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REVIEW

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Food-borne intestinal trematodiases in humans

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Abstract Food-borne trematodiases still remain a public health problem world-wide, despite changes in eating habits, alterations in social and agricultural practices, health education, industrialization, environmental alteration, and broad-spectrum anthelmintics. Food-borne trematodiases usually occur focally, are still persistently endemic in some parts of the world, and are most prevalent in remote rural places among school-age children, low-wage earners, and women of child-bearing age. Intestinal fluke diseases are aggravated by socioeconomic factors such as poverty, malnutrition, an explosively growing free-food market, a lack of sufficient food inspection and sanitation, other helminthiases, and declining economic conditions. Control programs implemented for food-borne zoonoses and sustained in endemic areas are not fully successful for intestinal food-borne trematodiases because of centuries-old traditions of eating raw or insufficiently cooked food, widespread zoonotic reservoirs, promiscuous defecation, and the use of "night soil" (human excrement collected from latrines) as fertilizer. This review examines food-borne intestinal trematodiases associated with species in families of the Digenea: Brachylaimidae, Diplostomidae, Echinostomatidae, Fasciolidae, Gastrodiscidae, Gymnophallidae, Heterophyidae, Lecithodendriidae, Microphallidae, Nanophyetidae, Paramphistomatidae, Plagiorchiidae, and Strigeidae. Because most of the implicated species are in the Echinostomatidae and Heterophyidae, emphasis in the review is placed on species in these families.

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Introduction

Current estimates indicate that 40–50 million people world-wide are infected with food-borne trematodes (Abdussalam et al. 1995; Lima dos Santos 1995). These infections are endemic in various parts of the world, particularly Southeast Asia (Dixon and Flohr 1997). More than 10% of the world population is potentially at risk of food-borne trematode infection (Abdussalam et al. 1995). Many factors contribute to this problem, including a lack of education on the part of the public and poor recognition of trematode infections by public health authorities (Dixon and Flohr 1997). Furthermore, there are indications that infections have been increasing in the last few years because of an increasing production of fish and shellfish in unhygienic fish ponds, and the popularity of raw, undercooked, or insufficiently processed food in many parts of the world (Abdussalam et al. 1995). Additionally, with increased international travel, food-borne trematodiases are important to understand, diagnose, and treat, particularly in areas where infection is common (Slifko et al. 2000).

Globally, about 70 species of intestinal trematodes have been reported to infect humans (Yu and Mott 1994). Almost one-half of these species belong to the families Heterophyidae and Echinostomatidae. In addition to these families, our literature search found 11 other families with digenean species that infect the human intestine. Table 1 provides an alphabetic listing of 13 families and 36 genera implicated in human intestinal trematodiases. Representative species from these genera are considered in the text. This review is organized on the basis of the family from the Brachylaimidae to the Strigeidae, as described by LaRue (1957). Wherever possible, the review considers briefly

Table 1 Food-borne intestinal trematode infections

Family	Genus	Disease and geographic area	Source of metacercariae
Brachylaimidae	*Brachylaima*	Brachylaimidiasis: Australia	Molluscs (snails)
Diplostomidae	*Neodiplostomum*	Diplostomidiasis: Korea	Amphibians and reptiles
Echinostomatidae	*Echinochasmus*, *Echinoparyphium*, *Echinostoma*, *Episthmium*, *Euparpyhium*, *Himasthla*, *Hypoderaeum*, *Paryphostomum*	Echinostomiasis: Japan, China, Korea, Taiwan, Indonesia, Thailand, Hungary, Italy, Romania, Japan, Philippines, India, Singapore, The Americas, Egypt	Fish (loach), molluscs (snails, clams), amphibians (tadpoles, frogs)
Fasciolidae	*Fasciolopsis*	Fasciolopsiasis: India, Bangladesh, Pakistan, Korea, China, Taiwan, Vietnam, Cambodia, Thailand, Indonesia, Laos	Water plants (water chestnut, caltrop, lotus roots, bamboo), other aquatic vegetation
Gastrodiscidae	*Gastrodiscoides*, *Gastrodiscus*	Gastrodiscoidiasis: India, Vietnam, Philippines, Thailand, China, Russia	Squid, plants, crustaceans (crayfish), amphibians (frogs, tadpoles)
Gymnophallidae	*Gymnophalloides*	Korea	Molluscs (oysters), vegetation
Heterophyidae	*Appophalus*, *Centrocestus*, *Cryptocotyle*, *Diorchitrema*, *Haplorchis*, *Heterophyes*, *Heterophyopsis*,, *Metagonimus*, *Phagicola*, *Procercovum*, *Pygidiopis*, *Stellantchasmus*, *Stichodora*	Metagonimiais or heterophyiasis: China, Japan, Korea, Indonesia, Spain, Israel, Balkans, Russia, Taiwan, Sudan, Tunisia, Turkey, Philippines, Indonesia, USA, Egypt, Brazil, Greenland	Fish (freshwater or brackish, carp, mullet, cyprinoids), crustaceans (shrimp)
Lecithodendriidae	*Paralecithodendrum*, *Phaneropsolus*, *Prosthodendrium*	Lecithodendriidiasis: Indonesia, Thailand, Laos	Arthropods (odonate insects)
Microphallidae	*Spelotrema*	Microphallidiasis: Philippines	Crustaceans (crabs, shrimp)
Nanophyetidae	*Nanophyetus*	Nanophyetiasis: Russia, USA	Fish (salmon, trout)
Paramphistomatidae	*Fischoederius*, *Watsonius*	Paramphistomatidiasis: Africa, China	Vegetation (aquatic plants)
Plagiorchiidae	*Plagiorchis*	Plagiorchiidiases: Philippines, Indonesia, Japan, Thailand, Korea	Insect larvae, arthropods, insects, molluscs (snails)
Strigeidae	*Cotylurus*	Strigeidiasis: China	Unknown

the morphology, biology, life cycle, epidemiology, and clinical aspects of human intestinal trematodes on a world-wide basis.

Brachylaimidae

The Brachylaimidae is represented by one species, i.e., *Brachylaima cribbi* (Table 1), which is a terrestrial fluke infecting mammals, birds, and humans (as incidental hosts; Butcher and Grove 2001). Human infections are reported from South Australia (Butcher et al. 2003) where the life cycle of *B. cribbi* is maintained between the common house mouse, *Mus musculus*, and/or poultry and European helicid and hygromiid snails (which are introduced species in Australia; Butcher et al. 1996; Table 1). Humans are infected by eating snails that harbor metacercarial cysts (Butcher et al. 1996). In areas where helicid snails are abundant, small snails are very frequently ingested intact with vegetables derived from house gardens or local markets (Butcher et al. 1996; 1998). The infections are predominantly reported from children (Butcher et al. 2003), although adults are also susceptible (Butcher et al. 1998). Infections with *B. cribbi* are usually chronic and can persist as long as 18 months (Butcher et al. 1996). Re-infections are very frequent and are related to constant exposure to infected helicid and hygromiid snails (Butcher et al. 1996). Clinical symptoms vary and depend on the worm burden (Butcher et al. 2003): they include diarrhea, abdominal pain, low-grade fever, and fatigue (Butcher et al. 1996). Diagnosis is based on identification of eggs in the feces; and treatment includes Praziquantel (Butcher et al. 1996).

Diplostomidae

The life cycle of the Diplostomidae includes snails, fish, and piscivorous birds and mammals as final hosts. *Neodiplostomum soulensis*, formerly named *Fibricola seolensis* (Chai and Lee 1991) has been reported from humans (Huh et al. 1994). Infections with *F. seolensis* are predominantly reported from Korea (Hong and Shoop 1994; Chai and Lee 2002; Chai and Shih 2002; Table 1). Examination of stool samples from military soldiers in Korea revealed the prevalence of infection was 0.4% (Huh et al. 1994).

Echinostomatidae

The Echinostomatidae flukes are small, typically 3–10 mm in length and 1–3 mm in width, with a large ventral sucker and distinctive collar spines. Human echinostomiasis, attributed to at least 16 species (Anonymous 1995a, 1995b) is endemic to Southeast Asia and the Far East, i.e., mainland China, Taiwan, India, Korea, Malaysia, Philippines, and Indonesia (Bandyopathy and Nandy 1986). Haseeb and Eveland (2002), in their excellent review on human echinostomiasis, indicated that about 20 species belonging to 8 genera are involved in this disease. Adult trematodes infect a variety of mammals (including humans) and aquatic birds (Bandyopathy and Nandy 1986; Anonymous 1995a). 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 zoonotic potential; Belding 1964; Carney et al. 1980; Bundy et al. 1991). 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 (Bundy et al. 1991) and 44% in the Philippines (Cross and Basaca-Sevilla 1986) to 5% in mainland China (Li 1991) and from 50% in northern Thailand (Sanchaisuriya et al. 1993) to 22% in Korea (Ryang 1990). The foci of transmission and natural reservoirs are widespread and linked to fresh- or brackish water habitats (Bundy et al. 1991). Metacercariae are ingested by humans in raw or undercooked fresh- or brackish water molluscs (pulmonate, opisthobranch snails or bivalves), fish, crustaceans, and amphibians (tadpoles or frogs) which constitute a substantial portion of the diet in endemic areas (Bandyopathy and Nandy 1986).

Human disease

Morbidity and mortality due to echinostomiasis are difficult to assess because of a prolonged latent phase, a short acute phase, asymptomatic presentations, and similarity of clinical symptoms to other intestinal helminthiasis (Chai and Lee 1990). Clinical symptoms are related to parasite load (Bandyopathy and Nandy 1986; Chai et al. 1994). In light to moderate infections, anemia, headache, dizziness, slight anemia stomachache, gastric pain, and loose stools have been reported (Chattopadyay et al. 1990; Bundy et al. 1991; Anonymous 1995a). Heavy infections are associated with eosinophilia, abdominal pain, profuse watery diarrhea, anemia, edema, and anorexia (Chattopadyay et al. 1990; Anonymous 1995a). Pathologically, echinostomes damage the intestinal mucosa, causing extensive intestinal and duodenal erosions and catarrhal inflammation (Anonymous 1995a).

Diagnosis and treatment

The diagnosis of echinostomiasis is done by finding characteristic operculate, non-embryonated, ellipsoidal, yellow to yellow-brown eggs in fecal specimens. As egg size varies among echinostome species (Bandyopathy and Nandy 1986), species identification can be done based on the morphology of adult worms following anthelmintic treatment. The diagnosis of animal, i.e., rodent, infections can be done based on serology (Graczyk and Fried 1994; 1995; Graczyk 1997). Infections can be terminated by mebendazole (Cross et al. 1976), albendazole (Cross 1984), Praziquantel, or niclosamide (Anonymous 1995b). Diagnosis and treatment programs should also include domestic animals.

Economic impact

Economic assessment and the assessment of disease morbidity and mortality are difficult, as quantitative data are not available. Considering the occurrence of other food-borne trematodiases in the areas where echinostomiasis is common, it is difficult to provide an accurate economic assessment exclusive for echinostomiasis (Graczyk 2000). However, it is evident that 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 (Lu 1982; Seo et al. 1985). In many countries, echinostomiasis is aggravated by socio-economic factors such as poverty, malnutrition, and an explosively growing free-food market; and a lack of food inspection, poor sanitation, other helminthiasis, and declining economic conditions also contribute (Ujiie 1963; Carney 1991). As in other food-borne zoonotic parasitoses, the endemicity of echinostome transmission depends upon the interplay of host, parasite, and environment (Yu et al. 1994). As demonstrated by epidemiologic surveys in Asia, the patterns of food-borne trematode diseases, including echinostomiasis, were altered following changes in habits, cultural practices, health education, industrialization, and social environment (Kian and Virik 1963; Ujiie 1963; Lu 1982; Carney 1991; Huh et al. 1994).

Control and prevention

The nature of echinostomiasis does not justify the establishment of a separate control program, because it can be controlled along with other food-borne diseases for which there are sustained WHO control programs (Ujiie 1963; Carney 1991; Yu et al. 1994). The control of human echinostomiasis via blocking or interruption of the life cycle can be achieved through proper diagnosis, followed by pharmacologic treatment and prevention of reinfection (Graczyk and Fried 1998). As human infections result from eating raw molluscs, fish, crustaceans, and amphibians, infections could be prevented if people change their eating habits (Graczyk and Fried 1998). Significant changes in the control of echinostomiasis include: (1) the development of effective broad-spectrum anthelmintics, (2) an understanding by WHO of the differences between intestinal helminths and arthropod-borne infectious agents, and (3) the implementation of control programs in school-age children, with strong community therapy programs delivering multiple treatments against concurrent helmintic infections (Waikagul 1991; Warren 1993; Yu et al. 1994). A decreasing pattern in some food-borne trematode diseases along with industrialization, health education, and alteration of environment has been observed in certain areas of Southeast Asia (Ujiie 1963; Lu 1982; Carney 1991). This is particularly true for Taiwan and mainland China, where industrial developments and wastewater discharges pollute streams and rivers, practically destroying those aquatic animals involved in trematode life cycles (Lu 1982). Although a reduced number of cases of paragonimiasis, fasciolopsiasis, fascioliasis, clonorchiasis, and metagonomiasis was reported in endemic regions, the prevalence of echinostomiasis was not changed, due to an extensive zoonotic reservoir of echinostomes (Ujiie 1963). The disease remains a public health problem in endemic areas (Ujiie 1963; Carney 1991). The WHO control programs operating through the essential components of diagnosis, treatment, and prevention for the control of human zoonotic trematodiases have not been successful against echinostomiasis, although they have been for other trematode diseases (Carney 1991).

Fasciolidae

Fasciolopsis buski is the only fasciolid species reported to frequently infect people. This is the largest fluke parasitizing humans (Kuntz and Lo 1967). Adult worms are typically 8–10 cm in length and 1–3 cm in width (Kuntz and Lo 1967). They inhabit the duodenum and jejunum in light infections and can also be found in much of the intestinal tract, including the stomach, in moderate and heavy infections. The eggs released in the feces embryonate in water in 3–7 weeks (Gilman et al. 1982; Weng et al. 1989). After hatching, miracidia infect pulmonate snails of the genera *Segmentina*, *Hippeutis*, and *Gyraulus*, which shed cercariae after 4–6 weeks (Graczyk et al. 2000). Cercariae encyst on the surface of aquatic plants, on debris, and also on the water surface (Weng et al. 1989). Metacercarial cysts are ingested through: (1) the consumption of raw or undercooked aquatic plants [such as water caltrop (*Trapa* sp.), water hyacinth (*Eichhornia* sp.), water chestnut (*Eliocharis* sp.), water bamboo (*Zizania* sp.), water lotus (*Nymphaea lotus*), water lily (*Nymphaea* sp.), watercress, gankola (*Otelia* sp.), or morning glory (*Ipomoea* sp.)], (2) the drinking or use of raw water, and (3) the handling or processing of water-derived plants, e.g., using one's teeth to peel plants (Kuntz and Lo, 1967; Gilman et al. 1982; Weng et al. 1989). Human and animal fasciolopsiasis is largely confined and endemic to the oriental countries of the Far East and Southeast Asia. In endemic areas, the disease occurs focally, is widespread, and is linked to freshwater habitats with stagnant or slow-moving waters. It is also associated with common social and agricultural practices and promiscuous defecation (Kuntz and Lo 1967; Gilman et al. 1982; Cross 1984; Weng et al. 1989). In foci of parasite transmission, the prevalence of infection in children ranges from 57% in mainland China (Lee 1972; Weng et al. 1989) to 25% in Taiwan (Shyu et al. 1984) and from 60% in India (Muttalib and Islam 1975) and 50% in Bangladesh (Rahman et al. 1981) to 10% in Thailand (Bunnag et al. 1983). The infections predominantly occur in children and the worm burden can exceed 800 flukes/child (Gilman et al. 1982; Weng et al. 1989).

Human disease

Morbidity due to fasciolopsiasis in endemic areas is high (Lee 1972; Idris et al. 1980; Gilman et al. 1982; Bunnag et al. 1983; Lee et al. 1986; Weng et al. 1989) and the disease can be fatal, depending on worm burden (Lee 1972; Idris et al. 1980; Gilman et al. 1982; Bunnag et al. 1983; Weng et al. 1989). Clinical symptoms are related to parasite load and, in light infections, they include anemia with eosinophilia, headache, dizziness, stomachache, gastric pain, and loose stools (Gilman et al. 1982). Moderate and heavy infections are associated with severe epigastric and abdominal pain, diarrhea or bowel obstruction, nausea (occurring especially in the morning and resolving after the first meal), acute ileus, anasarca, and marked eosinophilia and leucocytosis (Gilman et al. 1982). Moderate and heavy infections are associated with malnutrition (Jaroonvesama et al. 1986). Adult flukes damage the intestinal mucosa and cause extensive intestinal and duodenal erosions, ulceration, hemorrhage, abscesses, and catarrhal inflammation. Absorption of toxic and allergic worm metabolites causes ascites, general edema and facial edema, e.g., cheek and orbital edema (Jaroonvesama et al. 1986). Feces are profuse, yellow-green in color, and contain pieces of undigested food due to malabsorption (Jaroonvesama et al. 1986).

Diagnosis and treatment

Diagnosis is routinely done by examining fecal specimens for operculate, non-embryonated, ellipsoidal, yellow eggs, length 130–140 μm, width 80–85 μm, or expelled adult worms (Gilman et al. 1982; Weng et al. 1989). Historically, niclosamide and dichlorophen have been used to treat heavy *F. buski* infections in school-age children in an endemic area of Bangladesh (Idris et al. 1980). Therapeutic studies that utilize Praziquantel at dosages of 40, 25, and 15 mg/kg in school-age children heavily infected with *F. buski* were carried out in Central Thailand (Bunnag et al. 1983; Harinasuta et al. 1984). As Praziquantel administered at the lowest dose, i.e., 15 mg/kg, was highly efficacious and no side-effects occurred, a single Praziquantel dose of 15 mg/kg at bedtime was recommended for children (Bunnag et al. 1983; Harinasuta et al. 1984). Praziquantel treatment was also highly efficacious in school-age children with severe fasciolopsiasis in Taiwan (Lee et al. 1986). Currently, although not officially approved in the United States, a single dose of Praziquantel at 15 mg/kg is the treatment of choice (Bunnag et al. 1983; Harinasuta et al. 1984).

Economic impact

The economic impact of fasciolopsiasis, disease morbidity, and mortality are difficult to assess, as quantitative data exclusive for *F. buski* infections are not available (Graczyk et al. 2001). In the endemic areas, the disease is under-reported and is most prevalent in remote rural places and semi-urban areas among school-age children (Lee 1972; Shah et al. 1973; Idris et al. 1980; Rahman et al. 1981; Gilman et al. 1982; Bunnag et al. 1983; Harinasuta et al. 1984; Gai et al. 1995). Fasciolopsiasis is considered to be the main factor for the persistent poor nutritional status of children in endemic areas in underdeveloped countries (Lee 1972; Shah et al. 1973; Gilman et al. 1982). Pharmacologic termination of *F. buski* infections uses Praziquantel given to school-age children in endemic areas and the prevention of reinfection and is aimed to improve their health at a crucial time in their growth and development (Anonymous 1995a). In many oriental countries, fasciolopsiasis is aggravated by socio-economic factors, such as poverty, malnutrition, an explosively growing free-food market associated with a lack of food inspection, poor sanitation, other helminthiasis, and declining economic conditions (Muttalib and Islam 1975; Gilman et al. 1982; Cross 1984; Weng et al. 1989; Yu et al. 1994; Anonymous 1995a). As in other food-borne zoonotic trematodiases, the endemicity of *F. buski* transmission depends upon the interplay of human and animal hosts, the parasite, and the agricultural environment (Anonymous 1995a, 1995b; Graczyk 1997). As demonstrated by epidemiological surveys in Asia, the pattern of fasciolopsiasis shifted following changes in eating habits, socio-cultural and agricultural practices, health education, industrialization, and environmental alteration (Cross 1984; Yu et al. 1994; Anonymous 1995a, 1995b; Mott et al. 1995).

Control and prevention

Fasciolopsiasis is controllable by pharmacologic treatment and the institution of modern pig-farming. The control is theoretically very simple and the most practical method is to avoid eating raw, water-derived food. However, it is extremely difficult to enforce such a simple method in the face of centuries-old traditions. Infections with *F. buski* follow a familial trend, as food preparation and eating habits are passed from one generation to the next (Gai et al. 1995). In addition, water plants are a common food source because they are inexpensive and readily available (Gilman et al. 1982; Weng et al. 1989; Gai et al. 1995). The nature of fasciolopsiasis does not justify the establishment of a separate control program, because it can be controlled along with other food-borne parasitoses for which there are sustained WHO control programs (Anonymous 1995a, 1995b; Mott et al. 1995). The control of fasciolopsiasis by blocking or interrupting the parasite life cycle can be achieved through proper diagnosis followed by pharmacologic treatment of people and their livestock, i.e., hogs, and prevention of reinfection (Kuntz and Lo 1967; Muttalib and Islam 1975; Cross 1984; Gai et al. 1995). In countries where the eating of raw aquatic plants is customary and treated water is not available, prevention of reinfection relies on consistent educational propaganda, stressing the importance of thoroughly cooking all aquatic plants and boiling the water (Cross 1984; Weng et al. 1989; Gai et al. 1995). Dried aquatic plants are not dangerous because desiccation kills the metacercariae (Weng et al. 1989). Such educational efforts should be directed primarily toward school-age children, because they are less entrenched in their food and eating habits, behavior, and customs (Cross 1984). Significant changes in the control of intestinal helminthiasis rely on the development of effective broad-spectrum anthelmintics and the implementation of control programs in school-age children, together with strong community-therapy programs (Yu et al. 1994; Anonymous 1995a, 1995b; Mott et al. 1995). The aggressive education programs in Taiwan include lectures and demonstrations of *F. buski* flukes in primary schools and during home visits (Lee et al. 1986, 1989). Although a reduction in the number of cases of fasciolopsiasis and other trematodiasis was recognized in their endemic regions (Cross 1984), this tendency may not be stable because many cultures, particularly in China, still enjoy eating raw food products (Lee et al. 1989; Weng et al. 1989). In addition, there is a belief that cooking food destroys its flavor and nutritional value (Lee et al. 1989; Weng et al. 1989; Gai et al. 1995). The simplest control measures in endemic areas should include the boiling of raw water and the thorough cooking or steeping of aquatic plants in boiling water, restraining pigs from having access to ponds and canals, eliminating the intermediate snail hosts, and prohibiting the use of aquatic green fodder to feed pigs and unsterilized "night soil" as a fertilizer (Cross 1984; Weng et al. 1989; Gai et al. 1995).

Gastrodiscidae

The family Gastrodiscidae contains relatively large organisms, i.e., approximately 8–14 mm in length. The body is divided into two parts. In the species that infects man, *Gastrodiscus hominis*, the anterior part is short and cylindrical and the posterior part is large and discoidal. The characteristics of *G. hominis* include a subterminal pharynx, tandem, lobed testes, a post-testicular ovary, an ascending uterus, and a ventral genital pore (Kumar 1999). The life cycle is not completely understood and transmission of this parasite may occur when encysted metacercariae are swallowed with tainted vegetation or with animal products, such as raw or undercooked crustaceans, molluscs, or amphibians.

G. hominis is an intestinal fluke infecting people and their livestock, e.g., hogs, in Africa (Goldsmid 1975;

Hira 1983) and India (Murty and Reddy 1980). For other locations where this parasite has been reported, see Table 1. The disease condition associated with *G. hominis* is referred to as gastrodisciasis. The juvenile flukes do not penetrate the intestinal mucosa. Juvenile flukes, released from the excysted metacercariae in the small intestine, descend the intestinal tract to reach the cecum and colon. In these locations, the juvenile gastrodiscids mature and live as adults in the lumen by attaching to the intestinal mucosa with the aid of their acetabula (Kumar 1999).

Gymnophalidae

Gymnophalloides seoi is the only species reported from humans (Chai and Lee 1991; Lee et al. 1994). The infection is endemic to Korea and southwestern coastal islands (Chai and Lee 1991; Lee et al. 1994). *G. seoi* adults are small, 0.3–0.5 mm in length and 0.2–0.3 mm in width (Lee and Chai 2001). The first intermediate host is unknown (Lee et al. 1995; Lee and Chai 2001). People are infected by consuming raw oysters (*Crassostera gigas*), which represent the second intermediate host containing metacercarial cysts (Lee et al. 1995; Lee and Chai 2001). Humans, the oystercatcher (*Haematophus ostralegus*), and wading birds are natural definitive hosts and parasite reservoirs (Lee and Chai 2001). There has been an increase in the incidence of *G. seoi* infections in humans in Korea (Chai et al. 2003). The prevalence of infection in endemic areas ranges from 10% to 78% (Lee et al. 1993, 1994; Chai et al. 2000, 2001). The average worm burden determined after anthelmintic treatment and purgation of worms ranged over 1,006–26,373 specimens/individual (Lee et al. 1994). Further study showed that the average worm burden was 10,344 worms/individual within the range of 94–69,125 worms/person (Chai et al. 2000). There was an average of 1,015 eggs/g feces (Chai et al. 2000). There were no sex-related differences in the prevalence of *G. seoi* infection and the age distribution of infected people showed an even pattern (Lee et al. 1994). Further study demonstrated a strong age predilection: 95% of the infected people were over 40 years old; and females showed a slightly higher prevalence of infection than males (Chai et al. 2001). *G. seoi* infection is widely distributed in mainland Korea and southwestern coastal islands (Chai et al. 2000). The clinical symptoms include loose stools, pancreatitis, indigestion, diarrhea, and abdominal, i.e., epigastric, discomfort (Lee et al. 1994). *G. seoi* requires considerable medical attention, because of its relationship with pancreatitis and other pancreatic diseases (Lee et al. 1995). The infection can be diagnosed by finding eggs in the feces. However, an expert is needed to identify the eggs (Lee and Chai 2001; Chai and Lee 2002). Praziquantel, 10 mg/kg in a single dose, is effective for treatment (Lee and Chai 2001). Eating raw oysters in endemic areas is not recommended (Lee and Chai 2001; Chai and Lee 2002).

Heterophyidae

Numerous genera of heterophyids have species that are causative agents of human food-borne intestinal trematodiases. These genera are listed in Table 1. For a complete listing of the species in these genera that are human pathogens, see Chai and Lee (2002).

The family Heterophyidae contains small, i.e., typically less than 0.5 mm in length, egg-shaped organisms containing infective metacercariae that are usually encysted in fish second intermediate hosts. Adult worms are found in fish-eating birds and mammals in addition to humans. A striking morphological feature of members of this family is the possession of a *gonotyl*, or genital sucker that is retractile and aids copulation. Eggs of heterophyids contain fully developed miracidia when laid, but hatching does not occur until the eggs are ingested by the gastropod host. A good example that illustrates the life cycle of a typical heterophyid is the cosmopolitan species, *Cryptocotyle lingua*. This heterophyid has been reported from humans (Kumar 1999), but is usually found in seagulls, other fish-eating birds and pinniped mammals (e.g., seals). This heterophyid is not specific for its definitive host; and the laboratory rat is a suitable experimental host. The adult flukes live between the villi of the anterior region of the small intestine and release numerous eggs into seawater. The embryonated eggs are then ingested by littorine snails (particularly *Littorina littorea* and *L. scutulata*) and hatch within the snail's intestine. Intramolluscan development proceeds through sporocyst and redial stages and cercariae are released into the water where they penetrate shore-fish, such as cunners, gudgeon, and charr, and encyst on the surface of the fish. Cysts remain viable for years and serve as the source of infection to the definitive hosts.

Human disease

Chai and Lee (2002) listed 12 species of heterophyids that parasitize humans in Korea, including three species of *Metagonimus*, three species of *Heterophyes*, two species of *Stictodora*, and a single species in the genera *Heterophydosis*, *Pygidiopsis*, *Stellantchasmis*, and *Centrocestus*. Because heterophyids are important medical parasites in Korea, Chai and Lee (2002) provide considerable coverage of these digeneans in their excellent review.

In humans, heterophyiasis is associated mainly with species of *Heterophyes* and metagonimiasis is associated mainly with species of *Metagonimus*. Heterophyiases and metagonimiasis are the best known diseases associated with heterophyid parasitism. Human infections are usually acquired through the consumption of raw, undercooked, or inadequately processed freshwater, brackish, or marine fishes.

The two most prevalent species of human heterophyids are *H. heterophyes* and *M. yokogawai*. The former species has been reported in humans from Egypt, Sudan, Iran, Turkey, Tunisia, China, Taiwan, the Philippines, Indonesia, and India. Reservoir hosts include dogs, cats, foxes, jackals, and other fish-eating mammals. *Pirenella conica* and *Cerilbida cengulata* are gastropod first intermediate hosts of these heterophyids; and second intermediate hosts include brackish-water fishes in the genus *Mugil* (mullets), *Aphanius*, and *Acanthogobius*. Human infections with *H. heterophyes* occur in Egypt in the northern part of the Nile Delta and are acquired by the consumption of freshly salted or inadequately cooked fish. Kumar (1999) estimated that 10,000 people were affected by heterophyiases in Egypt in 1992 and reported a high prevalence of heterophyiasis in China with estimates of 230,000 infected individuals.

Adults of *H. heterophyes* inhabit the mucosa and crypts of Lieberkühn in the anterior region of the human small intestine (Marty and Andersen 2000). Numerous digeneans in these sites may cause inflammation and ulceration of the mucosa and superficial necrosis. Low-grade infections are of no clinical consequence, but cases with heavy infections are associated with diarrhea, mucus-rich feces, upper abdominal tenderness, pain, dyspepsia, anorexia, nausea, and vomiting. Occasionally, worm eggs may enter the lymphatic vessels through the crypts of Lieberkühn and reach the circulatory system. These egg emboli may occlude cardiac vessels and produce heart damage and fibrosis. Death due to cardiac involvement is rare but has been reported, as have rare occurrences of egg emboli in the spinal cord and brain of humans (Marty and Andersen 2000).

The most prevalent causative agent of metagonimiases in man is *Metagonimus yokogawai*. Its distribution is mainly in China, Japan, Korea, Taiwan, Indonesia, Russia, Israel, the Balkans, and Spain. Reservoir hosts include dogs, cats, pigs, and other fish-eating birds and mammals. Adult worms live in the small intestine of vertebrate hosts; and gastropods in the genus *Semisulcospira* are the first intermediate hosts. Cyprinid fish serve mainly as the second intermediate host, including species of *Plectoglossus*, *Tribolodon*, *Lateolabex*, and *Salmo*. These freshwater fishes harbor the encysted metacercariae in their gills, fins, tails, and under their scales.

M. yokogawai is prevalent in the Far East and the distribution of this species in Korea corresponds with the distribution of the Sweet oriental trout, *Plectoglossus altivelis*. Kumar (1999) estimated 500,000 cases of infection with *M. yokogawai* in Korea. The pathogenicity of this fluke in humans is similar to that reported for *H. heterophyes*. Treatment of heterophyiasis and metagonimiasis is usually done with a single dose of 25 mg/kg of Praziquantel.

Other genera of heterophyids have been reported in humans (Kumar 1999; Marty and Andersen 2000; Chai and Lee 2002). *Centrocestus* sp. occurs in humans in Russia, Korea, Taiwan, and Japan. Metacercariae of these heterophyids are encysted in fishes in the genera *Acheilognathus*, *Misgarnus*, *Pseudorasbora*, *Zacco*, *Mugil*, *Cyprinus*, *Gnathopogon*, and *Channa*. *Cryptocotyle lingua* has been reported from humans in Greenland, where the second intermediate hosts are fishes in the genera *Labris* and *Gobius* (Kumar 1999). Chai et al. (2002) reported six human cases of infection with *Stictodora lari* from patients in Korea who had eaten the raw flesh of infected mullet and gobie fish caught in an estuary near their village. Several species of digeneans in the genus *Haplorchis* have been reported from humans in Japan, China, Egypt, and Taiwan. The transmission of species of *Haplorchis* to humans occurs when cysts are obtained inadvertently from infected fishes in the genera *Gambusia*, *Acanthogobius*, *Glossogobius*, *Cyprinus*, *Mugil*, and *Ophiocephalus* (Kumar 1999).

Additional genera of heterophyids implicated in human heterophyiases are *Heterophyopsis*, *Phagicola*, *Procerovum*, *Pygidiopsis*, and *Stictodora*. Chieffi et al. (1992) reported human infection with *Phagicola* sp. In São Paulo, Brazil. Antunes et al. (1993) reported that gamma ionization of mugilid fish (mullets) was effective in destroying the cysts in the fish.

Diagnosis and treatment

Diagnosis of the heterophyids is facilitated by fecal examination. The eggs of these flukes are small, averaging about 25 μm in length and 15 μm in width. Some experience is needed to determine the presence of small digenean eggs in a fecal sample. Accurate diagnosis at the species level based solely on eggs is difficult and adult flukes are usually needed for this purpose. They are obtained following purgation of the patient with magnesium salts or treatment with Praziquantel (Radomyos et al. 1994). DNA analysis of heterophyids and scanning electron microscopic observation of the topography of adult flukes may help in clarifying identification problems with adult heterophyids found in humans. Representative measurements of various species of adult heterophyids and their eggs from Korea are given by Chai and Lee (2002).

Heterophyiases and metagonimiases frequently occur in geographical areas where certain liver fluke diseases occur in humans, such as clonorchiases and opisthorchiases. Since the dimensions of the eggs of the liver flukes *Clonorchis* and *Opisthorchis* overlap with those of most heterophyids, eggs must be examined with great care for a differential diagnosis. As mentioned previously, Praziquantel, administered as a single dose at 25 mg/kg, is very effective against most heterophyid infections (Kumar 1999).

Lecithodendriidae

The lecithodendriids have an oval body and a spinose tegument, a pharynx is present and the intestinal ceca are variable in length, the testes are opposite and a cirrus sac is present, the position of the genital pore is variable, the vitellaria are in lateral clusters in the hindbody, and the eggs are operculate and embryonated when laid. Adults of these digeneans are parasites of the digestive tract of amphibians, birds, or mammals (typically bats). The family is of medical significance, since species have been found in humans and other primates in the Far East. Schell (1985) listed two genera from North America and other genera have been reported from Europe and the Far East. At least three genera (see Table 1) have species that infect humans. Since species of *Prosthodendriim* have representatives that infect humans, the life cycle of *P. pyramidriim* is presented herein. Virgulate xiphidiocercariae develop in sporocysts in the snail, *Melania tuberculata*. The cercariae are ingested by anopheline mosquitoes in which they encyst; and adults develop in the intestine of bats that have fed on the mosquitoes.

Human disease, diagnosis, and treatment

Two lecithodrendriids, *Prosthodendriim molenkampi* and *Phaneropsolus bonnie*, infect humans in Thailand, Indonesia, and Laos (Kumar 1999). Both species have been found concurrently in the intestines of humans examined post mortem in Indonesia. The eggs of both species have been found in the feces of patients in Thailand and Laos. In some areas of the Far East, the prevalence rates of these infections range from 10% to 40% (Kumar 1999). Kaewkes et al. (1991) described a new species, *P. spinicionis*, collected in a stool from a Praziquantel-treated 44-year-old female patient in Thailand. It is distinct from *P. bonnie*, differing from the latter in the presence of a short spinose cirrus and the distribution of tegumentary spines. Kumar (1999) noted that, although thousands of these digeneans were voided in the feces of individual patients treated with Praziquantel in Thailand, these flukes appear not to produce significant clinical disease in humans. Praziquantel at a single dose of 40 mg/kg is an effective treatment for lecithodendriids.

Reservoir hosts of lecithrodendriids include monkeys in Thailand and Malaysia and insectivorous bats in India (Kumar 1999). The details of the life cycle of the human species are not well known. Eggs of these species resemble those of opisthorchiids and heterophyids and are difficult to distinguish unequivocally in fecal examinations. *Bithynia goniompaelus* (Gastropoda) is a suspected first intermediate host of some human lecithodendriids; and naiads of odonate insects, dragonflies, and damselflies are second intermediate hosts. The nymphal (naiad) stages of these insects harbor the encysted metacercariae and transmit the infective stage to humans. Human infection occurs via the consumption of raw small fishes which are contaminated with the metacercariae of infected naiads (Kumar 1999).

Pusterla et al. (2003) reported that two species of lecithodendriids, *Acanthatrium* sp. and *Lecithodrendrium* sp., can serve as the vectors of *Neorickettsia* (*Ehrlichia*) *risticii*, the agent of Potomac horse fever (PHF). These lecithodendriids infected with neorickettsiae were recovered from the intestines of naturally infected myotisital bats and species of swallows in northern California. Although PHF is an important problem in veterinary medicine, it is not known whether human neorickettsial disease can be transmitted to humans via lecithodendriids.

Microphallidae

Members of this family have a small pyriform body and a spinose tegument. Most genera have two ventral suckers, a pharynx, and short intestinal ceca. The testes are opposite and are located in the hindbody. The ovary is anterior to the right or left testis and the vitellaria are posterior to the testes. The uterus is confined to the hindbody; and the eggs are operculate and non-embryonated. The adults are parasites of vertebrates. There are numerous genera in this family and Schell (1985) listed 15 genera from North America alone. Of these genera, only *Spelotrema* (synonym = *Carneophallus*) has a species that infects humans: *S. brevicaeca* (= *C. brevicaeca*).

The generalized life cycle of microphallids usually involves three hosts: a mollusc, an arthropod, and a vertebrate. In some species, there is a tendency for the cycle to be abbreviated by eliminating the second intermediate (arthropod) host. In these species, the cercaria encysts within the sporocyst and the infected mollusc is eaten by the definitive host. The life cycle of species of *Spelotrema* follows this course. In *S. brevicaeca*, xiphidiocercariae of the *ubiquita* group (see Schell 1985) develop in daughter sporocysts within a prosobranch snail. Cercariae encyst in the abdomen and cephalothorax of shrimp. *S. brevicaeca* has been reported as the cause of fatal involvement in the heart and spinal cord of humans in the Philippines, when infected crustaceans (particularly shrimp in the genus *Macrobrachum*) were eaten raw or undercooked (Schell 1985). These tiny worms and their eggs can enter blood vessels and go to the heart or spinal cord. Specific diagnosis of microphallids in humans is difficult and must rely on the recovery of adult worms following purgation or treatment with Praziquantel, at a single dose at 40 mg/kg (Kumar 1999).

Nanophyetidae

These are small (about 1 mm or less) oval flukes with a non-spinose tegument. A pharynx is present and the intestinal ceca extend to the testes; and the testes are opposite and in the middle of the hindbody. The genital pore is median and posterior to the acetabulum; and the vitellaria fill the lateral regions of the body. The eggs are operculate, but not embryonated. The adults are parasites of the small intestine of mammals, including humans (Schell 1985). The major genus is *Nanophyetus* and the most important species is *N. salmincola*. A subspecies of this digenean, also considered as a geographic variant in some works, is *N. s. schikhobalowi*, a human parasite in Siberia (Kumar 1999).

The life cycle of *N. salmincola* involves the release of non-embryonated eggs in the feces of the mammalian host. Miracidial development within the egg takes about 4 months. The miracidium hatches and penetrates the freshwater prosobranch snail, *Oxytrema silicula*, in which microcercous cercariae develop. Cercariae emerge from snails, penetrate the skin and gills of salmonid fish, and encyst in the muscles and connective tissue. The adults develop in the intestine of numerous carnivorous mammals (including humans) that eat the infected fish (Schell 1985).

Human disease, diagnosis, and treatment

Eastburn et al. (1987) reported human infections of *N. salmincola* from ten patients in the northwest United States. The clinical presentation in most cases included a gastrointestinal complaint of abdominal discomfort, diarrhea, nausea, and vomiting; and peripheral blood eosinophilia was also observed. The fishes *Oncorhynchus* sp., *Salmo* sp., *Cottus perplexus*, *Dicamptodin ensatus*, and *Salvelinus fortinalis* transmitted the infection to humans in the United States.

N. salmincola is important in the Pacific Northwest (USA) because it transmits salmon-poisoning disease (by the rickettsial organism *Neorickettsia hexmentheca*) to dogs and other canids. As far as is known, this organism is not pathogenic in humans, but mortality in dogs may reach 90% (Schell 1985). Fritsche et al. (1989) recommended Praziquantel for the treatment of human nanophyetiasis.

Paramphistomatidae

Digeneans belonging to this family have thick, muscular, non-spinose bodies. The oral sucker is terminal and the ventral sucker is at the posterior end of the body. The pharynx is absent and the esophagus may have a muscular bulb at the posterior end. The intestinal ceca are long and the testes are in tandem or are oblique. The ovary is posterior and the vitellaria are distributed along the intestinal ceca. The eggs are operculate and may be embryonated or non-embryonated when laid. This family is characterized by the presence of an extensive lymphatic system (Kumar 1999). Members of this family are parasitic in the intestines or cloaca of vertebrates. In accord with Marty and Andersen (2000) and Chai and Lee (2002), we consider the family Paramphistomatidae distinct from the Gastrodiscidae.

The life cycles of most paramphistomatids involve freshwater pulmonate snails of various genera. Daughter rediae develop in the digestive gland–gonad region of the snail. Amphistome cercariae that have matured in both rediae and snail tissue emerge from the snail and encyst on a variety of aquatic vegetation. Vertebrate hosts that feed on the tainted vegetation become infected.

Human disease, diagnosis, and treatment

Information on the two genera of paramphistomes implicated in human infection is sparse. *Watsonius watsonius* is an inhabitant of the small intestine of humans. The adult flukes are about 1 cm in length and 0.5 cm in width; and the eggs are about 130 μm in length and 80 μm in width. The adults are pyriform and red-yellow. They have a large posterior acetabulum measuring about 1 mm in diameter and a subterminal oral sucker; and the eggs are non-embryonated, operculate, and light yellow. They have been reported as human parasites in Africa; and it is suspected that humans become infected by eating tainted vegetation (Marty and Andersen 2000). Information on the other paramphistome of humans, *Fischoederius elongates*, is scant. This is an amphistome of humans in China contracted by the ingestion of aquatic plants containing encysted metacercariae. Marty and Andersen (2000) note that heavy infection with paramphistomes can produce headache, epigastric pain, and diarrhea. The diarrhea may be a reaction to metabolites released by the worms (Marty and Andersen 2000).

Plagiorchiidae

According to Schell (1985), members of this family have oval bodies and a spinose tegument, the ventral sucker is in the anterior half of the body and a pharynx is present. The intestinal ceca are long, the testes are opposite, tandem or oblique and are located in the hindbody. A cirrus sac is present and the genital pore is anterior to the acetabulum. The ovary is pretesticular and the vitelline follicles are adjacent to the intestinal ceca and are variable in length. The uterus is confined to the hindbody and the eggs are operculate and embryonated. Plagiorchiids are parasitic in the intestine, gall bladder, bile duct, or cloaca of vertebrates.

Human disease

Schell (1985) noted 12 genera from North America and there are other genera in Europe and the Far East. The only genus with species that infect humans is *Plagiorchis*. The most representative species is *P. muris*, which has been reported from natural (Hong et al. 1996) and experimental (McMullen 1937) infections in humans. The life cycle of *P. muris* involves embryonated eggs being eaten by the pulmonate snail *Stagnicola emarginata*, in which sporocysts develop and produce xiphidiocercariae of the armatae group (see Schell 1985).

Cercariae emerge from the snail and encyst in chironomid larvae, but encystment in freshwater fishes also occurs. Natural definitive hosts are rats, dogs, nighthawks, robins, herring gulls, and sandpipers. In addition to humans, experimental infections have been established in mice, rats, and pigeons (McMullen 1937).

Kumar (1999) reported infections in the intestine of humans with *P. philippiniensis*, *P. javensis*, and *P. harinasutai* from the Philippines, Indonesia, and Thailand. Because differentiation of these species is difficult based solely on morphological features, the validity of some of the above-mentioned species is questionable. Molecular data including sequences from the nuclear rDNA/internal transcribed spacer region have been used to solve species problems in the *P. vespertilionis* group (Tkach et al. 2000) and these methods could be applied to species analysis of the human plagiorchids.

Hong et al. (1996) reported a human case of *P. muris* from a Korean man with a history of eating various freshwater fishes caught in a small stream near his village. The patient did not complain of gastrointestinal discomfort associated with this fluke. A survey of the local fish suggested that fishes of the genera *Liobagrus*, *Puntungia*, and *Odontolutes* were the probable source of infection for this patient.

Diagnosis and treatment

Diagnosis of plagiorchiids in humans is best done after treating patients with a single dose of 40 mg/kg of Praziquantel and recovering the adult worms (Kumar 1999). Use of fecal examinations alone to identify eggs to species is not possible because of the overlap in egg appearance with related digeneans.

Strigeidae

Members of the family Strigeidae contain a cup-shaped forebody with suckers, a pharynx, and an accessory structure known as the tribocytic organ (an accessory sucker). The hindbody is cylindrical or ovoid and contains the reproductive organs. The short uterus contains operculate, non-embryonated eggs. The excretory system is characterized by an extensive network of tubules and reservoirs. The adult flukes are parasites of the intestine of birds and mammals. Schell (1985) listed several genera of this family from North America, including the genus *Cotylurus*. It is in this genus that the only human representative, *C. japonicus*, has been reported. Eggs from *Cotylurus* worms hatch in fresh water about 3 weeks after they are laid; and the miracidia penetrate pulmonate snails in the genera *Stagnicola*, *Lymnaea*, *Physa*, and *Helisoma*. Fork-tailed pharyngeate strigeid cercariae develop in sporocysts, encyst in the same snail hosts, and become specialized metacercariae known as tetracotyles. Birds acquire the infection by ingesting the tetracotyls in infected snails. Strigeidiases of humans have been associated with infection by *C. japonicus* in China, but details about the fluke or the disease are sparse and the source of the metacercariae is unknown (Marty and Andersen 2000). Details on clinical symptoms or treatment in humans are not available.

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