 69.7% of loach, *Misgurnus anguillicaudatus*, examined from a local market were infected (Yu and Mott, 1994).

In experimental rats, infection produces villous atrophy, crypt hyperplasia, inflammation of the stroma, and decreased villus/crypt ratios (Chai and Lee, 2002). Mucosal damage is generally more severe than in heterophyid infections. Abdominal pain, diarrhea, and fatigue are the major symptoms. Chai *et al.* (1994b) reported that a patient with *E. hortense* infection suffered from severe ulcerative lesions and bleeding in the duodenum.

b- *Echinochasmus japonicus* (Tanabe, 1926): The genus *Echinochasmus* Dietz, 1909 is characterized by a plump, sometimes elongated, body and the presence of a head collar with a dorsally interrupted crown of spines (Yamaguti, 1958). Among the 40 species known, only four species have been found infecting humans; *Ech. japonicus*, *Ech. perfoliatus*, *Ech. liliputanus* and *Ech. fujianensis* (Yu and Mott, 1994). *Ech. japonicus* was first reported in Japan from experimental animals fed metacercariae from freshwater fish; it is now known to be distributed widely in the Far East, particularly in humans in the Republic of Korea (Chai and Lee, 2002) and Anhui, Fujian, Guangdong, Guangxi, and Jiangsu provinces of China (Lin *et al.*, 1985). In six counties of Fujian and Guangdong provinces, China, the infection rate among residents was 4.9% (178/3639) (Yu and Mott, 1994).

c- *Nanophyetus salmincola*, Chapin, 1927: It belongs to the Nanophyetidae Dollfus, 1939, and infects various mammals including humans, the dog, cat, raccoon, and fox, and three species of birds on the Pacific coast of North America and Canada, and Eastern Siberia. It is minute, pyriform, and possesses two large testes in the posterior half of the body. Its snail host is *Oxytrema silicula* and the second hosts are salmonid (trout, salmon) and non-salmonid fish (Millemann and Knapp, 1970). Nanophyetiasis is endemic in the far-eastern part of Russia including Amur and Ussuri valleys of Khabarovsk territory and north Sakhalin (Yu and Mott, 1994). In local ethnic minorities, the prevalence is 20%, and reaches up to 60% in some localities. In the USA, 20 human cases have been reported since 1974 (Eastburn *et al.*, 1987). Infected people may experience mild diarrhea, abdominal discomfort, and eosinophilia.

Cestodiasis: Diphyllbothriasis: This is the most important fish-borne zoonosis caused by a cestode parasite. Species of the genus *Diphyllbothrium* (Order Pseudophyllidae, Family Diphyllbothriidae) are responsible for most reported cestode infections in humans. The zoonosis occurs most commonly in countries where it is a frequent practice to consume raw or marinated fish. At least 13 of about 50 species of *Diphyllbothrium* have been reported from humans. All are gastrointestinal parasites as adults in a variety of piscivorous birds and mammals. Diphyllbothriasis is considered a mild illness and is not normally reportable; the understanding of the global distribution of this parasite infection is somewhat fragmentary and based on limited human and fish surveys or clinical case reports. Sturchler (1988) estimated that there were about 9 million human infections in the 1970s, but the accuracy of this figure currently is doubtful, and may even be an underestimate. Although *Diphyllbothrium* is generally associated with cold water intermediate and definitive hosts, there are sporadic case reports from

warm localities including the Middle East and Malaysia (Abo-Shehada and Ziyadeh, 1991; Rohela *et al*, 2002), although the sources are not clear; confusion with sparganum infections makes reports from such areas somewhat problematical.

Globally, the incidence of human infections has declined in recent years, particularly in North America (Kingston and Kilbourn, 1989; Dick *et al*, 2001) and Europe (Dupouy-Camet and Peduzzi, 2004). Until 1982, diphyllbothriasis was a reportable disease in the USA and CDC estimated that about 125–200 cases occurred during the period 1977–1981 (Ruttenber *et al*, 1984). CDC estimates only several dozen cases occurring annually in the USA (Deardorff, 1991). During 1981, CDC reported that 52 people residing in the west coast states of the USA became infected with *Diphyllbothrium*, apparently from fresh salmon shipped from Alaska. Surprisingly, 1% of school children in Baton Rouge, Louisiana carried *D. Latum* according to a survey (Christian and Perret, 1974). A recent discovery reported in France revealed that a patient became infected with *D. nihonkaiense* from a salmon (*Oncorhynchus*) imported from the Pacific Coast of Canada (Chai *et al*, 2005).

Most reported human infections in South America occur in Chile, Peru and Argentina (Von Bonsdorff, 1977). The first case in Chile was reported by Neghme *et al*. (1950). The prevalence of diphyllbothriids in some Chilean lake districts ranges from 0.1 to 2.8% (Torres *et al*, 2004). The presence of the marine species *D. pacificum* in humans in Peru has been estimated to be about 1.6% (Miranda *et al*, 1967), which is in line with recent findings from the analysis of ancient coprolites of the Chiribaya Culture populations (700–1476AD) in southern Peru (Holiday *et al*, 2003), suggesting that this zoonotic species has persisted in the region for a very long time.

Analysis of 20 years of diphyllbothriasis survey in Europe indicated that while this

zoonosis has declined overall, especially in the former ‘hotspot’ Scandinavian countries, it persists in several regions (Dupouy-Camet and Peduzzi, 2004). Currently Switzerland, Sweden, Finland and Estonia reported more than 10 cases per year, while Lithuania, Poland, Hungary, Italy and France average 2–10 cases annually. Only sporadic cases occur in Norway, Austria, and Spain. Most of the cases in Switzerland, France and Italy occur in the Alpine Lakes region. In Finland, the national prevalence has declined since 1981 when it was 1–4% (Raisanen and Puska, 1984). Diphyllbothriasis is a common infection in Far-East Russia, where *D. klebanovskii* is considered the important zoonotic species (Muratov and Posokhov, 1988; Lloyd, 1998 and Muratov, 1990). The parasite is widespread in all the major river drainages east of the Urals, including those of the Lena, Kolyma and Indigirka rivers (Suvorina and Simonova, 1993).

The Amur River region is also an endemic area (Khodakova *et al*, 1996), as are the coastal area of the Okhotsk Sea where human prevalences range from 1.0 to 3.3%. A major new focus has apparently developed during the 10 years since the completion of the Krasnoyarsk Reservoir on the Enisei River; one survey revealed a prevalence of 7.7% in people living along the reservoirs here (Ko, 1995). Diphyllbothriasis was frequently reported in Japan, especially along the coast of the Sea of Japan, averaging about 100 cases per year since the 1970s (Oshima, 1984). Until recently, most infections were considered due to *D. latum*. However, recent taxonomic studies strongly suggest that the majority of infections are due to *D. nihonkaiense* (Yamane *et al*, 1989). Infections by other species also cannot be ruled out, such as *D. yonagoensis* are known in the region (Yamane *et al*, 1981; Kamo *et al*, 1988).

As an example, in 1996 a large outbreak in Shizuoka Prefecture was discovered to be caused by another diphyllbothriid, *Diplogonoporus grandis*. Since 1894 there have

been more than 100 cases caused by this species in Japan (Kino *et al*, 2002a; b). Until recently, diphyllbothriasis has not been considered common in the Republic of Korea. Between 1921 and 2001, only 28 cases were reported and the results of a national prevalence survey for parasites revealed a prevalence of only 0.004%. However, the growing demand for fresh salmon, and the strong cultural fondness for raw fish may alter the status of this zoonosis in the future (Lee *et al*, 2001). As with Japan, the systematics of diphyllbothriids recovered in Korea are uncertain because most cases are attributed to *D. latum*, although the fish sources (salmonids) are not typical for this species. Because of their generally broad host specificities, *Diphyllbothrium* life cycles are maintained primarily in nature independent of humans, and therefore the cestode is not affected much by elimination from the human population (Torres *et al*, 2004). The host preferences of the various marine or freshwater diphyllbothriid species may be relatively specific for either piscivorous birds or a specific spectrum of mammals such as bears, cetaceans, pinnipeds or humans, and this can be very important in transmission and dissemination (Dupouy-Camet and Peduzzi, 2004). Other risk factors associated with infection are occupation, age and gender (Sagua *et al*, 2000). Although infection rates are usually highest in adults, especially males, there are reports of high rates in children (Khodakova *et al*, 1996).

An increasingly important factor in introducing or sustaining the zoonosis in human communities is the contamination of the local aquatic environment with faeces (Cross, 2001). The discharge of improperly treated sewage from lake-side dwellings, hotels and ships is an important source of contamination with eggs. Domestic animals, especially dogs, are another important source of environmental contamination and may help to maintain a natural *D. latum* cycle, which can be amplified by human activities (Dick *et al*,

2001). Despite its apparent global decline, diphyllbothriasis appears to have increased in some countries (Torres *et al*, 2004). The reasons for its persistence or re-emergence are not always clear. Zoonoses such as that caused by *Diphyllbothrium* spp. exist within a continuum that links animal and human populations, and this equilibrium may be disturbed by activities such as the intensification of fish production, environmental alterations, translocation of human and animal populations, tourism, changes in fish marketing (export and distribution) systems, and cultural changes in eating habits (Dazak *et al*, 2000; Murrell, 2002).

Certain projections indicate that the future worldwide demand for fish and fish-products will increase substantially (FAO, 1992), creating increasing pressure to exploit the marine environment for food (Deardorff, 1991). The growing awareness of the nutritional benefits of fish and fish products, the preferences in many countries for raw or lightly cooked foods, and the rising affluence in both developing and developed countries make this a reasonable prediction. This increased demand may increase the risk of diphyllbothriids entering the human food chain by increasing the harvesting and export of fish from areas of high endemicity. Higher risks for urban populations may also arise because of the incentive for exporters to ship fresh (non-frozen) fish by air to gain a competitive edge in the market (Deardorff and Overstreet, 1990; Kaferstein, 1994; Nawa *et al*, 2001). The global market in fish exports is quite large. For example, Europe and Canada, both endemic for diphyllbothriids, supply about one-third of the USA demand for seafood. In Korea, the demand for salmonids has increased with rising per capita incomes, and this has stimulated increased production of farmed salmonids. This increase in production concerns public health workers because of its link to the risk of diphyllbothriasis, which has occurred more frequently in the country in recent years (Lee *et al*, 2001).

It should be emphasized here, however, that there is little to implicate farm-raised salmonids in transmission of diphyllbothriids to humans; wild salmonids are at highest risk of becoming infected with diphyllbothriids and represent a major reservoir of infection. Freshwater non-salmonids are also important in certain regions, especially for infection of *D. latum*. Even among salmonid hosts not all species play a similar role. For example, *Oncorhynchus nerka* that spends extended periods in freshwater lacustrine systems prior to descending to the ocean, may be more important than other species of Pacific salmon in transmitting *Diphyllbothrium ursi* because of its greater vulnerability to human and animal fishing.

Seemingly unrelated environmental changes may also have unexpected effects on the epidemiology of this zoonosis. It has been suggested that the increase in infections by *D. pacificum* during the 1975-2000 period in Northern Chile was related to the cyclic appearance of El Niño phenomena in the Eastern Pacific, which not only affect fish populations but also that of the primary definitive host, the sea lion (Sagua *et al*, 2000). Another example is the increased risk of diphyllbothriid infection of fish because of growing marine mammal populations in the Northwest Pacific, a result of the 1972 Marine Mammal protection Act (Deardorff, 1991).

Effects of climate changes like these reflect the complexity of the aquatic food webs and the unpredictability of responses by biological systems. The stocking of imported fish in new aquatic habitats may be a significant risk for spreading diphyllbothriids, by providing potential intermediate hosts in the event of egg contamination. The appearance of *D. latum* in Argentina and Chile has been attributed to the introduction of rainbow trout (*Oncorhynchus mykiss*) and brown trout (*Salmo trutta*) in the early 20th century from North America.

Later these fish became infected by immigrants and tourists who, through poor sanitary practices, contaminated the aquatic en-

vironment with eggs. This led eventually to substantial areas becoming endemic for diphyllbothriasis (Torres *et al.*, 2004). However, the identity of the *Diphyllbothrium* reported from salmonid fish in Chile has been questioned because elsewhere *D. latum* fish intermediate hosts are typically non-salmonids (e.g. pike, perch) and it has been suggested that the *Diphyllbothrium* infecting trout and humans in Chile may be another species, which is endemic to the region, such as *D. dendriticum* (Dick *et al*, 2001).

They concluded that based on existing data and the results from their own experimental and field work, the life cycle of *D. latum* became well established in Canadian wilderness lakes without the participation of humans, and that distribution has changed little during the past 100 years, giving an evidence that favors a pre-European introduction in North America. They suggested, however, that phylogenetic analysis of the genotypes of *D. latum* from Alaska, Siberia and Europe may be the best means for settling the issue.

There is general agreement among experts in this field that the overriding obstacle to clarifying the distribution, host-associations, and epidemiology of diphyllbothriids, especially *D. latum*, is the poor state of the systematics of the genus (Holiday *et al*, 2003). The great difficulty in differentiating morphologically the plerocercoids and the adult strobila or proglottids of the various species, has produced confusion among researchers about the specific host ranges of the species, and therefore hindered the understanding of the epidemiology of the zoonoses in North and South America, Far-East Asia and Eurasia (Torres *et al*, 2004). Misunderstandings of the host associations for the freshwater species, *D. latum* and *D. dendriticum* have caused misinterpretations of their epidemiology in specific locales. Research carried out in recent years has convincingly demonstrated that the fish intermediate hosts for *D. latum* are primarily nonsalmonid fish such as pike and perches,

while *D. dendriticum* utilizes salmonid and coregonid species. The sites of pleuroceroid infection within the fish also differ between the two species (Andersen and Gibson, 1989; Dick *et al.*, 2001).

Confusion over *D. latum* in Japan was resolved when careful study of the diphylobothriids from man was identified as a new species, *D. nihonkaiense*, from salmon (*Oncorhynchus gorbusha* and *Oncorhynchus masu*) and the species *D. yonagoensis* from marine fish (Yamane *et al.*, 1986; Kamo *et al.*, 1988). In Siberia in the 1980s, it was also discovered that diphylobothriasis transmitted from salmonid fish (*O. gorbusha* and *O. keta*) was not, as long believed, *D. latum* but a new species, *D. klebanovskii* (Muratov and Posokhov, 1988). The discovery of *D. nihonkaiense* in salmon (*O. keta*) from the Canadian Pacific Coast (Gulf of Alaska) is a good example of why the current taxonomy and mapped distributions of the diphylobothriids are questionable, since this species may have long been present in this region—just undetected because of confusion with other *Diphylobothrium* species.

Nematodiasis: a- Anisakiasis: Anisakiasis refers to infection of people with larval stages of nematodes belonging to the families Anisakidae or Raphidascarididae. Although human infection have been reported with worms from a number of species within these families (Bouree *et al.*, 1995), the two genera most often associated with anisakiasis are *Anisakis* and *Pseudoterranova*. Anisakiasis occurs when people ingest third stage larvae found in the viscera or muscle of a wide range of fish and cephalopod mollusc species. Humans are accidental hosts in the life cycle, and the parasites almost never develop further within the human gastrointestinal tract. Nevertheless, anisakiasis is a serious zoonotic disease, and there has been a dramatic increase in its reported prevalence throughout the world in the last two decades.

Life cycle and distribution: The higher-level taxonomy of the superfamily Ascaridoidia is uncertain (Fagerholm, 1991; Anderson, 1992), but molecular studies using mitochondrial DNA (mtDNA) and nuclear ribosomal DNA (rDNA) sequences provide provisional support for a monophyletic origin of the family Anisakidae, which includes genera *Anisakis* and *Pseudoterranova* (Nadler and Hudspeth, 2000). Anisakids typically utilise marine mammals or piscivorous birds as definitive hosts, with aquatic invertebrates and fish as intermediate or paratenic hosts. Adults of *Anisakis spp.* are found mainly in the gastrointestinal tract of cetaceans (dolphins, porpoises and whales), and adults of *Pseudoterranova spp.* in pinnipeds (seals, sea lions and walrus), although the definitive host range of most species is still incompletely known (Anderson, 1992). Eggs are shed in the faeces and embryonate and hatch in the ocean, releasing free swimming, and apparently third stage larvae (Køie *et al.*, 1995). The larvae are ingested by crustaceans, such as decapods, copepods or amphipods, where they grow within the haemocoel. Fish and cephalopod molluscs become infected by eating crustaceans containing third stage larvae, which penetrate the intestine and invade the tissues of the paratenic host, where they may continue to grow or become encapsulated (Anderson, 1992). Definitive hosts are usually infected by eating fish or cephalopods containing the larvae. As people usually become infected with anisakids by eating larvae contained within the paratenic host, the distribution of larval nematodes within the tissues of the host is epidemiologically important. This distribution appears to be very variable, and may be affected by the species of parasite (Anderson, 1992), the fish species infected and the environmental conditions to which the fish are subjected after capture (Roepstorff *et al.*, 1993).

Some studies have found that larval nematodes migrate from the visceral organs to the muscle after the death of the paratenic host,

and that migration may be enhanced by the cold storage or processing of ungutted fish. Others, however, have not been able to demonstrate post-mortem migration of larvae in the paratenic host (Cattan and Carvalho, 1984; Roepstorff *et al*, 1993). At least three species have been described within the *A. simplex*: *A. simplex* (sensu stricto), found in the northern Atlantic, *A. simplex complex* found in the northern Pacific and southern waters and *Anisakis pegreffii*, found in the Mediterranean Sea (Mattiucci *et al*, 1997). Paggi *et al*. (1991) also described three species within the *Pseudoterranova* complex: *P. decipiens* A in the north east Atlantic and Norwegian Sea, *P. decipiens* C in the north west Atlantic and Barents Sea, and *P. decipiens* B throughout northern waters. Further genetic studies are required to confirm the geographical and host ranges of these species, and to establish their relationships with other species of *Anisakis* and *Pseudoterranova*, which have been described on morphological criteria. A very large number of fish species act as paratenic hosts for species of *Anisakis* and *Pseudoterranova*.

Pathology and epidemiology: Clinically, human anisakiasis can take a number of forms, depending on the location and histopathological lesions caused by the larvae. Larvae may remain in the gastrointestinal tract, without penetrating the tissues, causing an asymptomatic infection, which may only be discovered when the worms are expelled by coughing, vomiting or defecating (Acha and Szyfres, 1987). In invasive anisakiasis, larvae penetrate the gastric or intestinal mucosa, or more rarely other sites such as the throat (Amin *et al*, 2000). There is some evidence that gastric invasion is more often associated with infections by *Pseudoterranova* spp. and intestinal invasion with infections by *Anisakis* spp. (Oshima, 1987). Symptoms of gastric anisakiasis usually appear 1-7 hr after consumption of fish, while intestinal anisakiasis usually manifests 5-7 days after fish consumption. In both cases, there is severe pain, with nausea and vomit-

ing (Acha and Szyfres, 1987; Oshima, 1987).

A. simplex can cause different diseases in humans. Acute anisakidosis is probably caused by an inflammatory and/or allergic response in the digestive tract mucosa with abdominal pain. It can also induce IgE mediated reactions with several clinical manifestations ranging from urticaria and angioedema to anaphylaxis. Chronic anisakidosis results from abscesses or eosinophilic granulomas caused by parasite invasion (Alonso *et al*, 1997; Audicana *et al*, 2002; Farahnak *et al*, 2002). Anisakiasis occurs through the world, with foci in north Asia and western Europe. Over 90% of about 20,000 cases of anisakiasis were reported from Japan (where approximately 2000 cases are diagnosed annually), with most of the rest from the Netherlands, Germany, France and Spain (Feldmeier *et al*, 1993). As diagnostic methods improve, however, more cases are being reported from other areas of the world, including the USA (Amin *et al.*, 2000), Canada (Couture *et al*, 2003), Chile (Mercado *et al*, 2001), New Zealand (Paltridge *et al*, 1984) and Egypt (Cocheton *et al*, 1991).

In the last 30 years, there has been a marked increase in the prevalence of anisakiasis worldwide. This is probably due to a number of factors. First, the increase in reported cases coincides with new diagnostic techniques, particularly endoscopy; prior to the development of the gastrofiberscope many cases of gastric anisakiasis were probably misdiagnosed (Oshima, 1987). Second, the increasing global demand for seafood and a growing preference for raw or lightly cooked food, especially in many western countries, increase the risk of parasite exposure. Third, there has been speculation that greater regulatory controls over the exploitation of marine mammals has led to increasing population sizes of potential definitive hosts (McCarthy and Moore, 2000), although it should be recognised that the relationship between definitive host population size and parasite population size is not

straightforward for parasites such as anisakid nematodes, which have a complex, multi-host life cycle.

b- Capillariasis: Capillariasis is a zoonotic parasite caused by two different species: *C. hepatica* and *C. philippinensis*. *C. hepatica* is transferred through the fecal matter of infected animals and can lead to hepatitis. *C. philippinensis* is transferred through ingesting infected small freshwater fish and can lead to diarrhea and emaciation. According to Cross (1992), 1884 confirmed cases of the disease caused by this nematode were documented in human beings from 1967 to the end of 1990; 110 cases were fatal. Moravec (2001) redescribed and evaluated the systematic status of *C. philippinensis*.

Typically, unembryonated eggs are passed in the human stool and become embryonated in the external environment; after ingestion by freshwater fish, larvae hatch, penetrate the intestine, and migrate to the tissues. Ingestion of raw or undercooked fish results in infection of the human host. The adults of *C. philippinensis* (males: 2.3 to 3.2 mm; females: 2.5 to 4.3 mm) reside in the human small intestine, where they burrow in the mucosa. The females deposit unembryonated eggs. Some of these become embryonated in the intestine, and release larvae that can cause autoinfection. This leads to hyperinfection (a massive number of adult worms).

C. philippinensis is currently considered a parasite of fish eating birds, which seem to be the natural definitive host (http://www.cdc.gov/parasites/capillaria/biology_c_philippinensis.html). This highly pathogenic parasite, that causes serious illness in human beings, is known to be distributed in eastern, southern, and southeastern Asia and northern Africa (Philippines, Thailand, Japan, Korea, Taiwan, India, Iran, Egypt) (e.g., Chitwood *et al.*, 1968; Pradatsundarasar *et al.*, 1973; Mukai *et al.*, 1983; Hoghooghi-Rad *et al.*, 1987; Chen *et al.*, 1989; Youssef *et al.*, 1989; Lee *et al.*, 1993; Kang *et al.*, 1994; Khalifa *et al.*, 2000). More than 2,000 cases of intestinal capillariasis have been reported

in the Philippines and Thailand, and sporadic cases have been reported in Korea, Japan, Taiwan, India, Iran, Italy, the United Arab Emirates, Spain, and the United Kingdom (Cross, 1998; Austin *et al.*, 1999).

In Egypt, the first case of intestinal capillariasis was reported by Youssef *et al.* (1989) in a 41-year-old female from Cairo, the second case was a 38-year-old female living in Lower Egypt reported by Mansour *et al.* (1990). Many subsequent cases have been reported from different parts of Egypt, including Cairo (El-Dib *et al.*, 1992; Ahmed *et al.*, 1999) and the Menouf area (Austin *et al.*, 1999; Anis *et al.*, 1998). In Upper Egypt, the first reported case was a female patient in the Assiut Governorate (Khalifa *et al.*, 2000) and the second case was two sisters from the El Menia Governorate (El-Karakasy *et al.*, 2004). Attia *et al.* (2012) presented an overview of human infections with *Capillaria philippinensis* and a new emerging parasite in Upper Egypt.

Pathology and epidemiology: Intestinal capillariasis is a life-threatening disease in humans which causes severe enteropathy (Cross, 1998). Worms can be found in the lumen, the mucosa, or in the crypts of Lieberkuhn in the human jejunum. The most common pathological features are the thickening of the intestinal wall, the prominence of the vessels, the atrophy of the crypts, and the flattening of the villi (Sangcha *et al.*, 2007). The infestation of the small bowel by this parasite results in the severe derangement of intestinal functions, which leads to weight loss, chronic (continuous or intermittent) diarrhea, abdominal pain, borborygmi, muscle wasting, cachexia, weakness, and edema (Lu *et al.*, 2006; Saichua *et al.*, 2008).

Diagnosis of fish zoonotic parasites: Diagnosis of liver fluke infections can be made by the recovery of eggs from feces by cellophane thick smear (Chai *et al.*, 1982) or Kato-Katz techniques (Hong *et al.*, 2003). However, the eggs must be differentiated from those of heterophyids and from various other opisthorchiid species, a task which re-

quires considerable training and experience, and even then the lack of specific diagnostic tools such as molecular probes presents a challenge (Lee *et al*, 1984; Ditrich *et al*, 1992). Serological tests such as ELISA using excretory-secretory antigens are helpful in some cases (Choi *et al*, 2003). There is interest in developing specific molecular or immunological methods to aid this task, but such methods have not yet appeared or gained acceptance (Wongratanacheewin *et al*, 2003). However, progress in this area is encouraging, for example, a PCR-based technique to detect snail and fish infections with *O. viverrini*, often a difficult task, has been reported (Maleewong *et al*, 2003). There are a number of gene sequences now published in GenBank, which should spur development of needed diagnostic tools.

Intestinal flukes: The diagnosis is made by recovery of eggs in fecal examinations. Very important issue related to heterophyids is the difficulty of differentiating the eggs from those of the liver flukes in human fecal examinations, which may cause inaccurate estimates of the prevalences of both trematodes groups (Chai and Lee, 2002). New diagnostic techniques including PCR are needed to improve specific diagnosis of these flukes.

Diphyllobothriasis: Human infection can be easily identified by finding characteristic eggs or proglottids in feces. When species needs to be determined, restriction fragment length polymorphisms PCR can be effectively used (Schotz *et al*, 2009). Although the identification of plerocercoids from fish by morphological criteria is very difficult (Margolis and Arthur, 1979), progress in overcoming this obstacle has been made, particularly for the freshwater species (Dick and Poole, 1985; Yamane *et al*, 1986; Andersen *et al*, 1987; Andersen and Gibson, 1989). However, identifications based on morphological characters for marine species remain troublesome. Molecular approaches that have proved so powerful in resolving other parasite taxonomic problems have only

recently been applied to the diphylobothriids. Molecular investigations have shown that the morphological variation seen within *D. dendriticum* populations has a genetic basis (De Vos *et al*, 1990). Ribosomal genes have been identified that can differentiate between the two most important freshwater species, *D. latum* and *D. dendriticum* (De Vos and Dick, 1989). Molecular markers for differentiating *D. latum* and *D. nihonkaiense* have also been reported (Matsuura *et al*, 1992). Further efforts towards developing molecular tools for diagnostic use and for phylogenetic analysis should be strongly encouraged if many of the issues associated with this zoonosis, such as the origins and distributions of *D. latum* are to be resolved.

Anaskiasis: Endoscopic examination can often be used to provide a definitive diagnosis for gastric anisakiasis, but clinical diagnosis of intestinal anisakiasis is difficult and requires careful examination of clinical symptoms and patient history. From clinical symptoms, gastric anisakiasis is often misdiagnosed as a peptic ulcer, and intestinal anisakiasis as appendicitis or peritonitis (Acha and Szyfres, 1987; Oshima, 1987). Although immunological diagnosis of anisakid infection shows potential, it is complicated by antigenic cross-reactivity with other ascarids (Iglesias *et al*, 1996).

Capillariasis: Diagnosis of human infection depends mainly on stool examination for finding characteristic eggs, larvae or adults in feces (Khalifa *et al*, 2000) or detection of coproantigen by ELISA (El-Dib *et al*, 2004), immunodiagnosis (Intapan *et al*, 2010) or intestinal aspiration or biopsy (Lu *et al*, 2006).

Control and prevention: Strategies for prevention and control approaches are similar for all the liver flukes. The traditional human habit of eating raw or improperly cooked freshwater fish is a major reason for sustaining the zoonosis in endemic areas and a seemingly intractable obstacle to control; health education efforts aimed at changing such habits have not been very successful

(Guoqing *et al*, 2001; WHO, 2004). Currently, the major strategies for community prevention and control include fecal examination and treatment of individual cases with praziquantel (25 mg/kg, three times daily, for 2–3 days), health education to instill the need to consume only cooked fish, and environmental sanitation through the building and use of latrines in endemic areas. More recently, WHO (2004) has recommended mass chemotherapy of people at risk in endemic areas as the most practical and immediately effective control strategy. Mass chemotherapy with praziquantel (40 mg/kg in a single dose) is highly efficient and generally feasible to distribute (Lee, 1984).

Until more such control programs are implemented, however, and followed over time, the long-term effectiveness of this approach maybe problematic. Efforts to interrupt transmission at the intermediate host level apparently have not been extensive to date, judging by published reports. Several projects have been conducted on pond fish production in China, utilizing snail control and drug treatment of infected members of the household, along with intensive health education of the community on the risks of eating raw fish.

The effect on transmission over 2 years was mixed, however, with a decline in prevalence in people, but only a modest impact on snail populations, on the use of human feces as pond fertilizer and on the habit of eating raw fish (Guoqing *et al*, 2001). In Thailand, a FAO led HAACP approach to fish pond management was carried out that focused on water supply, fish fry, fish feed and pond conditions to eliminate contamination of the ponds with *O.viverrini* eggs and snail infections.

A preliminary report indicated some success with this intensive effort, but a full assessment of its sustainability over a period of years is needed (Khamboonraung *et al*, 1997). Irradiation of fish to control infectivity of metacercariae was tried for *C. sinensis* (Lee *et al*, 1989) and *O. viverrini* (Sornmani

et al, 1993); however, feasibility of the method economically, and consumer acceptance appear to be obstacles to the use of this prevention method. Strategies such as use of chemotherapy to reduce morbidity, interrupting transmission, and reducing risky human behavior (WHO, 2004) are reasonable and logical. However, because of local constraints, deeply embedded cultural traits, and inadequate national priorities, it is problematic whether this strategy will be implemented sufficiently to have significant public health impact any time soon. Compounding this difficulty is a number of gaps in knowledge and technology that should be addressed to facilitate implementation of any control efforts: i- Improved diagnostic tools are badly needed, especially those that can differentiate various species; ii- Guidelines for designing and implementing epidemiological studies are needed in order to obtain the impact data required by public health agencies in setting priorities; iii- The role of reservoir hosts in maintaining transmission in the absence of infected humans needs investigation in order to design sustainable control strategies; iv- Social/anthropological studies are needed to better understand the cultural and behavioral traits of people with regard to food choices in order to develop education strategies aimed at influencing risky behavior; v-Development of improved aquaculture systems that can prevent or mitigate the transmission of trematodes and vi- Long-term pilot control projects are needed to compare efforts targeted at multiple high risk factors identified in risk assessment studies with the current mass chemotherapy strategy.

Control measures include treatment of infected people, environmental sanitation, and health education. The drug of choice is praziquantel; the efficacy of a single oral dose of 10-20 mg/kg is satisfactory. Irradiation of the sweetfish by 200 Gy is highly effective in controlling infectivity of metacercariae (Chai *et al*, 1995). The infection can be prevented by the avoidance of eating uncooked

fresh water fish. The risk of anisakid larvae in these dishes may be enhanced if the fish are eaten whole (because worms are often found in the viscera rather than the flesh of fish) or if the fish have been kept whole for some time after capture, rather than gutted immediately (because worms may migrate from the viscera to the flesh after death of the fish). Most control measures for anisakiasis emphasise the importance of immediate evisceration of captured fish, and cooking or freezing fish product prior to consumption (Acha and Szyfres, 1987; Abollo *et al*, 2001). Consumption of live larvae in raw or undercooked fish, however, is not necessarily the only way in which the parasite can cause disease; in some cases there is evidence that occupational exposure to fish products may be sufficient to trigger an allergic response to anisakid allergens (Purrello-D'Ambrosio *et al*, 2000).

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