

INVITED REVIEW

Global status of fish-borne zoonotic trematodiasis in humans

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Abstract

Fishborne zoonotic trematodes (FZT), infecting humans and mammals worldwide, are reviewed and options for control discussed. Fifty nine species belonging to 4 families, i.e. Opisthorchiidae (12 species), Echinostomatidae (10 species), Heterophyidae (36 species) and Nanophyetidae (1 species) are listed. Some trematodes, which are highly pathogenic for humans such as *Clonorchis sinensis*, *Opisthorchis viverrini*, *O. felinus* are discussed in detail, i.e. infection status in humans in endemic areas, clinical aspects, symptoms and pathology of disease caused by these flukes. Other liver fluke species of the Opisthorchiidae are briefly mentioned with information about their infection rate and geographical distribution. Intestinal flukes are reviewed at the family level. We also present information on the first and second intermediate hosts as well as on reservoir hosts and on habits of human eating raw or undercooked fish.

Keywords

Clonorchis, *Opisthorchis*, intestinal trematodes, liver trematodes, risk factors

Fish-borne zoonotic trematodes

Fish-borne zoonotic trematodes (FZT) are found within four families, i.e. Opisthorchiidae, Heterophyidae, Nanophyetidae and Echinostomatidae (Class: Trematoda Rudolphi, 1808; phylum: Platyhelminthes Genenbaur, 1859). Fish serve as the second intermediate host in their life cycle (Fig. 1). FZTs inhabit mainly the liver or intestine of vertebrates, including humans (Chai *et al.* 2005a; Le 2000; Taylor *et al.* 2007).

Humans and fish-eating mammals and birds may serve as final hosts depending on trematode species involved (Le 2000; Murrell and Fried 2007; Taylor *et al.* 2007). People get infected with FZT if they eat raw or undercooked freshwater and sometimes brackish water fish containing active metacercariae (Chai *et al.* 2005a; Keiser and Utzinger 2009; Lemly and Esch 1983; Murrell and Fried 2007). When the fish tissue is broken down through digestion, metacercariae are released into the small intestine where they excyst and migrate to the suitable internal organs of the host and grow to adult trematodes. Fertilized eggs are released into the environment

with feces of their host and the eggs may reach water sources such as ponds, lakes, streams or rivers. Either eggs containing a miracidium are eaten by an appropriate snail and they hatch inside the snail (e.g. species of Opisthorchiidae, Heterophyidae) or the eggs hatch (Echinostomatidae) and a free-living miracidium is released in the water. The miracidium must locate and infect a snail within few hours. When eggs are ingested by snails, the miracidium is released in the intestinal tract of the snails, and it penetrates the rectal wall and develops into a sporocyst, which asexually generate rediae. The rediae in turn migrate to the digestive gland-gonad complex of the host snail where they asexually produce cercariae continuously throughout the life of the snail. Cercariae released from the snail will seek out a freshwater fish, penetrate its skin, and encyst as metacercariae in the skin or muscle of the fish. The asexual multiplication within the snail host results in thousands of cercariae being produced from one egg, and the duration of this process depends on the species and survival of the snail host (Le 1998; Keiser and Utzinger 2009; Toledo *et al.* 2011).

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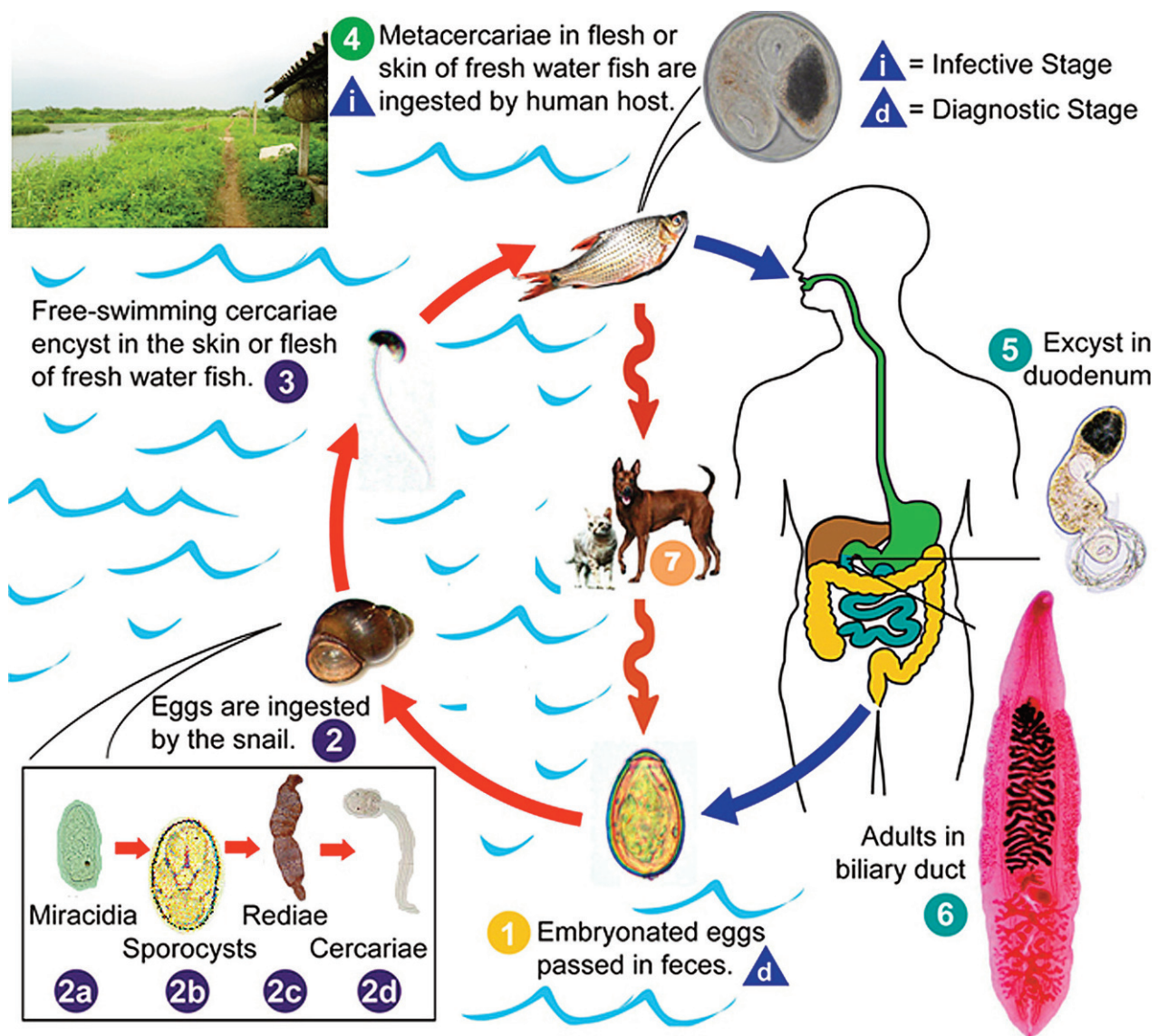


Fig. 1. The life cycle of *Clonorchis sinensis* (modified from <http://www.dpd.cdc.gov/dpdx>) as a representative for FZT species

The public health importance of fishborne zoonotic trematodes

Fish-borne zoonotic trematodiasis caused by flukes transmitted by fish products pose major public health problems worldwide. Among more than 100 trematode species infecting humans, 59 species are reported as FZT (Table 1). The number of people currently infected with only liver flukes (family Opisthorchiidae) exceeds 18 million and unknown millions are infected with intestinal flukes (Chai *et al.* 2009; World Health Organization 1995), but it is estimated that more than half a billion are at risk of infection (Lima dos Santos and Howgate 2011; World Health Organization 2004). Some of these parasites are highly pathogenic and human infection is the result of the consumption of raw or undercooked fish in-

fect by the parasites (World Health Organization 1995). Lima dos Santos and Howgate (2011) mentioned that these ichthyozoonoses have increased significantly in recent years for various reasons: (1) the development of new and improved diagnosis, (2) by the increase in raw fish consumption in those countries in which such dishes have commonly been eaten, (3) by the increased consumption elsewhere of regional fish dishes such as sushi, sashimi, ceviche, carpaccio based on raw or minimally processed fish, (4) by the growth in the international trade in fish and fish products, and (5) by the spectacular development of aquaculture.

The species of major importance to human health are the liver flukes (family: Opisthorchiidae) which parasitize the liver or bile-duct of the final host. The public health importance of these species is due to their wide geographical distri-

bution, high prevalence and severe morbidity (Chai *et al.* 2005a; Keiser and Utzinger 2009; Lima dos Santos *et al.* 2011; MacLean *et al.* 2006; Mas-Coma and Bargues 1997). They have long been known to cause serious disease in certain areas of the world. Cholangitis, choledocholithiasis, pancreatitis, and cholangiocarcinoma are the major clinical problems, associated with the long chronic pattern of these infections (Chai *et al.* 2009; Mas-Coma and Bargues 1997). The causative agents of human infections include *Clonorchis sinensis*, *Opisthorchis viverrini*, *Opisthorchis felinus* and several minor species e.g. *Metorchis conjunctus*, *M. albidus* and *Amphimerus pseudofelineus*. In contrast although the intestinal trematode infections are more focal in distribution, they have been reported from a larger number of countries, representing a far greater number of species and are acquired from a wide range of intermediate hosts.

Intestinal trematodes are the commonest parasitic infections in humans and animals (Chai *et al.* 2009, Yu and Mott 1994). Although less associated with mortality than other groups of parasites, intestinal trematodes are responsible for significant morbidity, food safety and quality problems (Toledo *et al.* 2006; Yu and Mott 1994), but they have not attracted the interest of international agencies until recently. The intestinal trematodes transmitted by fish belong to the Echinostomatidae, Heterophyidae, and Nanophyetidae but there are several other intestinal or liver trematodes within Diplostomidae, Fasciolidae, Gastrodiscidae, Gymnophallidae, Lecithodendriidae, Microphallidae, Paramphistomatidae, Plagiorchiidae and Strigeidae (Chai 2007; Chai *et al.* 2005a; Dawer 1956; Kumar 1999; Mas-Coma and Bargues 1997; Yamaguti 1971; Yu and Mott 1994). All of these species are acquired by humans from ingestion of raw or undercooked fish, mollusks, amphibians, terrestrial snakes, aquatic insects and aquatic plants (Chai *et al.* 2009; Yu and Mott 1994). About 70 species of intestinal food-borne zoonotic trematodes have been reported to infect people (Yu and Mott 1994) and 47 of these were transmitted through fish (Table I). The endemicity of the parasites is associated with cultural and eating habits. The current understanding of the epidemiological distribution and pathology of intestinal trematodes is generally based on individual case reports rather than on systematic investigations in populations with specific high risk food habits (Yu and Mott 1994).

Diversity, occurrence, geographical distribution of FZT in humans and their clinical/epidemiology

The transmission of fish-borne trematodiasis is restricted to areas where the first and second intermediate hosts coexist and where humans have the habit of eating raw, pickled, or insufficiently cooked fish (Keiser and Utzinger 2005, 2009; Sripa *et al.* 2007; Mas-Coma and Bargues 1997; World Health Organization 2004). These contextual determinants explain why the distribution of fish-borne trematodiasis is focal (Keiser and Utzinger 2009).

In the World, about 350 snail species are estimated to be of possible medical or veterinary importance (Keiser and Utzinger 2009). Several snail genera have been reported as second intermediate host for trematodes, i.e. *Pila conica*, of *Viviparus javanicus*, *Lymnaea rubiginosa brevis* are source of infection of *Echinostoma ilocanum* etc. (Yu and Mott 1994, Tropmed Technical Group 1986). First intermediate hosts of liver flukes (Opisthorchiidae) include: *Bithynia fuchsiana*, *B. chaperi*, *B. siamensis*, *B. funiculata*, *B. tentaculata*, *B. leachii*, *B. inflata*, *B. troscheli*, *Parafossarulus manchouricus* (Syn. *P. striatulus*), *P. anomalospiralis*, *P. sinensis*, *Alloconima longicornis*, *Melanoides tuberculata*, *Thiara scabra*, *Tarebia granifera*, *Assiminea lutea*, *Semisulcospira libertina*, *Amnicola limosa*, *Huaningpoensis*, and *Opisthorchophorus hispanicus*; some of the bithynid species may be referred to *Codiella* (World Health Organization 2004; Mas-Coma and Bargues 1997; Derrai 2008). The status of thiarid snail species e.g. *Melanoides* and *Thiara* as the first intermediate host of *Clonorchis sinensis* (De *et al.* 2003; Lun *et al.* 2005) has been refuted (Dung *et al.* 2010) and further research is required. Rohela *et al.* (2006) mentioned that *M. tuberculata* is not good host for *C. sinensis*.

A wide range of freshwater snails are the first intermediate hosts of minute intestinal trematodes, including *Bellamya*, *Melanoides*, *Thiara*, *Tarebia*, *Bithynia*, *Parafossarulus*, *Lymnaea*, *Radix*, *Gyraulus*, *Cipangopaludina*, *Hippeutis*, *Segmentina*, *Oxytrema*, *Heleobia*, *Semisulcospira*, *Melania*, *Stenomelania*, *Stagnicola*, *Koreanomelania* etc. (Tropmed Technical Group 1986, Dung *et al.* 2010; Le 2000; World Health Organization 2004). Brackish water snails of the genera *Cerithidea*, *Tympanotonus* and *Sermyla* have been reported as intermediate hosts of FZT.

Most of the second intermediate hosts of FZT species are freshwater fish, except for some cases where estuary fish (mullet) or marine fish (salmon) are hosts. Snails, however, can also be second intermediate hosts for some echinostome species, particularly species of the Viviparidae and Pilidae (Le *et al.* 1993; Yu and Mott 1994). The association between transmission of FZT diseases and wild- and aquaculture-fish is well documented (Lima dos Santos and Howgate 2011), and FZT infections in farmed fish is a concern for human health (World Health Organization 1995; Howgate 1998).

Fish belonging to the family Cyprinidae (carp) are the major intermediate hosts of liver flukes, especially *Clonorchis sinensis* and *Opisthorchis* spp. (Adam *et al.* 1997; IARC 1994; Le 2000; Mas-Coma and Bargues 1997). More than 100 species of freshwater fish have been shown to be naturally infected with *C. sinensis* and more than 35 with *Opisthorchis* spp. (Adam *et al.* 1997). The Cyprinidae also has been reported as the second intermediate hosts of many minute intestinal flukes. Marine fish (*Salmo* sp., *Oncorhynchus* sp., *Brachymystax* sp., *Coregonus* sp. and some non-salmon fish species) have been found to harbor metacercariae of *Nanophyetes salmincola* (Chai *et al.* 2005a; Yu and Mott 1994). Several estuary fish species, such as *Mugil* spp., *Liza* spp., *Acanthogobius* spp., and *Chaenogobius* spp. are the sec-

Table 1. Species of fish-borne zoonotic trematodes reported in humans and animals with their infection prevalence, distribution and host species

Echinostomatidae	
<i>Echinochasmus fujianensis</i> Cheng <i>et al.</i>, 1992	
Distribution	China
Infection in people	Prevalence of 3.2% in humans in 5 counties/cities of southern Fujian (China); patients were 3-15 years old. Infection rate in dogs was 29.2%
1 st int. host	Freshwater snails: <i>Oncomelania</i> spp., <i>Bellamya aeruginosa</i>
2 nd int. host	Snails. Freshwater fishes, such as: <i>Pseudorasbora parva</i> and <i>Cyprinus carpio</i> .
Final hosts	Dog, cat, pig, rat (<i>Rattus rattoides losea</i> , <i>Rattus norvegicus</i>), human
References	Chai <i>et al.</i> 2009; Cheng <i>et al.</i> 1992; Yu and Mott 1994
<i>Echinochasmus japonicus</i> Tanabe, 1926	
Distribution	China, Japan, Korea, Vietnam
Infection in people	Prevalence was 4.9% in humans in 6 counties of Fujian and Guangdong (China).
1 st int. host	Freshwater snail: <i>Oncomelania</i> spp., <i>Pila</i> spp., <i>Gyraulus</i> spp., <i>Parafossarulus manchouricus</i> , <i>Allocinma longicornis</i>
2 nd Int. host	Marsh clams: <i>Corbicula</i> spp. Freshwater fish, i.e. <i>Pseudorasbora parva</i> , <i>Hypomesus olidus</i> , <i>Gnathopogon strigatus</i> , <i>Macropodus opercularis</i>
Final hosts	Avian species, such as ducks, chickens, egrets. Mammalian species, such as dog, cat, rat, human
References	Chai <i>et al.</i> 2005a, 2009; Le 2000; Lin <i>et al.</i> 1985; Sohn and Chai 2005; Yu and Mott 1994
<i>Echinochasmus jiufuensis</i> Liang and Ke, 1988	
Distribution	China
Infection in people	Found in 6 months old girl in Guangzhou
1 st int. host	Fresh water snails: <i>Oncomelania</i> spp.
2 nd int. host	Molluscs and fishes
Final hosts	Dog, cat, pig, human
References	Chai <i>et al.</i> 2009; Yu and Mott 1994
<i>Echinochasmus liliputanus</i> (Looss, 1896) Odhner, 1910	
Distribution	China, Egypt, Palestine, Syria
Infection in people	In Anhui province (China), prevalence was 13.4% among 2,426 people. Higher prevalence was recorded in a 3-15 years (22.7%) and a 16-30 years (16.4%) age group. Prevalence in dog and cat was 50% and 45% respectively.
1 st int. host	Freshwater snails: <i>Parafossarulus manchouricus</i> , <i>Oncomelania</i> spp.
2 nd int. host	Freshwater fishes: <i>Pseudorasbora parva</i> , gold fish
Final hosts	Dog, cat, fox (<i>Vulpes vulpes hoole</i>), badger (<i>Meles meles leptorynchus</i>), racoon (<i>Nyctereutes procyonoides procyonoides</i>), human
References	Chai <i>et al.</i> 2005a, 2009; Yu and Mott 1994
<i>Echinochasmus perfoliatus</i> (Ratz, 1908) Geddoelst, 1911	
Distribution	China, Denmark, Hungary, Italy, Japan, Rumania, Russia, Taiwan, Vietnam
Infection in people	In Guangdong, Fujian, Anhui, Hubei province (China), prevalence was 1.8% (34/1846). This species has been reported in humans in Hanoi (Vietnam) but the prevalence was not reported
1 st int. host	Freshwater snails: <i>Parafossarulus manchouricus</i> , <i>Bithynia leachi</i> , <i>Lymnaea stagnalis</i> , <i>Oncomelania</i> spp.
2 nd int. host	Freshwater fishes: <i>Carassius</i> sp., <i>Zacco platypus</i> , <i>Z. teminckii</i> , <i>Pseudorasbora parva</i>
Final hosts	Dog, cat, pig, fox, rat, badger, human
References	Chai <i>et al.</i> 2005a, 2009; Le 2000; Saeed <i>et al.</i> 2006; Taylor <i>et al.</i> 2007; Toledo <i>et al.</i> 2006; Yu and Mott 1994
<i>Echinoparyphium paraulum</i> Dietz, 1909	
Synonyms	Probably a synonym of <i>Echinostoma revolutum</i>
Distribution	Asia, Europe, New Zealand, and Brazil
Infection in people	Infected humans were found in Yunnan, Guangdong (China), Thailand, Indonesia, Russia. In 1929 in Taiwan, prevalence was estimated between 2.8% and 6.4%

1 st int. host	Freshwater snails: <i>Lymnaea stagnalis</i> , <i>Physa</i> sp., <i>Paludina</i> sp., <i>Segmentina</i> sp., <i>Helisoma</i> sp., <i>Stagnicola palustris</i> , <i>Planorbarius corneus</i> , <i>Radix peregra</i> , <i>Acroloxus</i> spp., <i>Planorbis</i> sp.
2 nd int. host	Tadpoles, snails, clam (<i>Corbicula</i>), freshwater fish
Final hosts	Avian: duck (<i>Anas boschas fereae</i>), goose, swan, and dove. Mammal: muskrat (<i>Ondatra zibethica</i>), human
References	Yu and Mott 1994; Murrell and Fried 2007

***Echinostoma angustitestis* Wang, 1997**

Distribution	China
Infection in people	Two infected humans were reported in Fujian (China)
1 st int. host	Freshwater snails: <i>Oncomelania</i> spp., <i>Parafossarulus</i> sp.
2 nd int. host	Freshwater fish
Final hosts	Dog, human
References	Cheng <i>et al.</i> 1992; Yu and Mott 1994

***Echinostoma cinetorchis* Ando and Ozaki, 1923**

Distribution	Indonesia, Japan, Korea, Taiwan, Vietnam
Infection in people	Infected people were found in Japan, Korea, Taiwan but no information of the infection prevalence in these countries.
1 st int. host	Freshwater snails: <i>Hippeutis cantori</i> , <i>Segmentina nitidella</i> , <i>Gyraulus convexiusculus</i> , <i>Autropeplea ollua</i>
2 nd int. host	Freshwater fishes: <i>Misgurnus anguillicandatus</i> . Freshwater snails: <i>Radix auricularia corcanus</i> , <i>Physa acuta</i> , <i>Planorbis compressus</i> , <i>Lymnaea japonica</i> and <i>Cipangopaludina</i> spp., <i>Hippeutis cantori</i> , <i>Segmentina nitidella</i> . Tadpoles and frogs (<i>Rana nigromaculata</i> , <i>R. catesbiana</i>). Larvae of salamander
Final hosts	Dog, cat, rat (<i>Rattus norvegicus</i> , <i>R. flavipectus</i> , <i>R. edwardsi</i> , <i>E. sladeni</i>), mouse (<i>Bandicota indica</i>), human
References	Chai <i>et al.</i> 2009; Chai and Lee 2002; Le 2000; Yu and Mott 1994

***Echinostoma hortense* Asada, 1926**

Distribution	China, Japan, Korea (Cheongsong-gun)
Infection in people	Liaoning province (China): 6/10 patients who had eaten raw loach were found infected. In Cheongsong-gun area (Korea), prevalence was 22.4%.
1 st int. host	Freshwater snails: <i>Planorbis</i> spp., <i>Oncomelania</i> spp., <i>Lymnaea pervia</i> , <i>Radix auricularia correana</i>
2 nd int. host	Freshwater fishes: <i>Misgurnus anguillicaudatus</i> , <i>M. mizolepis</i> , <i>Odontobutis obscura</i> , <i>Moroco oxycephalus</i> , <i>Coreopeca kawamebari</i> , <i>Squalidus coreanus</i>
Final hosts	Dog, cat, rat (<i>Rattus norvegicus</i>), human
References	Chai <i>et al.</i> 2005a, 2009; Fan and Sun 1989; Sohn and Chai 2005

***Episthmium caninum* (Verma, 1935) Yamaguti, 1958**

Distribution	Thailand, Vietnam, India
Infection in people	Several human cases have been reported in Thailand
1 st int. host	Freshwater snails
2 nd int. host	Freshwater fish
Final hosts	Bird, dog, pig, human
References	Chai <i>et al.</i> 2009; Le 2000; Radomyos <i>et al.</i> 1991; Toledo <i>et al.</i> 2006; Yu and Mott 1994.

Heterophyidae

***Apophalus donicus* (Skrjabin and Lindtrop, 1919) Price, 1931**

Synonyms	<i>Rossicotrema donicus</i> Skrjabin et Lindtrop, 1919; <i>Cotylophallus venustus</i> Ransom, 1920; <i>C. similis</i> Ransom, 1920
Distribution	Canada, East Europe, United States
Infection in people	Human infection was found in the United States; the prevalence was unknown
1 st int. host	Snails: <i>Flumenicola virens</i> , <i>Lithoglyphus naticoides</i>
2 nd int. host	Fishes: <i>Perca</i> sp., <i>Lusioperca</i> sp., <i>Blicca</i> sp., <i>Scardinius</i> sp.
Final hosts	Dog, cat, rat, fox, rabbit, human
References	Niemi and Macy 1974; Toledo <i>et al.</i> 2006; Yamaguti 1958; Yu and Mott 1994

***Ascocotyle longa* Ramson, 1920**

Synonyms	<i>Phagicola</i> sp.
Distribution	Asia, Africa, America, Europe
Infection in people	Human infection was reported in Brazil; 9 out of 92 adults who lived in Sao Paulo were found egg-positive. The infection prevalence in dog was 1.6%.
1 st int. host	Freshwater snail: <i>Heleobia australis</i>
2 nd int. host	Estuary fish: <i>Mugil liza</i>
Final hosts	Hamster, mammals
References	Fried <i>et al.</i> 2004; Simões <i>et al.</i> 2010; Yu and Mott 1994

***Ascocotyle* sp.**

Distribution	Asia, Africa, Americas, Europe
Infection in people	Unknown
1 st int. host	Unknown
2 nd int. host	Estuary fish: <i>Mugil</i> sp.
Final hosts	Dog, cat, human
References	Bray <i>et al.</i> 2008

***Centrocestus armatus* (Tanabe, 1922) Price, 1932**

Distribution	Japan, Korea
Infection in people	Reported case: 42 year old man in Kyeongsangnam-do, Korea. In Japan, a successful experimental human infection was reported.
1 st int. host	Freshwater snails: <i>Semisulcospira libertina</i> .
2 nd int. host	Freshwater fishes: <i>Pseudorasbora parva</i> , <i>Pelteobagrus fulvidraco</i> , <i>Zacco platypus</i> , <i>Z. temminckii</i> , <i>Rhodeus ocellatus</i> , <i>Gobius similis</i>
Final hosts	Egret (<i>Egretta alba modesta</i>), dog, cat, rabbit, rat, human
References	Chai <i>et al.</i> 2009; Chai and Lee 1990; Hong <i>et al.</i> 1988; Sohn and Chai 2005

***Centrocestus caninus* (Leiper, 1912) Yamaguti, 1958**

Synonyms	<i>Stephanopirumis longus</i> Onji and Nishio, 1916
Distribution	Taiwan, Thailand.
Infection in people	Human infection in Taiwan and 2 reported cases in Thailand
1 st int. host	Freshwater snail: <i>Melanoides tuberculata</i>
2 nd int. host	Freshwater fishes: <i>Anabas testudineus</i> , <i>Channa formosana</i> , <i>Channa striata</i> , <i>Cyprinus carpio</i> , <i>Carrassius auratus</i> , <i>Gnathopodon elongates</i> , <i>Glossogobius giuris</i> , <i>Hampala dispar</i> , <i>Hyporhamphus dussumieri</i> , <i>Puntius</i> spp., <i>Cyclocheilichthys</i> sp., <i>Tilapia nilotica</i> , <i>Terapon plumbeus</i> . Frog: <i>Rana limnochairis</i> , <i>Bufo melanostictus</i>
Final hosts	Dog, fox, cat, rat, human
References	Chai <i>et al.</i> 2009; Yamaguti 1958; Waikagul <i>et al.</i> 1997; Yu and Mott 1994

***Centrocestus cuspidatus* Looss, 1896**

Distribution	Egypt and Taiwan
Infection in people	Human infection reported in Egypt and in Taiwan; no information on prevalence
1 st int. host	Freshwater snail: <i>Oncomelania formosana</i>
2 nd int. host	Freshwater fish
Final hosts	Yellow-billed Kite (<i>Milvus parasiticus</i>), rat, human
References	Yu and Mott 1994

***Centrocestus formosanus* Nishigori, 1924**

Distribution	China, Japan, Hawaii, Mexico, Philippines, Taiwan and Vietnam
Infection in people	Human infection reported in Taiwan and Philippines
1 st int. host	Snail: <i>Stenomelania newcombi</i> , <i>Oncomelania hupensis</i>
2 nd int. host	Freshwater fishes: <i>Macropodus opercularis</i> , <i>Puntius semifasciolatus</i> , <i>Carassius auratus</i> , <i>Misgurnus anquillicaudatus</i> , <i>Cyclocheilichthys repasson</i> , <i>Puntius brevis</i> , <i>Osteochilus hasseltii</i> , <i>Chana formosana</i> . Frogs: <i>Rana limnochairis</i> , <i>Bufo melanostictus</i>
Final hosts	Chicken, duck, dog, cat, rat (<i>R. flavipectus</i> , <i>R. norvegicus</i>), human
References	Chai <i>et al.</i> 2009; Le 2000; Scholtz and Salgado-Maldonado 1999; Toledo <i>et al.</i> 2006; Yamaguti 1958; Yu and Mott 1994

***Centrocestus kurokawai* Kurokawa, 1935**

Distribution	Japan
Infection in people	Human infection reported in Japan but no information on prevalence
1 st int. host	Freshwater snail: <i>Oncomelania nosophora</i>
2 nd int. host	Freshwater fish
Final hosts	Human
References	Chai <i>et al.</i> 2009; Yu and Mott 1994

***Centrocestus longus* Onji and Nishio, 1916**

Synonyms	Probably a synonym of <i>C. canius</i>
Distribution	Taiwan
Infection in people	Human infection reported in Taiwan but no information on prevalence
1 st int. host	Unknown
2 nd Int. host	Freshwater fish
Final hosts	Human
References	Yu and Mott 1994

***Cryptocotyle lingua* (Creplin, 1825) Fischoeder, 1903**

Distribution	Denmark, Greenland, North America, Russia, Japan
Infection in people	Human infection reported in Greenland
1 st int. host	Snails: <i>Tautogladius</i> spp.
2 nd int. host	Periwinkle: <i>Littorina littorea</i> . Fishes: <i>Gobius ruthensparri</i> , <i>Labrus bergylta</i>
Final hosts	Dog, cat, rat, wild animals, human
References	Chai <i>et al.</i> 2005; Chai and Lee, 2002; Saeed <i>et al.</i> 2006; Toledo <i>et al.</i> 2006; Yamaguti 1958; Yu and Mott 1994

***Haplorchis microchis* Matsuda, 1932**

Distribution	Japan
Infection in people	Human infection reported in Japan
1 st int. host	Snails
2 nd int. host	Fish: e.g. mullet
Final hosts	Dog, cat, human
References	Yu and Mott 1994

***Haplorchis pleurolophocerca* Sonsino, 1896**

Distribution	Egypt
Infection in people	Human infection reported in Egypt
1 st int. host	Snails
2 nd int. host	Fish: <i>Gambusia affinis</i>
Final hosts	Cat, human
References	Yu and Mott 1994

***Haplorchis pumilio* (Looss, 1886) Looss, 1899**

Synonyms	<i>Monorchotrema taihokui</i> (Nishigori, 1924) Chen, 1936; <i>Haplorchis taihokui</i> Nishigori, 1924
Distribution	China, Egypt, Laos, Philippines, Taiwan, Thailand, Vietnam
Infection in people	In Thailand, 12 of 411 patients who were treated for opisthorchiasis were infected with <i>H. pumilio</i> . In Nam Dinh province (Vietnam), 33 of 610 examined persons were found with this species.
1 st int. host	Freshwater snails: <i>Melanooides</i> spp., <i>Stenomelania</i> sp., <i>Melania reiniana</i> , <i>M. hitachiensis</i>
2 nd int. host	Freshwater fishes: <i>Ophiocephalus striatus</i> , <i>Glossogobius giurus</i> , <i>Acanthogobius</i> sp., <i>Mugil</i> sp., <i>Cyprinus</i> sp., <i>Carassius</i> sp., <i>Misgurnus</i> sp. Anura: Toad <i>Bufo spinulosus</i> , Frog <i>Rana esculenta</i>
Final hosts	Bird, dog, cat, human
References	Chai <i>et al.</i> 2005a, 2009; Dung <i>et al.</i> 2007; Yamaguti 1958; Yu and Mott 1994

***Haplorchis taichui* (Nishigori, 1924) Chen, 1936**

Synonyms	<i>Monorchotrema taichui</i> Nishigori, 1924; <i>M. microrchia</i> Katsuda, 1932; <i>H. microrchis</i> Yamaguti, 1958
Distribution	Bangladesh, China, Egypt, Laos, Palestine, Philippines, Taiwan, Thailand, Vietnam
Infection in people	Human infection reported in Philippines, Laos, Thailand, Taiwan, Bangladesh, and Vietnam. In Nam Dinh province (Vietnam) 23 of 610 examined people were infected with this species.

1 st int. host	Freshwater snails: <i>Melania obliquegranosa</i> , <i>M. juncea</i> , <i>Melanoides tuberculata</i>
2 nd int. host	Freshwater fishes: <i>Gambusia affinis</i> , <i>Ctenopharyngodon idellus</i> , <i>Cyprinus carpio</i> , <i>Carassius auratus</i> , <i>Cyclocheilichthys repasson</i> , <i>Hampala dispar</i> , <i>Labiobarbus leptocheila</i> , <i>Puntius binotatus</i> , <i>P. brevis</i> , <i>P. gonionotus</i> , <i>P. leicanthus</i> , <i>P. orphoides</i> , <i>P. palata</i> , <i>Pseudorasbora parva</i> , <i>Rhodeus ocellatus</i> , <i>Zacco platypus</i> , <i>Raiamas guttatus</i> , <i>Mystacoleucus marginatus</i> , <i>Henichorhynchus siamensis</i>
Final hosts	Hawk (<i>Milvus migran</i>), Dog, cat, human
References	Chai <i>et al.</i> 2005a, 2009; Dung <i>et al.</i> 2007; Le 2000; Toledo 2006; Yu and Mott 1994

***Haplorchis vanissimus* Africa, 1938**

Distribution	Philippines, Australia
Infection in people	Human infection reported in Philippines
1 st int. host	Snails
2 nd int. host	Estuary fish: e.g. mullet
Final hosts	Pelicans, cat, dog, human
References	Chai <i>et al.</i> 2009; Murrell and Fried 2007; Yu and Mott 1994

***Haplorchis yokogawai* (Katsuta, 1932) Chen, 1936**

Synonyms	<i>Monorchotrema yokogawai</i> Katsuda, 1932
Distribution	Taiwan, China, India, Philippines, Malaysia, Australia, Egypt, Laos, Indonesia, Thailand, Vietnam
Infection in people	Human infection reported in Philippines, Thailand, China, Taiwan and Vietnam. In Nam Dinh province (Vietnam) 1 of 610 examined people were infected with this species.
1 st int. host	Freshwater snails: <i>Melanoides tuberculata</i> , <i>Stenomelania newcombi</i>
2 nd int. host	Fishes: <i>Mugil</i> spp., <i>Puntius</i> spp., <i>Misgurnus</i> sp., <i>Ophicephalus striatus</i> , <i>Cyclocheilichthys armatus</i> , <i>Hampala dispar</i> , <i>Labiobarbus leptocheila</i> , <i>Onychostoma elongatum</i> . Shrimp: <i>Perracus</i> spp.
Final hosts	Dog, cat, human
References	Chai <i>et al.</i> 2005a, 2009; Le 2000; Toledo <i>et al.</i> 2006; Yamaguti 1958; Yu and Mott 1994

***Heterophyes dispar* Looss, 1902**

Distribution	Egypt, North Africa, the Eastern Mediterranean, Korea, Thailand
Infection in people	Human infection reported in Korea and Thailand
1 st int. host	Snail: <i>Pirenella conica</i>
2 nd int. host	Fish of several genera: <i>Mugil cephalus</i> , <i>Epinephelus fasciatus</i> , <i>Tilapia</i> sp., <i>Lichia</i> sp., and <i>Barchus callipterus</i>
Final hosts	Dog, cat, human
References	Chai and Lee 1990; Yu and Mott 1994

***Heterophyes heterophyes* (v. Siebold, 1852) Stiles and Hassall, 1990**

Synonyms	<i>Distoma heterophyes</i> v. Siebold, 1852; <i>Heterophyes aegyptiaca</i> Cobbold, 1866; <i>Heterophyes nocens</i> Onji and Nishio, 1915
Distribution	Egypt, Turkey, Sudan, Palestine, Brazil, Spain, Iran, India, Russia, Japan, China, Philippines, Taiwan, Indonesia
Infection in people	Human infection reported in Korea, Egypt (0.01-1% in the 5 governorates), China (Guangdong, Hubei, Beijing) and Taiwan.
1 st int. host	Freshwater snails: <i>Parafossarulus manchouricus</i> , <i>Pirenella conica</i>
2 nd int. host	Fishes: <i>Mugil cephalus</i> , <i>Tilapia nilotica</i> , <i>Aphanius fasciatus</i> and <i>Acanthogobius flavimanus</i> , <i>Chelon haematocheilus</i> .
Final hosts	Dog, cat, fish-eating mammals, human
References	Chai <i>et al.</i> 2005a; Bray <i>et al.</i> 2008; Le 2000; Taraschewski and Nicolaidou 1987; Toledo <i>et al.</i> 2006; Yu and Mott 1994

***Heterophyes katsuradai* Ozaki and Asada, 1926**

Distribution	Japan
Infection in people	Human infection reported in Japan
1 st int. host	Snail: <i>Cerithidia cingulata</i>
2 nd int. host	Fish: <i>Mugil cephalus</i>
Final hosts	Dog, human
References	Yu and Mott 1994

***Heterophyes nocens* Onji and Nishio, 1916**

Distribution	Korea, Japan, Philippines, China
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Infection in people	The prevalence ranged from 10 to 70% among residents in southwestern coastal areas in Korea. In Japan, <i>H. nocens</i> was reported in Kochi, Chiba, Yamaguchi, Chugoku, Hiroshima, Shizuoka.
1 st int. host	Snails: <i>Pirenella conica</i> , <i>Cerithidia cingula alata</i>
2 nd int. host	Estuary fishes: <i>Mugil cephalus</i> , <i>Liza</i> sp., <i>Acanthogobius</i> sp., and <i>Chaenogobius</i> sp.
Final hosts	Dog, cat, fish-eating mammals, human
References	Chai <i>et al.</i> 2005a; Chai and Lee 1990; Yu and Mott 1994

***Heterophyopsis continua* (Onji and Nishio, 1916) Yamaguti, 1958**

Synonyms	<i>Heterophyes continuus</i> Onji et Nishio, 1916; <i>Heterophyes expectans</i> Africa et Garcia, 1935
Distribution	Philippines, Japan, China, Korea
Infection in people	Human infection reported in Japan (2 cases), and Republic of Korea (8 cases), and China
1 st int. host	Freshwater snail: <i>Parafossarulus manchouricus</i>
2 nd int. host	Fishes: <i>Mulgi cephalus</i> , <i>M. affinis</i> , <i>Larus argentatus</i> , <i>Cyprinus carpio</i> , <i>Acanthogobius flavimanus</i> , <i>Lateolabrax japonicus</i> , <i>Clupadon punctatus</i> , <i>Conger myriaster</i> , <i>Plecoglossus altivelis</i> , <i>Konosirus punctatus</i> , <i>Boleophthalmus pectinirostris</i> , <i>Scartelaos histophorus</i> , <i>Harengula zunasi</i> , <i>Dorosoma thrissa</i> .
Final hosts	Cat, dog, chick, human
References	Chai <i>et al.</i> 2009; Chai and Lee 1990; Toledo <i>et al.</i> 2006; Yamaguti 1958; Yu and Mott 1994

***Isthimiophora melis* (Schränk, 1788) Lühe, 1909**

Synonyms	<i>Euparyphium melis</i> Railliet, 1919; <i>Euparyphium jassyense</i> Leon et Ciurea, 1922
Distribution	China, Europe, North America, Taiwan
Infection in people	Human infection reported in Rumania, China, and Taiwan.
1 st int. host	Freshwater snail : <i>Stagnicola emarginata</i>
2 nd int. host	Freshwater fishes: loach, tadpoles and <i>Misgurnus</i> spp.
Final hosts	Domestic and wild animals, human
References	Chai <i>et al.</i> 2009

***Metagonimus minutus* Katsuta, 1932**

Distribution	Taiwan
Infection in people	Human infection reported in Taiwan
1 st int. host	Snails
2 nd int. host	Fish: mullet
Final hosts	Cat, mice, human
References	Chai <i>et al.</i> 2009; Yu and Mott 1994

***Metagonimus miyatai* Saito, Chai, Kim, Lee and Rim, 1997**

Distribution	Japan, Korea
Infection in people	Human infection reported in Korea (from people along the Gum River)
1 st int. host	Freshwater snails: <i>Semisulcospira globus</i> , <i>S. libertine</i> , <i>S. dolorosa</i>
2 nd int. host	Freshwater fishes: sweetfish, dace, common fat-minnow <i>Morocco steindachneri</i> , pale chub <i>Zacco platypus</i> , and dark chub <i>Zacco temmincki</i>
Final hosts	Mice, rats, hamsters, dog, human
References	Chai <i>et al.</i> 2009

***Metagonimus takahashii* Suzuki, 1930**

Distribution	Korea, Japan
Infection in people	Human infection reported in Korea (Umsong-gun, Chunchungnam-do, and along upper reaches of the Namhan River)
1 st int. host	Freshwater snails: <i>Semisulcospira coreana</i> , <i>Koreanomelania nodifila</i>
2 nd int. host	Freshwater fishes: <i>Cyprinus carpio</i> , <i>Carassius carassius</i> , <i>C. auratus</i> , <i>Gnathopodon</i> sp., <i>Tribolodon taczanowskii</i> , <i>Lateolabrax japonicus</i>
Final hosts	Mice, dog, human
References	Chai <i>et al.</i> 2009; Yu and Mott 1994

***Metagonimus yokogawai* Katsurada, 1913**

Synonyms	<i>Losotrema ovatum</i> Kobayashi, 1912; <i>Metagonimus ovatus</i> Yokogawa, 1913; <i>Loossia romanica</i> (Ciurea, 1915)
Distribution	China, Far East of Russia, Indonesia, Japan, Korea, Siberia, Spain, Taiwan

Infection in people	Human infection reported in China (Guangdong, Anhui, Hubei, and Zhejiang provinces), Japan (Hamana Lake), Korea, Siberia, Israel, Balkan states, and Spain. In Korea, the prevalence was highest in Gangwon-do (20%-70%). In Russia, the endemic areas include Amur and Ussuri valley (Khabarovsk territory) where the prevalence was between 20 and 70%. In the north of Sakhalin Island, the infection rate was 1.5% in Russians.
1 st int. host	Freshwater snails: <i>Thiara</i> spp., <i>Semisulcospira coreana</i> , <i>S. libertine</i>
2 nd int. host	Freshwater fishes: sweet oriental trout <i>Plecoglossus altivelis</i> , dace <i>Tribolodon taczanowskii</i> , perch <i>Lateolabrax japonicus</i> , <i>Salmo perryi</i> , <i>Odontobutis obscurus</i> , etc.
Final hosts	Dog, cat, rat, pig, fish-eating animals, human
References	Chai <i>et al.</i> 2009; Chai and Lee 2002; Taylor <i>et al.</i> 2007; Toledo <i>et al.</i> 2006; Yu and Mott 1994

***Phagicola* sp.**

Distribution	Brazil, United States, Philippines
Infection in people	Human case reported of 31 year-old female in Southern Sao Paulo State, Brazil
1 st int. host	Freshwater or brackish water snails
2 nd int. host	Estuary fish: Mullet: <i>Mugil</i> sp., <i>Ambassis buruensis</i>
Final hosts	Raccoon (<i>Procyon lotor</i>), human, fish-eating animals
References	Chieffi <i>et al.</i> 1990; Hamir <i>et al.</i> 1993; Toledo <i>et al.</i> 2006; Athur and Lumanlan-Mayo 1997

***Procerovum calderoni* (Africa and Garcia, 1935) Price, 1940**

Distribution	Africa, China, Philippines
Infection in people	Human infections reported in Africa, China, Philippines
1 st int. host	Brackish water snails, <i>Sermyla riqueti</i> (= <i>Thiara riquetii</i>)
2 nd int. host	Fishes: <i>Ophiocephalus striatus</i> , <i>Glossogobius giurus</i> , <i>Creisson validus</i> , <i>Mollienesis latipinna</i> , <i>Mugil</i> sp.
Final hosts	Cat, dog, human
References	Chai 2007; Chai <i>et al.</i> 2009; Toledo <i>et al.</i> 2006; Yu and Mott 1994

***Procerovum varium* Onji and Nishio, 1916**

Distribution	Australia, China, Korea, India, Philippines
Infection in people	Human infection reported in Japan
1 st int. host	Snail: <i>Thiara riquetii</i>
2 nd int. host	Fish: <i>Mugil affinis</i>
Final hosts	Cat, dog, human
References	Chai <i>et al.</i> 2009; Sohn and Chai 2005; Yu and Mott 1994

***Pygidiopsis summa* Onji and Nishio, 1916**

Distribution	Japan, Korea
Infection in people	Human infection reported in Japan in 1965; in two coastal areas of Korea 18 and 5 people were found positive with this fluke.
1 st int. host	Brackish water snails: <i>Cerithidea</i> sp., <i>Tympanotonus</i> sp.
2 nd int. host	Fishes: <i>Mugil cephalus</i> , <i>Liza menada</i> , <i>Acanthogobius flavimanus</i>
Final hosts	Dog, cat, rat, human
References	Chai <i>et al.</i> 2009; Chai and Lee 2002; Sohn and Chai 2005; Toledo <i>et al.</i> 2006; Yu and Mott 1994

***Stellantchasmus falcatus* Onji and Nishio, 1916**

Distribution	Hawaii, Japan, Korea, Palestine, Philippines, Thailand, Vietnam
Infection in people	Human infection reported in Hawaii, Japan, Korea, Palestine, Philippines, Thailand, and Vietnam. In Nam Dinh province (Vietnam) 2 of 610 examined people were found infected with this species.
1 st int. host	Snails: <i>Stenomelania newcombi</i> , <i>Tarebia granifera</i>
2 nd int. host	Fishes: mullet <i>Mugil cephalus</i> and half-beaked fish <i>Dermogenus pusillus</i>
Final hosts	Dog, cat, rat, human
References	Chai <i>et al.</i> 2009; Chai and Lee 2000, 2002; Le 2000; Sohn and Chai 2005; Toledo <i>et al.</i> 2006; Yu and Mott 1994

***Stellantchasmus formosanum* (Katsuta, 1932)**

Distribution	Taiwan
Infection in people	An experimental human infection was reported in Taiwan
1 st int. host	Snail

2 nd int. host	Fish: <i>Mugil cephalus</i>
Final hosts	Cat, rat, human
References	Chai <i>et al.</i> 2009

***Stellantchasmus pseudocirratum* (Witenberg, 1929) Yamaguti, 1958**

Synonyms	<i>S. amplicaealis</i> Katsuta, 1932
Distribution	Hawaii, Palestine, Philippines, Taiwan
Infection in people	Human infection reported in Hawaii, Philippines
1 st int. host	Snail
2 nd int. host	Fish: <i>Mugil cephalus</i>
Final hosts	Dog, cat, human
References	Chai <i>et al.</i> 2009; Fahmy and Selim 1959; Toledo <i>et al.</i> 2006

***Stictodora fuscatum* (Onji and Nishio, 1916) Yamaguti, 1958**

Distribution	Japan, Korea
Infection in people	First human case was found in a young Korean man; 13 additional human cases were detected in this village in the south western coastal area.
1 st int. host	Brackish water snails
2 nd int. host	Fishes: mullet <i>Mugil cephalus</i> , goby <i>Acanthogobius flavimanus</i> , <i>Pseudorasbora parva</i> , <i>Liza macrolepis</i> , <i>Gobio gobio</i>
Final hosts	Cat, human
References	Chai V, 2009; Chai and Lee 1990; Toledo <i>et al.</i> , 2006; Yu and Mott 1994

***Stictodora lari* Yamaguti, 1939**

Distribution	Korea, Japan
Infection in people	In 2 southern coastal villages, 6 Korean people were detected with this species.
1 st int. host	Blackish water snail: <i>Velacumantus australis</i>
2 nd int. host	Estuarine fish, including goby <i>Acanthogobius flavimanus</i>
Final hosts	Dog, cat, human
References	Chai <i>et al.</i> 2002, 2009

Nanophyetidae***Nanophyetus salmincola* (Chapin, 1927)**

Synonyms	<i>Nanophyes salmincola</i> Chapin, 1926; <i>Troglorema salmincola</i> (Chapin, 1926) Witenberg, 1932
Distribution	Russia, United States
Infection in people	The infection prevalence in Amur and in Ussuri valleys of Khabarovsk territory (Russia) was 5%, and some localities, the average prevalence was 20% and reached up to 60%.
1 st int. host	Snail: <i>Oxytrema silicula</i>
2 nd int. host	Salmon fishes: <i>Salmo</i> sp., <i>Oncorhynchus</i> sp., <i>Brachymystax</i> sp., <i>Coregonus</i> sp. and some non-salmonid fish species
Final hosts	Human
References	Chai <i>et al.</i> 2005a; Yu and Mott 1994

Opisthorchiidae***Amphimerus noverca* (Braun, 1902) Barker, 1911**

Synonyms	<i>Distoma conjunctum</i> Lewis et Cunningham, 1872; <i>Opisthorchis noverca</i> Braun, 1902
Distribution	Indian
Infection in people	Two cases have been reported in India
1 st int. host	Aquatic snails
2 nd int. host	Fishes
Final hosts	Dog, fox, pig, human
References	Kassirsky and Plotikov 1969; Mas-Coma and Bargues 1997; Yamaguti 1971

***Amphimerus pseudofelineus* (Ward, 1901) Barker, 1911**

Synonyms	<i>Amphimerus guayaquilensis</i> (Ward, 1901) (Artigas and Perez, 1964; Thatcher 1970); <i>Opisthorchis guayaquilensis</i> Rodríguez, Gómez Lince and Montalvan, 1949
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Distribution	Brazil, Canada, Colombia, Ecuador, Panama, United States, Venezuela
Infection in people	Reported from Ecuador, 245 persons in lowland area were examined; 18 of them passed eggs of this fluke
1 st int. host	Aquatic snails
2 nd int. host	Fish: white sucker <i>Catostomus commersoni</i>
Final hosts	Dog, coyote, cat, marsupial (<i>Didelphis marsupialis</i> , <i>Philander opossum</i>), human
References	Chai <i>et al.</i> 2005a; MacLean <i>et al.</i> 2006; Mas-Coma and Bargues 1997

***Clonorchis sinensis* (Cobbold, 1875) Looss, 1907**

Distribution	China, Far East of Russia, Japan, Korea, North Vietnam, Taiwan
Infection in people	About 7-10 million people are infected, and 290 million people are at risk.
1 st int. host	Freshwater snails: <i>Parafossarulus manchoricus</i> , <i>P. anomalospiralis</i> , <i>P. sinensis</i> , <i>Bithynia fuchsiana</i> , <i>B. chaperi</i> (Bithyniidae), <i>Allocinma longicornis</i> (Hydrobiidae), <i>Melanoides tuberculata</i> , <i>Tarebia granifera</i> (Thiaridae), <i>Assiminea lutea</i> (Assimineidae), <i>Semisulcospira libertine</i> (Pleuroceridae)
2 nd int. host	Cyprinid fish: <i>Macropodus opercularis</i> , <i>Hypophthalmichthys molitrix</i> , top mouth minnow: <i>Pseudo rasbora parva</i> , grass carp: <i>Ctenopharyngodon idella</i> , common carp: <i>Cyprinus carpio</i> , Crucian carp: <i>Carassius auratus</i> , long nose barbel: <i>Hemibarbus longirostris</i> , goby minnow <i>Pseudogobio esocinus</i> , black striped gudgeon: <i>Pungtungia herzi</i> , <i>Zacco</i> spp., etc.
Final hosts	Cat, dog, pigs, rats, hog, wild cat, marten, badger, mink, weasel, fish-eating animals, rat (<i>Rattus norvegicus</i>), human
References	Bray <i>et al.</i> 2008; Chai <i>et al.</i> 2005a; Choi 1976; De <i>et al.</i> 2003; IARC 1994; Keiser and Utzinger 2009; Le 2000; Mas-Coma and Bargues 1997; Traub <i>et al.</i> 2009; Yu and Mott 1994; Zhang <i>et al.</i> 2007

***Metorchis albidus* (Braun, 1883) Looss, 1899**

Distribution	Denmark, France, Germany, England; Russia
Infection in people	No information in human, this species have been found in cat
1 st int. host	Snails: <i>Ammicola limosa</i> , <i>Bithynia troscheli</i> (= <i>Codiella troscheli</i>)
2 nd int. host	Freshwater cyprinoid fishes
Final hosts	Cat, fox, gray seal, birds, human
References	Bray <i>et al.</i> 2008; Bowman <i>et al.</i> 2012; Serbina and Iurlova 2002; Sherrard-Smith <i>et al.</i> 2009

Metorchis bilis

Distribution	Europe
Infection in people	Human infections have reported from the Ob River basin (West Siberia)
1 st int. host	Snail: <i>Bithynia</i> spp.
2 nd int. host	Freshwater fish
Final hosts	Fox, dog, cat, seal, raccoon
References	Eckert <i>et al.</i> 2005; II'inskikh <i>et al.</i> 2007; Schuster <i>et al.</i> 2007; Taylor <i>et al.</i> 2007; Mordvinov <i>et al.</i> 2012

***Metorchis conjunctus* (Cobbold, 1860) Looss, 1899**

Synonyms	<i>Distoma conjunctum</i> Cobbold, 1860; <i>Parametorchis canadensis</i> Price, 1929; <i>P. intermedius</i> Price, 1929; <i>P. manitobensis</i> Allen and Wardle, 1934; <i>P. noveboracensis</i> Hung, 1926
Distribution	Canada, North United States
Infection in people	Human infection reported from an Indian patient in Canada
1 st int. host	Freshwater snail: <i>Ammicola limosa porata</i>
2 nd int. host	Fish: common sucker <i>Catostomus commersonii</i>
Final hosts	Fish eating mammals, dog, cat, wolf, fox, raccoon, mink, fish-eating mammals, human
References	Axelson 1962; Bowman <i>et al.</i> 2012; Chai <i>et al.</i> 2005a; Mas-Coma and Bargues 1997; Taylor <i>et al.</i> 2007

***Metorchis orientalis* Tanabe, 1919**

Synonyms	<i>Metorchis albidus</i> Hsü, 1934
Distribution	China, Japan
Infection in people	In Ping Yuan country of Guangdong province (China), the infection rate was 4.2%
1 st int. host	Freshwater snail: <i>Parafossarulus striatulus</i>
2 nd int. host	Freshwater cyprinoid fishes
Final hosts	Dog, cat
References	Bowman <i>et al.</i> 2012; Lin <i>et al.</i> 2001

***Opisthorchis felineus* (Rivolta, 1884) Blanchard, 1895**

Synonyms	<i>Campula feline</i> Cholodkowsky, 1898; <i>Dicrocoelium felineus</i> Moniez, 1896; <i>Distoma conus</i> Gurlt, 1831; <i>D. felineum</i> Rivolta, 1884; <i>D. lanceolatum felis cati</i> Siebold, 1836; <i>D. lanceolatum canis familiaris</i> Tright, 1889; <i>D. sibiricum</i> Winogradoff, 1892; <i>D. winogradoffi</i> Jaksch, 1897; <i>Opisthorchis tenuicollis felineus</i> Erhardt, 1935; <i>O. wardi</i> Wharton, 1921
Distribution	France, Germany, Greece, Italy, Russia, Spain, Poland
Infection in people	The global infection is estimated at about 1.6 million
1 st int. host	Freshwater snails: <i>Bithynia inflata</i> (= <i>Codiella inflata</i>), <i>Bithynia troscheli</i> (= <i>Codiella troscheli</i>), <i>Bithynia tentaculata</i> (= <i>Codiella tentaculata</i>), <i>B. leachi</i> (= <i>Codiella leachi</i>), <i>B. fuchsiana</i> , <i>Parafos sarulus manchouricus</i> , <i>Alloclinma longicornis</i> , <i>Hua ningpoensis</i> , <i>Opisthorchophorus hispanicus</i>
2 nd int. host	Freshwater fishes: <i>Abramis balerus</i> , <i>A. bramae</i> , <i>A. sapa</i> , <i>Alburnus alburnus</i> , <i>Aspius aspius</i> , <i>Barbus barbus borysthenticus</i> , <i>Blicca bjoerkna</i> , <i>Carassius carassius</i> , <i>Chondrostoma nasus</i> , <i>Cobitis taenia</i> , <i>Cyprinus carpio</i> , <i>Gobio gobio</i> , <i>Leucaspis cephalus</i> , <i>L. delineates</i> , <i>Leuciscus idus</i> , <i>L. leuciscus</i> , <i>L. rutilus</i> , <i>Phoxinus chekanowskii</i> , <i>P. phoxinus</i> , <i>Polecus cultratus</i> , <i>Rutilus rutilus</i> , <i>Scardinius erythrophthalmus</i> , <i>Tinca tinca</i> , <i>Idus melanotus</i>
Final hosts	Dog, red-, silver- and polar foxes, cat, wolverine, domestic and wild hogs, maren, beaver, common otter (<i>Lutra lutra</i>), European (<i>Mustela putorius</i>), Siberian weasel (<i>Mustela sibirica</i>), sable (<i>Martes zibellina</i>), rat (<i>Rattus norvegicus</i>), water vole (<i>Arvicola terrestris</i>), lagomorphs (<i>Oryctolagus cuniculus</i>), grey seal (<i>Halichoerus grypus</i>), Caspian seal (<i>Phoca caspica</i>), bearded seal (<i>Erignathus barbatus</i>), lion (<i>Felis leo</i>), pig, human
References	Armignacco <i>et al.</i> 2008; Chai <i>et al.</i> 2005a; Dawes 1956; Eckert <i>et al.</i> 2005; Le 2000; Mas-Coma and Bargues 1997

***Opisthorchis tenuicollis* (Rudolphi, 1819) Stiles and Hassall, 1896**

Synonyms	<i>Distoma tenuicollis</i> Rudolphi, 1819; <i>D. viverrini</i> Poirier, 1886; <i>Opisthorchis viverrini</i> Stiles and Hassall, 1896; <i>O. tenuicollis-felineus</i> Looss, 1899 etc.
Distribution	Asia, Europe
Infection in people	Human infection was reported but the exact locality was unknown.
1 st int. host	Snail
2 nd int. host	Cyprinid fishes
Final hosts	Dog, cat, civet cat, bearded seal, grey seal, common porpoise, human
References	Dawes 1956; Bowman and Georgi 1963

***Opisthorchis viverrini* (Poirier, 1886) Stiles and Hassall, 1896**

Distribution	Cambodia, Laos, South Vietnam, Thailand
Infection in people	About 9 million people globally are estimated to be infected with this fluke
1 st int. host	Freshwater snails: <i>Bithynia siamensis goniomphalus</i> , <i>B. s. funiculata</i> , <i>B. s. siamensis</i> , <i>B. s. laevis</i> , <i>Melanoides tuberculata</i>
2 nd int. host	Cyprinid fishes, mainly <i>Barbodes gonionotus</i> , <i>Carassius auvatus</i> , <i>Cyclocheilichthys apogon</i> , <i>C. repasson</i> , <i>C. siaja</i> , <i>Puntius brevis</i> , <i>P. leiocanthus</i> , <i>P. partipentazona</i> , <i>P. orphoides</i> , <i>Esomus metallicus</i> , <i>Hampala dispar</i> , <i>H. macrolepidora</i> , <i>Osteochilus</i> sp.
Final hosts	Cat, rabbits, guinea pigs, albino rats, dog, rat, civet cat, fish-eating mammals, human
References	Chai <i>et al.</i> 2005a; De <i>et al.</i> 2003; IARC 1994; Keiser and Utzinger 2009; Kumar 1999; Le 2000; Mas-Coma and Bargues 1997; Yu and Mott 1997

***Pseudamphistomum aethiopicum* Pierantoni, 1942**

Distribution	Ethiopia
Infection in people	Human infection reported in Ethiopia
1 st int. host	Snail
2 nd int. host	Fish
Final hosts	Mammals, human
References	Mas-Coma and Bargues 1997; Yamaguti 1971

***Pseudamphistomum truncatum* (Rudolphi, 1819) Lühe, 1908**

Distribution	Europe (France, Germany, Hungary, Italy, Russia, etc.) and North America
Infection in people	Human infection reported in River Kama (USSR) where this species was found in 31 patients.
1 st int. host	Snail
2 nd int. host	Cyprinoid fishes
Final hosts	Cat, dog, fox, seal, skunk, mink, otter, human
References	Bray <i>et al.</i> 2008; Bowman <i>et al.</i> 2012; Mas-Coma and Bargues 1997

and intermediate hosts of some minute intestinal trematodes (Chai *et al.* 2005a; Yu and Mott 1994; Toledo *et al.* 2006).

Fish-borne zoonotic trematodes in aquaculture

Aquaculture plays an important role in providing food for domestic consumption and generating foreign currency through export of aquaculture products (General Directorate of Statistics of Vietnam 2012). The aquaculture systems include marine, brackish water and freshwater aquaculture. The freshwater aquaculture environments include ponds, canals, cages, net enclosures and pens in reservoirs, lakes, rivers, canals, and paddy fields (Phan *et al.* 2010a). Depending on the production mode and the cultivation area, they can be divided into commercial fish culture system and small-scale poly- or monoculture farming systems (Thien 2011).

Aquaculture practices are similar throughout Asia (Guo 2001) and in endemic areas these practices may directly impact prevalence and persistence of FZTs (Phan *et al.* 2010a, b; Chi *et al.* 2008). Particularly in northern Vietnam where small-scale family-based systems are mainly practiced (Phan *et al.* 2010b). Cultured fish is a main protein source for the households and consumed by the families at any time of the year (Thien 2011). This system is named the VAC system in Vietnam and is considered as an ecological way of using farm products in natural cycles (Tai *et al.* 2004). In the traditional form, the system has three functional units, including a garden (Vuon in Vietnamese), a fish pond (Ao), and an animal shed (Chuong). Manure from the husbandry is used to fertilize ponds, so as to stimulate algal growth and subsequently fish growth, and remnants from garden products and fish remains can be fed to dogs, cats or pigs. Mud from fish ponds is used to fertilize gardens or fields (Dung *et al.* 2010). The recirculation of waste material including human and animal manure is conducive for the life cycle of FZT. Eggs of trematodes will go with feces of their host into the pond, where snails and fishes are available as the first and the second intermediate hosts.

Fishborne zoonotic liver flukes

The human liver flukes are a closely related group of trematodes belonging to the family Opisthorchiidae, and have similar life cycles and epidemiologies (Chai *et al.* 2005a). Almost all of them have in common the hepatic location (bile ducts, gall bladder) of the adult stage of the parasite at the level of the definitive host. The most important species are *Clonorchis sinensis*, *Opisthorchis viverrini* and *O. felinus* but nine other species have been reported to infect humans.

Clonorchis sinensis

Clonorchis sinensis is the most important species of FZT in East Asia (Rim 1990; Chen *et al.* 1994; Hong 2003). It is widely distributed in this region (Table I). In Japan, this para-

site was formerly quite prevalent, but has been successfully controlled since the 1960s (Chen *et al.* 1994; Hong 2003). Current endemic areas of clonorchiasis include China, South Korea, North Vietnam, Taiwan, and the Far East of Russia (Mas-Coma and Bargues 1997). In this wide geographical zone, the incidence of clonorchiasis varies considerably from one district to another, even within small regions (Rim 1982a). Infections with *C. sinensis* have been reported in Thailand, Malaysia, Singapore, Laos and Philippines (Cross and Basaca-Sevilla 1984) but these were among immigrants or acquired from fish imported from endemic countries.

In China, clonorchiasis has been detected in 24 provinces, municipalities and autonomous regions (Chen *et al.* 1994). Southern regions, such as Guangdong, Guangxi, Zhuangzu, and northern regions, such as Heilongjiang, Jilin and Liaoning appear to be the zones with highest infection with prevalence ranging from 1 to 57% (Li 1991).

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). The disease continues to be found in almost every city/county, with prevalence in the range 0 and 57%; prevalence over 20% was considered as heavy endemic areas (Chen 1991; Cross 1984; Rim 1986). That disease is extending to new endemic localities in which human prevalence of up to 10–20% are found (Chen 1991).

In Korea, endemic areas are scattered over the country and the most extensive and intensive endemic regions are found mainly along Nakdong River and lower reaches of other rivers (Rim 1982a, 2005), with prevalence of up to 40% (Rim 2005). According to Rim (1990, 2005), Joo and Hong (1991) and Maurice (1994) the overall prevalence slowly decreases due to mass treatment programmes from 4.6% in 1971 to 2.4% in 2004.

In Vietnam, the most heavily infected area is found in the northern parts of the country, in the Red River delta e.g. Nam Dinh, Ninh Binh, Thai Binh, etc. provinces and some provinces in the center e.g. Thanh Hoa, Nghe An (Hop *et al.* 2007; Le 2000; Rim 1986).

In Russia, human cases have been reported in the far eastern part, namely in the Amur River Territory and Khabarovsk Territory (Korablev and Koltsov 1992; Posokhov 1982; Posokhov *et al.* 1987).

The distribution of *C. sinensis* is partly dependent on the distribution of the first intermediate host snails. Nine species of fresh water snails have been reported as first intermediate host for *C. sinensis*, including *Parafossarulus manchouricus* (Syn. *P. striatulus*), *P. anomalospiralis*, *P. sinensis*, *Bithynia fuchsiana*, *B. chaperti*, *Allocinma longicornis* (Family: Bithyniidae), *Tarebia granifera* (Syn. *Thiara granifera*), *Melanoides tuberculata* (Family: Thiaridae), *Assiminea lutea* (Family: Assimineidae) and *Semisulcospira libertina* (Family: Pleuroceridae) (Mas-Coma and Bargues 1997). The status of the thiarid species, *Tarebia granifera* and *Melanoides tuberculata*, however, is questionable (Dung *et al.* 2010). Bithynid snail species are the main first intermediate hosts in all the endemic

regions where transmission of the parasite is accomplished, such as in China, Taiwan, Korea, Japan, Vietnam and Far East of Russia (Mas-Coma and Bargues 1997). Generally the prevalence of *C. sinensis* in snails is low (Mas-Coma and Bargues 1997; Zhang *et al.* 2007). The release of cercariae from snails is high and occurs over a fairly long period thus ensuring propagation (Keiser and Utzinger 2009; Mas-Coma and Bargues 1997).

A crude estimate of the global number of people infected with *C. sinensis* was about 19 million (Stoll 1947), while Lun *et al.* (2005) and Fang *et al.* (2008) mentioned that 35 million people are infected globally, and 15 million of these are from China. However, according to several documents, it has been estimated to be about 7–10 million (World Health Organization 1995; Crompton 1999) and 290 million people are at risk (Rim *et al.* 1994).

Mas-Coma and Bargues (1997) mentioned that parasites lodge and mature in the medium and large intrahepatic ducts in the liver, especially those of the left liver lobe. Early changes seen in the biliary ducts are excessive mucin formation, desquamation, and adenomatous hyperplasia of the duct epithelium with goblet cell metaplasia (Markell and Goldsmith 1984). In the chronic stage, progressive bile duct thickening dilatation, ductal, and periductal fibrosis are noted. Biliary stasis results in secondary infection leading to pericholangitis, pyelophlebitis, cholangiohepatitis, and multiple abscesses (Markell and Goldsmith 1984). Fibrosis rarely appears in the portal tracts, and portal cirrhosis has been described only infrequently. The flukes may cause dilation and fibrosis (Markell and Goldsmith 1984). The organ may be enlarged to 2 or 3 times normal size in massive infection cases (Dooley and Naefie 1976). The external surface of the liver may show pale cystic areas and linear whitish streaks corresponding to dilated bile ducts may be observed (Dooley and Naefie 1976). The cut surface reveals a normal parenchyma punctuated by bile ducts with walls 2 to 3 times their normal thickness (Dooley and Naefie 1976).

The infection may persist up to 26 years in human hosts (Attwood and Chou 1978). Lightly infected persons (<100 flukes) usually show no symptoms, but in moderate or progressive cases the clinical symptoms show loss of appetite, indigestion, fullness of abdomen, epigastric distress unrelated to meals, discomfort in the right upper quadrant, diarrhea, edema and some hepatomegaly (Belding 1965; Keiser and Utzinger 2009). In heavily infected cases (101 to 1,000 flukes) the symptoms are weakness and lassitude, epigastric discomfort, paresthesia, loss of weight, palpitation of heart and tachycardia, diarrhea, vertigo, tetanic cramps and tremors, and toxemia from liver impairment (Belding 1965; Keiser and Utzinger 2009). In patients with a very heavy worm burden (up to 25,000 flukes) the symptoms include acute pain in the right upper quadrant, marked gastrointestinal disturbances, with a syndrome associated with portal cirrhosis, splenomegaly, ascites and edema (Keiser and Utzinger 2009; Mas-Coma and Bargues 1997).

Opisthorchis viverrini

Opisthorchis viverrini is a particularly serious liver fluke (Rim 1982b; Kaewkes 2003) and is highly prevalent in South-east Asia, including Thailand, Laos, Cambodia and South Vietnam (IARC 1994; Keiser and Utzinger 2009; Le 2000; Mas-Coma and Bargues 1997; Yu and Mott 1994). Fish-eating mammals such as cat, rat, dog, and civet cat are definitive hosts other than humans, and they are often found infected with *O. viverrini*, even in regions where the infection is not known to occur in humans (Mas-Coma and Bargues 1997). In Malaysia and southern China, reports on human infection by *O. viverrini* are limited; however, it has been found in cats (Mas-Coma and Bargues 1997; Bisseru and Chong 1969). Worth mentioning is the frequency of *O. viverrini* infection as reported in studies on human emigrants from these endemic countries and carried out in other parts of the world, such as Thais in Japan; Laotians and Thais in the United States; Laotians in Germany; Laotians, Vietnamese and Cambodians in France; Thais, Laotians and Vietnamese in Czech Republic or Thais in Kuwait (Mas-Coma and Bargues 1997). About 9 million people are estimated to be infected globally (Yossepowich *et al.* 2004).

The transmission of the parasite to the fresh-water snail hosts is related to the defecating habits of the definitive hosts, mainly human but also other fish-eating mammals, especially cats and dogs (Mas-Coma and Bargues 1997; Yu and Mott 1994; IARC 1994). In highly endemic areas of Thailand, *Bithynia* spp. snails are normally present in water bodies. The absence of latrines and disposal of untreated faeces into the environment around villages constitutes an important factor responsible for the propagation of the parasite (Forrer *et al.* 2012; Nithikethkul *et al.* 2004; Sayasone *et al.* 2007). The habit of people defecating on the ground in the bush not far from their houses, many of which are situated around the lakes, ponds, streams, etc., results in contamination of the water by the faeces containing *O. viverrini* eggs during the rainy season (Mas-Coma and Bargues 1997). Human and other animals acquire the infection by ingestion of fish, primarily cyprinoid fishes, containing metacercariae. The transmission of *O. viverrini* from humans to fish via snails is the net result of complex interplay between hosts and parasites that is invariably regulated by seasonal environmental conditions, especially water temperature and duration and amount of rainfall (Brockelman *et al.* 1986).

Thailand is the most endemic country for opisthorchiasis due to *O. viverrini* (Chai 2005; IARC 1994; Mas-Coma and Bargues 1997; Kaewpitoon *et al.* 2008; Sripa *et al.* 2003; Sithithaworn *et al.* 1997). 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 in Chai *et al.* 2005a). The estimated number of infected people is currently about 6 million (Jongsuksuntigul and Imsomboon 2003; Sripa *et al.* 2003).

It was estimated that 1.7 million people were infected with *O. viverrini* in Laos in 1992 (Rim *et al.* 1994; World Health Organization 1995). The Mekong River basin is the most heavily infected area in Laos (Chai *et al.* 2005a) and the parasite is widespread because of geographical location and similar eating habits of people. Detailed investigations on *O. viverrini*, however, are scarce in this country (Sayasone *et al.* 2007). Most surveys have been done in the Vientiane province (Chai *et al.* 2005b) and its immediate surrounding areas (Chai *et al.* 2005b, 2007; Forrer *et al.* 2012; Sayasone *et al.* 2007). Sayasone *et al.* (2007) found a prevalence of 58.5% of people infected with *O. viverrini* in a southern rural district, while Chai *et al.* (2007) found 67.1% people in Savannakhet province infected with both small liver fluke and intestinal flukes. An exact knowledge on the distribution of human infection by *O. viverrini* in the interior of Laos is still lacking (Mas-Coma and Bargues 1997), although Forrer *et al.* (2012) presented the risk map of *O. viverrini* in Champasack province, and found 61.1% people infected with this parasite.

Only few official reports or published data on *O. viverrini* infection in Cambodia prior to 1997 are available (Mas-Coma and Bargues 1997). A small survey in primary schoolchildren from Kampongcham province showed a prevalence of *Opisthorchis* spp. of 4% from 251 fecal specimens in 2002 (Lee *et al.* 2002). Current studies have confirmed high prevalence of *O. viverrini* in several provinces of this country, e.g. Takeo province with average prevalence of *O. viverrini* infection in human was 47.5% (Yong *et al.* 2012) and Kratie province 4.6% (Sohn *et al.* 2012).

In Vietnam, several southern provinces such as Phu Yen, Binh Dinh, Dak Lak have reported infections with *O. viverrini* and with prevalence about 10% (De *et al.* 2003; De 2004b).

The life span of *O. viverrini* is over 10 years (Harinasuta and Harinasuta 1984; International Agency for Research on Cancer 1994). Patients infected with *O. viverrini* were found to have pathological changes in the extra- and intrahepatic bile ducts and gall bladder (Mas-Coma and Bargues 1997). The movement of flukes along the biliary ducts results in adenomatous hyperplasia of the biliary epithelium and thickening of their walls with the fibrous connective tissue, bile ducts becoming hypertrophied and dilated (Kim 1984). Enlargement of the liver is observed in most cases, particularly in massive infections. The gross hepatic pathology in heavy infection is characterized by subcapsular bile duct dilatation on the liver surface (Pairojkul *et al.* 1991a, b). In early infection, there is no hyperplasia of epithelium, no proliferation of fibrous connective tissues, and the ducts are lined by a single layer of columnal epithelium. Suppurative cholangitis occurs, and the infection may extend into the parenchyma of the liver tissue, causing hepatitis with the formation of micro and macroabscesses (Pairojkul *et al.* 1991a; Mas-Coma and Bargues 1997; Rim 1982b).

Morbidity in *O. viverrini* infection is not clear. Few infected people, even among those with heavy infection, suffer detectable signs or symptom by physical examination, but this

does not mean that the parasite is non-pathogenic (Mas-Coma and Bargues 1997; International Agency for Research on Cancer 1994). Unfortunately, the asymptomaticity of *O. viverrini* infections becomes extremely dangerous since it contributes to enhancement of carcinogenesis, a leading cause of death among northeast Thais (Mas-Coma and Bargues 1997). The frequency of hepatobiliary abnormalities, e.g. gall bladder enlargement and poor function and simultaneously the odds of cholangiocarcinoma, rise sharply with intensity of infection (Khuhaprema and Srivatanakul 2007; Sithithaworn *et al.* 1994; Sripa and Pairojkul 2008; Sriamporn *et al.* 2004). This risk is clearly the highest incidence of liver cancer in the world (Sithithaworn *et al.* 1994).

Opisthorchis felineus

Opisthorchis felineus is a species very close to *O. viverrini* from the morphological point of view; however, several differences have been distinguished e.g. body size, oesophagus, distance between the anterior testis and ovary (Mas-Coma and Bargues 1997).

This species infects several species of fish-eating mammals, including humans in southern, central and eastern Europe, i.e. Italy, Albania, Greece, Switzerland, Holland, Germany, Poland, Ukraine, Russia and in Asia it is present in Turkey (Zavoikin 1991; World Health Organization 1995). The distribution of *O. felineus* in freshwater fish and human opisthorchiasis do not coincide; human infection occurs at some distance from the main endemic areas because of the natural fish migration patterns and transport of fish for sale (World Health Organization 1995).

Although humans may be considered an accidental host, this liver fluke is now known to infect approximately 1.2 million people in Russia and 1.5 million in the former Union of Soviet Socialist Republics (Rim *et al.* 1994). The global number of cases is estimated to be about 1.6 million (Yossepowitch *et al.* 2004). The largest number of registered infections (over 900,000 extrapolated cases) were reported from the two districts of T'umen' and Tomsk in the Russian Federation (IARC 1994; Mas-Coma and Bargues 1997). High prevalences were also observed in areas along the Volga-Kama river basin, along river basin in the Novosibirsk, Krasnojarsk, Kurgan, Kemerovo, Serdlovsk, Omsk and Tomsk districts and the Altaj territory (Iarotski and Be'er 1993; IARC 1994).

Infections also occur in Ukraine and Kazakhstan (Iarotski and Be'er 1993; IARC 1994). Reports from Ukraine indicate that infection is found in the Sumy, Poltava and Černigov districts within the Dnepr River basin, with prevalences of 5–40%. In Kazakhstan, the average prevalence in six endemic districts was less than 10% (Iarotski and Be'er 1993). In Germany, 8% of the population of one rural area was reported to be infected in 1929, but more recent surveys on parasitic zoonosis in this region indicated that the infection no longer persists (Hinz 1991).

Hepatic lesions produced by *O. felineus* are similar to those caused by *O. viverrini* (IARC 1994; Mas-Coma and Bargues 1997). During the course of their development, they initiate inflammatory and proliferative changes of the biliary epithelium, which continue after the worms have matured and are accompanied by fibrosis of the distal biliary ducts. If the infection is intensified by continued exposure, the pathological process may extend to the bile ducts and gall-bladder and result in cirrhosis (IARC 1994). The degree of pathogenicity and clinical involvement depends largely on the number of parasites and the duration of infection (IARC 1994). Normally, small numbers of worms do not cause serious damage and do not give rise to clinical signs. In the Russian Federation, many apparently healthy people have been found to be infected. However, their worm burden was light, with average of no more than 200 eggs/g faeces (Bronstein *et al.* 1991). When several hundred or thousand worms are present, severe damage to the liver and pancreas can occur (Rim 1982b).

Other fishborne zoonotic liver flukes

Amphimerus pseudofelineus has apparently a wide geographic range and low specificity for its definitive hosts. It is a parasite of the bile-ducts of dogs, coyotes, domestic cats and marsupials (*Didelphis marsupialis*, *Philander opossum*) in the USA, Panama, Colombia, Venezuela, Ecuador and Brazil. Rodriguez *et al.* (1949) made fecal examinations of 245 persons in a lowland area of Ecuador and found 18 of them infected with this species. Restrepo (1962) reported finding 6 cases out of 176 persons residing on the Amazon River, in Colombia. No additional human report and the pathology, symptom of this species appears in the literature (Mas-Coma and Bargues 1997).

Amphimerus noverca has been reported in the gall bladder at autopsy of two people in India (McConnell 1876 quoted in Mas-Coma and Bargues 1997). Proliferative changes in pancreatic duct epithelium and some epithelial desquamation and periductal fibrosis have been observed in pigs, in case of heavy infection in the pancreas (Sinha 1968).

Metorchis conjunctus was reported in the stool from an Indian patient in Saskatchewan, Canada (Cameron 1945 in Mas-Coma and Bargues 1997). Eggs of this species have also been reported in stools of humans native of Greenland (Baboti *et al.* 1961). The life cycle of this species is similar to that of species of *Clonorchis* and *Opisthorchis*. At the level of the bile ducts, adult worms may cause lesions similar to those produced by *Clonorchis sinensis* and *Opisthorchis felineus*: proliferation of biliary epithelium, biliary congestion and some degree of cirrhosis (Mills and Hirth 1968).

Metorchis albidus affects carnivorous mammals, but they are considered as a potential source of infection to humans, at least in Kazakhstan (Sidorov and Belyakova 1972) and Lithuania (Linnik 1983).

Metorchis bilis infections have occurred in people living in several regions of the Ob River basin in the West Siberia.

The infection of this species was more common in many of the serologically tested people than *Opisthorchis felineus* (Il'inskikh *et al.* 2007). The disease caused by *M. bilis*, is very close to opisthorchiasis in symptomatology.

Metorchis orientalis was originally described from a dog and cat in Japan and China (Bowman *et al.* 2012). Lin *et al.* (2001) reported a prevalence of infection of this species of 4.2% in human populations in Ping Yuan County of Guangdong Province, China. The infection rate of ducks, cats, and dogs are available 66.7%, 78.6% and 23.5%, respectively.

Opisthorchis tenuicollis is very similar to *O. felineus* (Dawes 1956). Infections in people have been reported (Bowman and Georgi 1963). There are few reports about its prevalence of infection in cats and pigs in India (Gatne *et al.* 2008; Chakrabarty and Sinha 1960).

Pseudamphistomum truncatum parasitizes bile ducts of various mammals, including humans. Instances of human infection are relatively few (Bittner 1928; Petrov 1940; Delianova 1957 in Mas-Coma and Bargues 1997). In a district near the River Kama (USSR), *P. truncatum* was found in bile of up to 31 patients (Khamidullin *et al.* 1991). Vinogradov (1892) reported young stages of a fluke from a human source in Russia. There are no studies on the pathology caused in humans, but liver pathological effects are known in seals.

Pseudamphistomum aethiopicum has been found in humans in Ethiopia and caused cyst-like nodules in the internal wall of the small intestine (Cacciapuoti 1947 in Mas-Coma and Bargues 1997).

Intestinal flukes

Among 47 fishborne zoonotic intestinal fluke species of 3 families which have been detected in humans, Nanophyetidae has only one species, while Echinostomatidae has 10 species (Table I). The family Heterophyidae has the highest number, with 36 species. In this section, we only review material at the family level.

Heterophyidae

The species of Heterophyidae are considered minute intestinal flukes because of their small sizes, i.e. typically less than 0.5 mm in length. Adult worms are found in fish-eating birds and mammals in addition to humans (Chai 2005a; Yu and Mott 1994). Although generally not considered of significant clinical importance compared to the liver flukes, several species, including *Stellantchasmus falcatus*, *Haplorchis* spp. and *Procerovum* spp., can cause significant occasionally fatal pathology, i.e. diarrhea, mucus-rich faeces, abdominal pain, dyspepsia, anorexia nausea, and vomiting (MacLean *et al.* 2006; Toledo *et al.* 2006, 2011; World Health Organization 1995; Yu and Mott 1994). In one case, an adult heterophyid was found in the epicardium of the heart (Yu and Mott 1994), and sometime eggs were found in the brain and in sections of the spinal

cord of humans (MacLean *et al.* 2006; World Health Organization 1995; Yu and Mott 1994). The exact mechanisms of pathogenesis responsible are not clear but may be related to invasion of the circulatory system by trematode eggs (Chai *et al.* 2005a). Disease is usually related to worm burden which in some cases can be very heavy (MacLean *et al.* 2006). Another very important issue related to heterophyids is the difficulty of differentiating eggs from those of the liver flukes in human fecal examinations, which may cause inaccurate estimates of the prevalence of both trematode groups (Chai and Lee 1991, 2002; Johansen *et al.* 2010).

Chai and Lee (2002) listed 12 species of heterophyids that parasitize humans in Korea, including a single species in the genera *Heterophydosis*, *Pygidiopsis*, *Stellantchasmus* and *Centrocestus*, two species of *Stictodora*, three species of *Metagonimus*, and three species of *Heterophyes*. In humans, heterophyiasis and metagonimiasis are the best known diseases associated with heterophyid parasitism (Fried *et al.* 2004). The two most prevalent species of human heterophyids are *Heterophyes heterophyes* and *Metagonimus yokogawai* (Toledo *et al.* 2011). The former species has been reported in humans from Egypt, Sudan, Iran, Turkey, Tunisia, Siberia, Europe, Russia, China, Taiwan, Philippines, Indonesia, India and Vietnam (Yu and Mott 1994). Kumar (1999) estimated that 10,000 people were affected by heterophyiasis in Egypt in 1992 and reported a high prevalence of heterophyiasis in China with estimates of 230,000 infected individuals (Fried *et al.* 2004).

Adult flukes inhabit the mucosa of the middle part of the small intestine, and eggs released by the worms may penetrate the gut and travel to vital organs via the circulatory/lymphatic system (MacLean *et al.* 2006). Eggs of different heterophyid species have been recovered from capillaries of the brain, heart, lungs, spleen and liver, where space-occupying granulomatous lesions may induce clinical pathology (MacLean *et al.* 2006). The flukes appear to live for less than a year. In light infections, fatigue and mild gastrointestinal concerns such as epigastric pain, diarrhea and anorexia are present; in heavy infections, abdominal cramps, malabsorption and weight loss may occur (MacLean *et al.* 2006). The diagnosis is made by recovery of the eggs in fecal examinations (Chai *et al.* 2005a).

Echinostomatidae

The Echinostomatidae flukes are small, typically 3–10 mm in length and 1–3 mm in width (Fried *et al.* 2004). At least 30 genera and more than 200 species of this family are known in the world, 15 species are reported to infect humans (Chai *et al.* 2005a; Huffman and Fried 1990). Among them, 10 species were reported as fish-borne echinostome species (Table I). Human echinostomiasis is endemic to Southeast Asia and the Far East, i.e. mainland China, Taiwan, India, Korea, Malaysia, Philippines, Indonesia, Thailand and Vietnam (Bandyopadhyay and Nandy 1986; Le 2000), but infections probably occur also in Africa (Yu and Mott 1994). *Echinostoma hortense* and

Echinochasmus japonicus are the most important species because of their wide distribution and high prevalence in endemic areas (Chai *et al.* 2005a). Two separate life cycles for several different species of echinostomes were demonstrated to occur in endemic areas, i.e., the “human cycle” and the “sylvatic cycle”, which has a zoonotic potential (Fried *et al.* 2004). In endemic areas, the disease occurs focally and is associated with common socio-cultural practices (Carney 1991). The prevalence of infection ranges from 65% in Taiwan and 44% in the Philippines to 5% in mainland China and from 50% in northern Thailand to 22% in Korea (Fried *et al.* 2004). However, the disease is under-reported in the endemic areas and is most prevalent in remote rural places among the low-wage earning population and among women of child-bearing age (Fried *et al.* 2004). In many countries, echinostomiasis is aggravated by socio-economic factors such as poverty, malnutrition and an explosively growing free-food market; and lack of food inspection, poor sanitation, other helminthiasis and declining economic conditions also contribute (Carney 1991; Fried *et al.* 2004).

Chai and Lee (1990) mentioned that morbidity and mortality due to echinostomiasis are difficult to assess. It is because of a prolonged latent phase, asymptomatic presentations, a short acute phase, and similarity of clinical symptoms to other intestinal helminthiasis. Clinical symptoms are related to parasite load (Chai *et al.* 1994; MacLean *et al.* 2006). In light to moderate infections, patients have been observed to have anemia, headache, dizziness, stomach ache, gastric pain, and loose stools (Bundy *et al.* 1991; Chattopadhyay *et al.* 1990; Field *et al.* 2004). Other symptoms such as eosinophilia, abdominal pain, profuse watery diarrhea, anemia, edema, and anorexia are associated with heavy infections (Chattopadhyay *et al.* 1990). Pathologically echinostomes damage the intestinal mucosa, causing extensive intestinal and duodenal erosions and catarrhal inflammation (Fried *et al.* 2004).

Nanophyetidae

These are small (about 1 mm or less) flukes and the most important species is *Nanophyetus salmicola* (Fried *et al.* 2004). A subspecies of this digenean, also considered as a geographic variant by some researchers, is *N. s. schikhobalowi*, a human parasite in Siberia (Kumar 1999).

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. In animals such as dogs, foxes, and coyotes, however, the fluke has been shown to be the vector of a rickettsia, *Neorickettsia helmintheca*, which causes a serious and often fatal systemic infection known as “salmon poisoning” (Fried *et al.* 2004; Yu and Mott 1994). The *Neorickettsia* bac-

teria is not pathogenic in humans, but mortality in dogs may reach 90% (Schell 1985).

The major risk factors in human infections

In some cultures, raw animals and plants are eaten for medicinal as well as nutritional purposes and this is associated with various diseases, including FZT. Raw crayfish is used to treat measles and transmits paragonimiasis. In Cameroon, raw crab is thought to increase fertility and in Ecuador macerated crab supernatant is given to sick children (Huss *et al.* 2004). Transmission of fish-borne trematodes is associated with behavioral patterns determined by socio-economic and cultural conditions in endemic areas. Consumption of raw fish and shellfish occurs most often around lakes, streams and ponds. Throughout Asia, up to 750 million people are at risk of infection by fish-borne liver flukes (Lima dos Santos and Howgate 2011; Kaiser and Utzinger 2009; World Health Organization 2004). Food safety education may be the most expedient way to control the spread of infections because prevalence is inherently linked to human behavior (Ziegler *et al.* 2011). However, eating habits are deeply rooted in cultures and are resistant to changes.

In Japan, sushi and sashimi are traditional dishes known world-wide. They are prepared from relatively expensive marine fish such as tuna, red snapper, salmon, etc. in the restaurants or sushi bars (Nawa *et al.* 2005). Although various marine fish species may harbor *Anisakis* larvae, fish that are preferentially served in these restaurants are less contaminated or free from *Anisakis* larvae (Nawa *et al.* 2005). Other popular and cheaper marine fish, such as cod, herring, mackerel, etc. tend to be heavily infected with *Anisakis* larvae and are mainly consumed at home or at local restaurants. In rural areas, freshwater or brackish-water fish are consumed as sushi and sashimi (Nawa *et al.* 2005). Various wild animals e.g. frogs, land snails, snakes, backyard chicken, and wild boar are also served as sushi and sashimi, especially in the mountainous areas. They are also consumed raw or undercooked in a variety of ethnic dishes in many Asian countries as well. Because of this, zoonotic parasites are transmitted to humans. Thus, travelers dining in local restaurants or street shops can be expected to have much higher risks of infections with various parasites (Nawa *et al.* 2005). Nowadays, there are several remarkable parasitic diseases associated with eating raw fish in Japan, i.e. (1) anisakiasis, an acute gastrointestinal disease caused by infection with herring worm, *Anisakis* species or the cod worm – *Pseudoterranova decipiens*, (2) diphyllbothriasis (an intestinal infection caused by the fish tapeworm *Diphyllbothriasis latum*), (3) gnathostomiasis, primarily a disease of the skin caused by migration of the larvae of a *Gnathostoma* sp. nematode, (4) paragonimiasis, caused by infection with *Paragonimus* spp. (lung flukes), (5) clonorchiasis/opisthorchiasis, (6) minute intestinal flukes. Infection with *Metagonimus yokogawai*, are still prevalent because people prefer to eat sushi and sashimi prepared from a locally famous freshwater fish “Ayu”

– *Plecoglossus altivelis* (Nawa *et al.* 2005). Examination of stool samples for parasite eggs at Mitsui Memorial Hospital in Tokyo showed that 10–20% of samples were infected with *M. yokogawai*, angiostrongyliasis, an acute or subacute infectious disease of the central nervous system caused by the larval stage of the nematode *Angiostrongylus cantonensis*, and sparganosis, caused by larva of tape worm *Sparganum mansoni* (Nawa *et al.* 2005). Approximately 500 cases of people infected with *Sparganum mansoni* have been reported in Japan but realistic figures are certainly higher (Nawa *et al.* 2005).

Korean cuisine has various raw food dishes e.g. Saengseon hoe or hwal-eo hoe which is thinly sliced raw fish or other raw sea food (similar to Japanese sashimi); yukhoe is raw food made with raw beef and seasoned with soy sauce, sesame oil, and rice wine; gan hoe is raw beef liver with a sauce of sesame oil and salt. Chu (1970) estimated that in South Korea 4.5 million people are infected with *Clonorchis sinensis* and 1.5 million with *Paragonimus westermani*, and both fluke species infect humans through consumption of raw food. Prevalences of these trematodes, however, are slowly decreasing due to mass treatment programmers (Joo and Hong 1991; Maurice 1994).

In South China and Hong Kong, people like to eat congee (rice gruel) with slices of raw fish (Chai *et al.* 2005a; Fried *et al.* 2004). Half roasted or undercooked fish in Guangdong province and raw shrimps in Fujian province are other dishes commonly served in daily meal in China (Chai *et al.* 2005a; Chen *et al.* 1994). Paragonimiasis is acquired by eating wine soaked ‘drunken’ crabs in parts of China. And in Thailand and the Philippines crab juice is used for medicinal purposes as well as using it in food preparations (Huss *et al.* 2004). Echinostome infections are contracted from eating undercooked snails and raw fish in Northern Luzon in the Philippines and in Korea.

In Southeast Asia, the most important of the parasitic diseases is opisthorchiasis, which is distributed throughout the Lower Mekong sub-region, including Northeast of Thailand, West of Laos, central of Cambodia and in the South of Vietnam (Chai *et al.* 2005; Fried *et al.* 2004; Lima dos Santos and Howgate 2011; MacLean *et al.* 2006; Mas-Coma and Bargues 1997; Sripa *et al.* 2003; World Health Organization 1995). The Lower Mekong Basin has numerous rivers, streams, human-made water diversion, irrigation ditches, reservoirs, natural lakes, aquaculture pond, and paddy fields (Grundy-Warr *et al.* 2012) and fisheries are a key source of livelihood, providing the major source of animal protein to large populations. Fishing is occupation by which many farmers supplement their incomes and family diets through small-scale fishing activities (Friend 2007; Gregory and Guttman 1996; Hortle 2008; Poulsen 2003).

In Laos, many rural areas in the Mekong River basin, sticky rice, fermented and raw fish locally known as “pla ra”, “som fak”, and “pla som” are regularly consumed, sometimes on a daily basis (Chai and Hongvanthong 1998; Chai *et al.* 2005a; Rangsin *et al.* 2009). Other traditional raw food is “koi

pla” (a dish made from finely chopped raw fish mixed with chili, lemon-juice, vegetables, and spices) eaten on special occasions (Chai *et al.* 2005a; Grundy-Warr *et al.* 2012). Consumption of koi pla is popular in the fishing and farming villages of northeast Thailand and Lao PDR as a cheap form of protein for local people. Koi pla is relatively quick and easy to prepare, taking approximately 20 minutes, and therefore it is very convenient for fishers and farmers who may be preparing the dish at some distance from their homes (Grundy-Warr *et al.* 2012). High consumption (92%) of raw or partially cooked fish in local dishes, such as koi pla, as well as “pla som” (moderately fermented fish) and “pla ra” or “pa dek” (Laos) (long-term fermented and highly salted fish) undoubtedly help the spread of liver fluke infections in human populations (Grundy-Warr *et al.* 2012). Research in Laos indicates that mostly men eat raw fish dishes and men are resistant to any alteration in their habits (Chai *et al.* 2005; Grundy-Warr *et al.* 2012). However, the same study also notes that women are still at risk because they often taste food, including raw fish dishes, during preparation.

Research in Thailand has indicated that alcohol was portrayed as having the ability to strengthen the body and prevent illness, as a means of pain relief, and a mood enhancer (Grundy-Warr *et al.* 2012). Local fishermen believe that strong alcohol kills germs and worms. There are also associated beliefs that plenti of lime juice on raw fish (nam manao) removes parasites (Grundy-Warr *et al.* 2012). Some women fish-traders consume lao-kao with the men (Fordham 1995). Nevertheless, it is a common practice mostly amongst fishermen, partly due to the fact that after a night’s fishing activity, they are able to consume koi pla and whiskey before they go to sleep in the late morning, whereas, the women still have many activities to do relating to fish processing, marketing, and helping with their families (Grundy-Warr *et al.* 2012).

Cambodia is potential hot-spot for multiple water-borne and food-borne parasitic infections. Average fish dependence of Cambodians is the highest of all countries in the Mekong Basin, and Mekong River and Tonle Sap Lake receive many migratory cyprinid species that are also found in Thailand and Laos (Grundy-Warr *et al.* 2012). Unlike Lao PDR and Thailand, eating “raw fish” is less common in Cambodia while the consumption of the hugely popular “prahoc” (Khmer fermented fish paste) which is popular in both urban and rural contexts (Grundy-Warr *et al.* 2012). However, there has yet to be a systematic study of whether *Opisthorchis viverrini* metacercariae can survive in prahoc made from small cyprinid fishes (Grundy-Warr *et al.* 2012).

Vietnam has two big river systems, the Red River in the North and the Mekong River in the South. In northern Vietnam, common fish species used to prepare raw fish dish, also called “gỏi cá”, are silver carp (*Hypophthalmichthys molitrix*), grass carp (*Ctenopharyngodon idellus*), rohu (*Labeo rohita*), and mrigal (*Cirrhinus mrigala*) (Chi *et al.* 2009; Phan *et al.* 2011). In the rural areas, slices of raw fish are soaked twice in a mild saline (1–3% NaCl) solution, before mixed with rice

powder and eaten with herbs and sauce (Chi *et al.* 2009; Phan *et al.* 2011). Mostly adult men eat raw fish, whereas women mainly eat herbs dipped into the sauce. Children also have meals together with those eating raw fish, but the children consumed other types of food. In these places 32.2% of fish farm household members were infected with FZT (Phan *et al.* 2011). In restaurants, raw fish is prepared in two different ways, i.e. (1) fillets placed on ice and eaten wrapped in vegetables and dipped in various sauces e.g. mustard or wasabi, or (2) fillets served in a sauce of lemon or vinegar (Chi *et al.* 2009). Chi *et al.* (2009) found that 11.8% dishes from Nam Dinh restaurants were infected with heterophyids, while 3.1% of dishes from Hanoi restaurants were infected. Chi *et al.* (2009) also compared metacercariae density in fish meat served raw with that in the remainder of the same fish and found that density in the meat was very low compared to the density in the remainder and it appears that heterophyids are located rather superficially in the fish, i.e. in the skin. This, however, may not be the case for *C. sinensis*. In the mountain areas, local people consume lightly fried crabs and this constitutes a high risk of infection with lung fluke of *Paragonimus* spp. Doanh *et al.* (2007, 2008, 2012) and Le *et al.* (2006) isolated metacercariae of several *Paragonimus* species in crab and experimentally infected cats. The recovered flukes were collected and identified and two of these species were new. The prevalence of paragonimiasis in humans detected by Kato-Katz method ranged from 0.3% in Lang Son, 0.6% in Nghe An province to 0.9–10.9% in Yen Bai and 3.3–11.3% in Hoa Binh province (De 2004a). Doanh *et al.* (2011) used ELISA method for diagnosing infections and they found a prevalence of 12.7% among people in Sinho district of Lai Chau province and 3.3% in Lucyen district of Yenbai province. In parts of southern Vietnam, people eat live fish with raw vegetables, chili and this is always accompanied by intake of strong alcohol, for example rice vodka (De 2009). De (2009), however, did not identify the fish used, nor did he determine the prevalence of metacercaria in these fish nor the prevalence of people infected with FZT. According to the reports from national hospitals and public communication, some patients were reported to be infected with taeniasis/cysticercosis, gnathostomiasis, anisakiasis when they consumed undercooked meat of mammals, frogs, snakes and fishes (De 2009).

Options for FZT control

With the primary purpose to develop a control strategy against FZT infections in aquaculture and thus providing safe food, several approaches have been developed to intervene at various stages of the trematodes’ transmission cycle, i.e. interventions against the adult parasites, preventing eggs from reaching aquaculture ponds, control of the intermediate host snails so as to reduce infection risks in fish, and preventing metacercariae reaching the final host. Due to the complexity of the dynamics of transmission, integration of most of these options should probably be the optimal strategy for control.

Education

In endemic areas, health programs and hygiene instructions may have an important role in the promotion of a safe environment. Instructions cover topics such as hygienic excreta disposal, use of latrines, and the relationship between aquaculture practices and the life cycle of the parasites. Farmers should be provided with guidelines on how to improve their ponds. This could include removal of the top 3–5 cm of mud from the pond bottom and letting the pond dry out for several days before restocking, removal of all aquatic vegetation from the pond to reduce snails and their habitat (Clausen *et al.* 2012). The banks of ponds could be lined with concrete to help control vegetation and possibly thereby reduce snail density (Clausen *et al.* 2012). Furthermore, the inlet tube could be fitted with a mesh filter to help reduce snail entry into the pond; if the mesh size is small the mesh filter must be long, otherwise it could be clogged by mud, vegetation or waste and eventually break due to water pressure (Clausen *et al.* 2012). Reduction of FZT egg contamination of ponds could perhaps be achieved by constructing a 10–15 cm elevated cement barrier all along the pond bank to prevent surface runoff water from entering the pond. Furthermore, the pond could be completely fenced by a 50 cm high fine meshed net placed very close to the pond edge to keep dogs and cats out (Clausen *et al.* 2012). Also farmers should not utilize liquid waste from pigpens and human latrines as fertilizer of ponds and this could be achieved by blocking drains with cement and bricks to prevent fecal contamination from surface runoff water (Clausen *et al.* 2012). In addition, the habit of eating raw or inadequately cooked fish should be changed through propaganda and education.

Treatment

Humans in endemic areas should be examined for FZT eggs and infected humans with clonorchiasis and opisthorchiasis should be treated with specific drugs e.g. praziquantel (Biltricide) at a dose of 40mg/kg body weight in a single administration or three times daily at 25 mg/kg body weight for 3 consecutive days (World Health Organization 2011, 2012). For treatment of infected people with intestinal flukes, single dose of 10–20 mg/kg is satisfactory (Chai and Lee 2002). According to the recommended strategy of World Health Organization (2012), in districts where the prevalence of infection is more than 20%, mass treatment of all residents should be done every 12 months. When the infection rate is less than 20%, all residents should be treated every 24 months or alternatively just treat those individuals reporting the habit of eating raw fish every 12 month (World Health Organization 2012). In Vietnam about 100,000 Vietnamese people were treated in 2008–2009 (World Health Organization 2011). It should be noted that the Ministry of Health recommended 75 mg praziquantel/kg body weight, given in three equivalent doses in one day, but now they adopted a standard regimen of praziquantel

50 mg/kg body weight, administered as two doses in one day (World Health Organization 2011).

In hospitals or health centres in communities, the doctors or technicians are using Kato-Katz smear method to diagnose the liver flukes (Chai and Lee 2002; Dung *et al.* 2007). But eggs from liver flukes are very similar to eggs of intestinal flukes and this can cause inaccurate estimates of prevalence of both trematode groups (Chai and Lee 2002). Thus some of the areas reported to have very high prevalences in Vietnam (De 2004b) could be partly due to misdiagnosis, although *Clonorchis sinensis* also is present (Dung *et al.* 2007). Hence new methods for accurate diagnosis and easily applicable in the field should be developed. Similarly, high prevalences of infections in the snail hosts in Vietnam (De 2004b) based on cercariae morphology alone could be misleading (Dung *et al.* 2010).

In addition, in the endemic areas, mass treatment should also be applied for domestic animals (dogs, cats, pigs, chicken etc.) (World Health Organization 2011). It is also highly desirable that the anthelmintic is active against both larval and adult parasitic stages. Especially, treatment of animals is difficult for various reasons, i.e. dog and cats can be difficult to catch; the cycle production of breeding animals is non-stop, so there is rapid exchange of animals (Clausen *et al.* 2012).

Snail control

One method to control FZT is to disrupt the life cycle of the snails. Snails can be controlled indirectly by reducing the suitability of their habitat or directly by removing them through chemical, physical, or biological control (Hoffman 1970; Sturrock 1995; Terhune *et al.* 2003). For chemical control, molluscicides such as niclosamide, copper compounds, hydrated lime, sodium chloride and calcium cyanamide could be used in ponds (Hoffman 1970; Rondelaud and Dreyfuss 1996; Sturrock 1995; Khallaayoune *et al.* 1998; Terhune *et al.* 2003; Wada 2004; Mostafa *et al.* 2005; Campbell *et al.* 2002; Wui and Engle 2007). Most molluscicides, however, are toxic to fish as well and therefore their use in aquaculture ponds may be limited to ponds with out fish. Physical alteration of culture ponds by draining or scraping of the banks can affect snail density through destruction or removal of snails along the periphery of ponds. Removal of aquatic vegetation may have some effect on snail density, although intermediate host snails for FZT do not show a strong association with aquatic plants (Dung *et al.* 2010). Flushing of drained ponds by washing with high pressure water hoses may reduce snail populations (Hoffman 1970). Many natural enemies of snails may have the potential to reduce snail density, but emphasis has been on competitor snails or predators (Madsen 1983). Biological control of snails may be achieved by the introduction of competitor snails, and there have been examples of the natural displacement of snails transmitting schistosomes in the field (Pointier and McCullough 1989; Pointier *et al.* 1989; Pointier and Jourdan 2000; Pointier 2001; Giovanelli *et al.* 2005).

With varying success, species of mollusk-eating fishes have been tested as snail control agents (Shelton *et al.* 1995; Venable *et al.* 2000; Rothbard and Rubinshtein 2000; Ben-Ami and Heller 2001; Terhune *et al.* 2003; El-Deeb and Ismail 2004; Ledford and Kelly 2007; Wui and Engle 2007), e.g. the Haplochromine cichlid *Astatoreochromis alluaudi*, Reader Sunfish *Lepomis microlophus*, Blue Catfish *Ictalurus furcatus* etc., especially, Black Carp, *Mylopharyngodon piceus*, stands out as an efficient predator of snails.

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