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REVIEW

Food-borne trematode infections of humans in the United States of America

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Abstract This review examines the literature on imported (allochthonous) and local (autochthonous) cases of food-borne trematode (FBT) infections in the United States of America (USA) from 1890 to 2009. Most of the literature is concerned with imported cases of the opisthorchiids *Clonorchis sinensis* and *Opisthorchis viverrini.* These flukes cause serious pathology in the liver and biliary system of humans. Chronic cases may induce liver (hepatocarcinoma) and bile duct (cholangiocarcinoma) cancers in humans. Clonorchiasis and opithorchiasis are preventable diseases that can be avoided by eating properly cooked freshwater fish products. Several species of lung flukes in the genus *Paragonimus* are local or imported FBT in the USA. The endemic cycle occurs in the USA with various local snails and crustaceans serving as intermediate hosts. Paragonimids are acquired when humans eat raw or improperly cooked freshwater crustaceans containing metacercarial cysts. Infection can cause severe lung disease and the symptoms of paragonimiasis often mimic those of tuberculosis and other non-helminthic diseases. Paragonimiasis can be avoided by not eating raw or improperly cooked shellfish. The liver fluke *Fasciola hepatica* can be acquired by eating raw or uncooked vegetation. The cycle exists in the USA involving local snails and aquatic vegetation. Although some cases are local, most are imported by travelers or immigrants. Fascioliasis can cause serious liver and biliary diseases in humans and consumption of tainted vegetation should be avoided. Lesser known FBT have been reported in the USA including species of *Alaria*, echinostomids, heterophyids, troglotrematids, and a self-induced infection of *Plagiorchis*. Treatment of the FBT mentioned in this review consists of various regimens of praziquantel, except for *F. hepatica* where the drug of choice is triclabendazole.

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Introduction

Food-borne trematode (FBT) infections in humans are a major global concern affecting millions of people. These are infections acquired following the consumption of raw or improperly cooked food, mainly freshwater fish and aquatic invertebrates, crabs, crayfish, snails and clams, containing metacercariae (cysts) of various digenetic trematodes. Additionally, aquatic vegetation of various kinds, e.g., watercress, may contain cysts that are infective to humans. Consumption of raw or improperly cooked seafood and vegetation is common in many parts of the world, and the tendency to eat such food continues to increase in developed countries where feeding on sushi, sashimi, and ceviche is now commonplace.

The major organisms that serve as FBT globally are various species of liver flukes in the genera *Fasciola*, *Clonorchis*, and *Opisthorchis*, lung flukes in the genus *Paragonimus*, intestinal flukes such as *Fasciolopsis*, and various miscellaneous species, mainly heterophyids and echinostomatids. See the review of Keiser and Utzinger

(2009) for an update of the numerous species of flukes that serve as FBT globally. Several reviews on FBT and their trematodiases have been published in the past 5 years including those of Fried et al. (2004), Keiser and Utzinger (2005), Fried and Huffman (2008), and Keiser and Utzinger (2009).

Although FBT are mainly problems in Southeast Asia and other sites distant to the continental USA, there are concerns about these flukes in the western hemisphere, mainly because of imported (allochthonous) infections brought in by immigrants or travelers and also by local (autochthonous) infections that may have been acquired from tainted imported foodstuff. Moreover, some infections may be acquired locally in the USA where infected first and second intermediate hosts may be present. This is the case with some species of *Paragonimus* which are endemic in the USA. For instance, in the USA, the snail *Pomatiopsis* is a first intermediate host of *Paragonimus* and the crayfish *Cambarus* is a second intermediate host.

A review by Dixon and Flohr (1997) on FBT and their associated trematodiases described local and imported human trematode infections in Canada. That review also mentioned some cases of FBT in the USA. Our search of the literature on human FBT in the USA indicated that a review on this topic was not available. Both Medline (1950–2009) and Web of Science (1975–2009) were searched using the names of the human trematodes listed in Fried et al. (2004) as well as their accompanying trematodiases. Relevant citations were also checked that appeared in papers identified in our database searches. Following the footnote trail proved especially important for locating earlier publications. Relevant citations to the *Morbidity and Mortality Weekly Report* (MMWR) were examined but excluded from our tables since they provided minimal information on cases infected with the organisms under review (e.g., Kappus et al. 1991).

The purpose of this review is to provide information on imported and local FBT and their trematodiases in the USA during an approximately 120 years. The review contains four tables, starting with *Clonorchis* and *Opisthorchis* (Table 1) which has the greatest number of entries, followed by *Paragonimus* (Table 2) and then *Fasciola* (Table 3), and finally miscellaneous FBT (Table 4). Information in each table is arranged chronologically and the first column contains the entry numbers for that table. Further clarification of the entry numbers is made in each section related to a particular FBT. In all tables, the labeling of column 4, except in Table 3 where it is column 3, indicates the difficulty of ascertaining the exact location where the infection was acquired, i.e., locally or not. Where symptoms are omitted, they were not provided in the original paper or were not specific for the trematode under consideration.

Clonorchis and *Opisthorchis*

We have included *Clonorchis sinensis* and *Opisthorchis* sp. in the same section since these species have close morphological and biochemical similarities. Both genera are in the family Opisthorchiidae. See Sithithaworn et al. (2007) for an excellent review of opisthorchiid liver flukes. In addition to being human flukes of importance with concerns about host pathology of the biliary system, both *O. viverini* (the main *Opisthorchis* species of humans) and *C. sinensis* have been classified as group 1 carcinogens by IARC (2009). The presence of these flukes in humans, and other unknown factors, may lead to cholangiocarcinoma (bile duct cancer) and hepatocarcinoma (liver cancer) (see review in Mayer and Fried 2007).

Species in both genera, particularly *O. viverini* and *C. sinensis*, are usually acquired when humans eat raw or improperly cooked freshwater fish (mainly cyprinids) infected with the metacercarial cysts. In brief, the life cycle of these flukes involves prosobranch snails not typically endemic in the USA, numerous species of freshwater fishes, and humans or vertebrates that serve as definitive hosts. Eating of raw or improperly cooked freshwater fish containing metacercariae may lead to biliary infection in humans. Diagnosis of infection is based on finding typical opisthorchiid eggs in the stool, although immunodiagnostic and molecular tests are available and particularly useful to detect chronic infections (Sithithaworn et al. 2007). Establishment of the parasite occurs when ingested metacercariae excyst in the small intestine enter the biliary system and become sexually mature. Mature worms establish in the bile ducts and induce pathology in the biliary system.

Although species of *Bithynia* and related snails are available in the USA (*Bithynia* hosts opisthorchiids), it is uncertain if human liver fluke infections are vectored by these snails in the USA or even if local cases of opisthorchiids have occurred in humans in the continental USA. Most cases of *Clonorchis* and *Opisthorchis* reported in the USA are allochthonous and a long history of such cases is documented in Table 1.

Most case reports of *Clonorchis* and *Opisthorchis* presented in Table 1 indicate that the infections have been mainly imported to the USA. Through the 1970s, imported infections were noted in Chinese, Japanese, and Korean immigrants (see entry numbers 1–4,8,9,11–14,19 in Table 1) as well as Caucasians who resided in China for several years (see entry numbers 6,7,11,19 in Table 1). The earliest imported case is from Biggs (1890), who found trematodes ("*Distoma sinense*") present at autopsy in the bile ducts of a Chinese male in New York City. This was followed a few years later by White (1906), whose autopsy results during a series of plague investigations detected the organism in 18

Chinese who died of other causes, many of whom had not been out of this country for 12 or more years. Lack of understanding of the transmission cycle and treatment for *Opisthorchis* at that time caused public health concerns, and stool samples became mandatory at certain ports of entry during the 1920s (see entry number 4 in Table 1) when it was designated "a loathsome and contagious disease" (see entry number 5 in Table 1). Estimates of prevalence from this period indicate that at least 20% of Chinese immigrants (see entry number 3 in Table 1) were infected, many without symptoms (see entry number 4 in Table 1). Comparable estimates were made a number of years later by Kammerer et al. (1977); that study found a prevalence of 26% among older Chinese immigrants in New York City.

Beginning in 1979, case reports and surveys indicate that Southeast Asians from Laos, Cambodia, and Vietnam were a major source of imported infections in the USA (see entry numbers 15–18, 20–39, 41–43, 45, 46, 48, 49, 51, 52 in Table 1). Prevalence estimates were highest during 1980–1982, when several surveys found up to 20% and 31.2% prevalence in the groups under study (38 and 28, respectively). Numerous reports document that Southeast Asian refugees who had been in Thai refugee camps may have acquired the infection there (e.g., entry numbers 17, 25–27, 31, 32, 38, 42, 46 in Table 1). Many papers, especially those with high prevalence estimates, indicate coinfection with other parasites (see entry numbers 4, 15–17, 22, 24, 25, 28, 32, 38 in Table 1). Recent studies of established immigrant populations in the USA for a year or more found a prevalence of approximately 2% or less in Southeast Asian immigrants (see entry numbers 48 and 52 in Table 1). These individuals may represent cases that were not detected upon arrival. Several surveys have noted higher rates in individuals under 39 years of age (e.g., see entry numbers 15, 17, 42 in Table 1). Occasional reports among Chinese immigrants during this period were also noted (see entry numbers 40, 44, 47, 50 in Table 1) and also for immigrants from Thailand (see entry numbers 39 and 53 in Table 1). Stauffer et al. (2004) indicated that the former Soviet Union and Ecuador are countries of origin for imported USA cases.

There have been several reports of infection in the USA, probably locally acquired (see entry 5 in Table 1). Binford (1934) reported four cases of *Clonorchis* infection among native born Hawaiians where the suspected source was local pond fish or freshwater fish imported from China. The possibility of infection from the consumption of imported fish in the continental USA was raised in a few reports (e.g., see entry numbers 8 and 50 in Table 1), particularly when the time since emigration to the USA was lengthy. Determining the definite geographic site of infection is particularly problematic for *Clonorchis* and *Opisthorchis* as cases may present years after infections were acquired, including one case which may have presented 25 years after the infection was acquired (see entry number 12 in Table 1) and another after 30 years (see entry number 50 in Table 1).

Common symptoms of infection with *Opisthorchis* include fever, jaundice, right upper quadrant pain, epigastric pain, nausea, diarrhea, and an eosinophilia of 3–20% (e.g., entry numbers 1, 4, 6, 8, 11, 12, 35, 39, 40, 43, 45, 46, 49–51, 53 in Table 1). Cases also commonly present with hepatomegaly, cholangitis, cholecysitits or other bile duct disorders, and pancreatitis (e.g., entry numbers 1, 8, 12, 13, 40, 44, 49, 50, 51 in Table 1). Several cases of cholangiocarcinoma were noted among Chinese, Laotian, and Thai immigrants (see entry numbers 40, 43, 46, 53 in Table 1). The onset of symptoms for *Clonorchis* or *Opisthorchis* infection may also be delayed, as documented in a number of studies where eggs were detected in stool specimens among individuals who were otherwise asymptomatic (e.g., entry numbers 4, 7, 25, 27, 32 in Table 1). For the treatment of clonorchiasis and opisthorchiasis, 25 mg/kg praziquantel three times a day for two consecutive days is recommended (Keiser and Utzinger 2009).

Paragonimus

Species of *Paragonimus* cause paragonimiasis in the USA. Some species are autochthonous, whereas others are allochthonous. Since species of the snail first intermediate host occur in the USA, the cycle exists with numerous local freshwater crustaceans, i.e., crabs and crayfish, serving as second intermediate hosts. Humans and various mammals that feed on infected crustaceans are the definitive hosts of these lung flukes. Metacercariae, in the duodenum of the definitive host, penetrate the gut and then the diaphragm, then migrate to the lung capsule and become adult worms in loosely formed cysts in the lungs. Adults become ovigerous and the eggs exit the host via the sputum and the feces. The egg is an important diagnostic tool for detecting this trematode in the host, although other types of immunological and molecular detection tests are available (Blair et al. 2007).

Table 2 summarizes the information on *Paragonimus* and paragonimiasis from 34 case reports and one prevalence survey from 1910 to 2009. These entries were reported from numerous locations in the USA. Of the 35 entries, at least ten are local (see entry numbers 1, 20, 25–28, 30, 32, 33, 35 in Table 2) and more than 20 are imported (see entry numbers 2, 5–19, 21–24, 29, 31, 34 in Table 2); a few are of uncertain origin (see entry numbers 3 and 4 in Table 2). Although numerous species of *Paragonimus* have been described globally (Blair et al. 2007), as seen in Table 2, only three species have been described from the USA, *P. westermani*, *P. kellicotti*, and *P. mexicanus*.

Table 1 A summary of studies on *Clonorchis sinenus* and *Opisthorchis* sp. in the USA

Entry #	Reference	Opisthorchiidae genera and species	Reporting locale for presumed local (L) or imported (I) infections	Case reports, survey and medical presentation
1	Biggs 1890	*Opisthorchis* sp.	New York, NY (I)	A Chinese male; 5 months history of partial paralysis, GI disturbance, diarrhea, sudden onset of fever, pulmonary edema, followed by death, bile duct obstruction
2	White 1906	*Opisthorchis* sp.	San Francisco, CA (I)	18 Chinese, most in USA for 2–12 years, including one canneryman from Alaska; death due to other causes unrelated to infection
3	Gunn 1916	*C. sinensis*	San Francisco, CA (I)	Survey of 686 Chinese and 32 Japanese immigrants, most checked upon arrival; others in USA for <9 years; many asymptomatic, several with hepatomegaly or spleenomegaly; 20% Chinese immigrants infected (125 cases); 29% sick Chinese residents infected (24 cases); 4% sick Japanese residents infected (4 cases)
4	Shattuck 1923	*C. sinensis*	Boston, MA (I)	Two Japanese and 52 Chinese immigrants; a few with weight loss, fever, 5–11% eos; most cases asymptomatic and detected by stool samples submitted upon arrival
5	Binford 1934	*C. sinensis*	Honolulu, HI (L)	Four (2 male and 2 female) native born Hawaiians, one with Korean ancestry, age 14–48 years, detected through routine stool samples during leprosy segregation
6	Edelman and Spingarn 1949	*C. sinensis*	New York, NY (I)	Four Caucasians, recent immigrants/visitors, with prior residence in Shanghai, China; 3 females, 1 male, age 4–34 years; symptoms include fever, 3–20% eos, nausea, epigastric pain, loose stool, jaundice, hepatomegaly
7	Augustine and Isenberg 1950	*C. sinensis*	Boston, MA (I)	Three German born male Caucasians with prior residence in Shanghai, China; 36–47-year-olds in USA for >2 years; mild infections detected through stool samples
8	Lee and Hirst 1957	*C. sinensis*	Oakland and Los Angeles, CA (L[a])	Two Chinese males, 43 and 56-year-olds, in USA for 20–30 years; history of gallbladder disease, 5.5% and 35% eos
9	Coleman et al. 1958	C. *sinensis*	Chicago, IL (I)	A 36-year-old Chinese male immigrant from Hong Kong in USA for 5 years; abdominal distention, epigastric and right upper quadrant pain; followed by severe diarrhea, 8% eos; hepatic failure and severe cholyangitis resulting in death. Coinfected with *H. heterophytes*
10	Ching 1961	*C. sinensis* and *Opisthorchis* sp.	Honolulu, HI (I)	Survey of stool samples from 1,380 Hilo and Honolulu in USA for ≤7 years during 1959–60, primarily of Hawaiian or Filipino decent, some with Chinese ancestry; *C. sinensis* 1.09% prevalence (15 cases—mostly Chinese or with travel history to China); *Opisthorchis* sp.: 0.07% prevalence (1 case)
11	Strauss 1962	*C. sinensis*	San Francisco, CA (I)	105 cases, 57 in Chinese (some USA born), and 48 Caucasian (45 USA born) during 1945–1960; some with epigastric pain, rt upper quadrant pain, diarrhea, nausea, vomiting, enlarged liver or spleen, 2.5–3.0% eos
12	Shugar and Ryan 1975	*C. sinensis*	Edison, NJ (I)	A 43-year-old Canton Chinese male in USA for 25 years; abdominal pain radiating to back, nausea and vomiting, hepatomegaly, pancreatitis
13	Ameres et al. 1976	*C. sinensis*	New York, NY (I)	A 37-year-old Korean male in USA for 5 years; fever, cholecystitis
14	Kammerer et al. 1977	*C. sinensis*	New York, NY (I)	A 38-year-old Chinese born female, with hepatitis, hepatoma, clonorchiasis; and, survey of stool samples from 200 Chinese residents of NYC: 26% prevalence in Chinese born from Kwantung Province (39 cases), 0 cases in USA born
15	Holtan et al. 1979	*C. sinensis*	St Paul, MN (I)	Survey of stool samples from 56 Laotians immigrating 1976–78, age 0–40 years: 5% prevalence (3 cases, all 10–19 years)
16	Lindes 1979	*C. sinensis*	Columbus, OH (I)	Survey of stool samples from 70 Laotian refugees, recent immigrants, 1 month–70 years: 10% prevalence (7 cases)

17	Erickson and Hoang 1980	*C. sinensis*	Hartford, CT (I)	Survey of 194 SEA refugees immigrating 1979–80, 0–79 years: 9% prevalence (14 cases, most under 39 years)
18	Jones et al. 1980	*C. sinensis*	Mayo Clinic, MN (I)	Survey of blood and stool specimens from 100 SEA refugees in USA 1 day to 5 years, most age 1–71 years: 2% prevalence (2 cases)
19	Sun 1980	*C. sinensis*	New York, NY (I)	A 42-year-old Caucasian female, a 45-year-old Japanese female, two Cantonese males 50–56 years; symptoms vary but include diarrhea, fever, epigastric pain, jaundice, hepatomegaly, liver nodules
20	Traylor et al. 1980	*C. sinensis*	CO (I)	Survey of stool specimens from 195 patients with SEA surnames including refugees: 10% prevalence (19 cases)
21	Weisenthal et al. 1980	*C. sinensis*	Kankakee and Will Co., IL (I)	Survey of stool specimens from 165 Meo Laotians refugees in 1979, all in USA for ≤1 year; prevalence: <1% (1 case)
22	Arafaa 1981	*C. sinensis*	Contra Costa County, CA (I)	Survey of stool specimens from 186 SEA refugees immigrating 1978–80: 15% prevalence in males (16 cases), 12% in females (10 cases), most under 40 years
23	Borchardt et al. 1981	*C. sinensis*/ *O. viverrini*	San Francisco, CA (I)	Survey of stool specimens from 6,241 SEA refugees screened 1979–80, 57.3% male: 3% prevalence (182 cases)
24	Hoffman et al. 1981	*Opisthorchis* sp.	San Diego, CA (I)	Survey of stool specimen from 217 SEA refugees with symptoms or hematologic findings suggesting parasitism during 1976–79: 18% prevalence (40 cases, all Laotian)
25	Wilson et al. 1981	*C. sinensis*	Mobile, AL (I)	A male Laotian refugee; asymptomatic
26	Catanzaro and Moser 1982	*Opisthorchis* sp.	San Diego, CA (I)	Survey blood and stool specimens from 618 SEA refugees screened 1980–81, 50% 0–18 years, 54% male: 5.6% prevalence (35 cases, 61% Laotian)
27	Lerman et al. 1982[b]	*Opisthorchis* sp.	San Diego, CA (I)	Survey of stool and blood specimen from 226 asymptomatic SEA refugees in 1980, 90% in USA for <12 months, ages 20–79 years: 11% prevalence (26 cases); some eos noted
28	Skeels 1982	*C.sinensis*/ *Opisthorchis* sp.	Albuquerque, NN (I)	Survey of stool specimens from 776 SEA immigrating 1979–80, 57% Laotian: 31.2% prevalence (242 cases)
29	Taylor and Swett 1982	*Opisthorchis* sp.	New Haven, CT (I)	A 31-year-old Laotian female refugee; cough, chest pain, pleural infiltrates, 36% eos; coinfected with *Paragonimus westermani*
30	Tittle et al. 1982	*C. sinensis*	Oakland, CA (I)	Survey of medical records and stool samples from 98 SEA children, age 2 weeks to 17 years; 4% prevalence (4 cases, in Laotians and Cambodians only)
31	DeGirolami and Kimber 1983	*Clonorhis*/ *Opisthorchis* sp.	Boston, MA (I)	Survey of stool specimens from 1478 SEA refugees (80% Cambodian, 10% Laos) immigrating 1981–82: 10% prevalence (146 cases)
32	Johnson et al. 1983	*C. sinensis*	Seattle, WA (I)	A 34-year-old male Laotian refugee in USA for 2 years; infection discovered during investigation for *Paragonimus*
33	Sutherland et al. 1983[c]	*C. sinensis*	Mayo Clinic, MN (I)	Survey of 426 SEA refugees seeking care during 1975–81, ~50% Vietnamese, 25% Laotian, 6 months–72 years, 55.2% male: 12.5% prevalence (53 cases)
34	Dao 1984	*C. sinensis*	Nashville, TN (I)	A 20-year-old pregnant Laotian female refugee, recent arrival in USA; no symptoms other than eggs in stool
35	Navab et al. 1984	*C. sinensis*	Little Rock, AK (I)	A 52-year-old Laotian female in USA for 2 months; rt upper quadrant pain, fever, weight loss, 10% eos; prior treatment for gallstones, mass in porta hepatis
36	Woolf et al. 1984	*C. sinensis*/*O. viverrini*	North Carolina (I)	26 Laotians refugees; elevated serum IgE levels
37	Parish 1985	*C. sinensis*	Seattle, WA (I)	Survey of stool specimens from 338 SEA refugee children, age 5 weeks–16 years, examined 1981–1982; 48 cases (92% Laotian)
38	Roberts et al. 1985	*C. sinensis*	Philadelphia, PA (I)	Survey of 97 pregnant SEA refugees during 1980–82, avg age 23.3 years, 42% Vietnamese, 29% Laotian: 20% prevalence (19 cases)
39	Wong et al. 1985	*O. viverrini*	Washington, DC and Bethesda, MD (I)	A 27-year-old Thai female in USA for 2 months; abdominal pain, fever, jaundice, upper GI bleeding, hemobilia, WBC 14–22% eos; coinfected with *F. hepatica*

Table 1 (continued)

Entry #	Reference	Opisthorchiidae genera and species	Reporting locale for presumed local (L) or imported (I) infections	Case reports, survey and medical presentation
40	Schwartz 1986	*C. sinensis*	Philadelphia, PA (I)	A 51-year-old Chinese male immigrant; epigastric discomfort, jaundice, dark urine, light stools, pruritis, hepatomegaly, cholangiocarcinoma, resulting in death
41	Nutman et al. 1987	*Opisthorchis* sp.	Washington, DC (I)	Survey of 128 SEA refuges between 1981 and 1984 with eos; 53% male, 87% Cambodian; 10% prevalence (13 cases)
42	Molina et al. 1988	*C. sinensis*	San Diego, CA (I)	Survey of stool specimens from 2520 SEA refugees, 98% Cambodian, 65% <20 years, in USA avg of 2 years: 1.7% prevalence in Cambodians (42 cases) and 5.8% in Hmong (3 cases); most cases under 39 years
43	Sher et al. 1989	*C. sinensis*	Pittsburgh, PA (I)	A 41-year-old Laotian male in USA for 7 years; fever, jaundice, rt upper quadrant pain, bile duct strictures, cholangiocarcinoma
44	Nishioka et al. 1990	*C. sinensis*	Boston, MA (I)	A 72-year-old Chinese female from Hong Kong in USA for 10 years; acute abdominal pain, fever, nausea, diarrhea, abdominal mass, cholangitis
45	Dao et al. 1991	*Opisthorchis* sp.	Nashville, TN (I)	A 66-year-old Laotian immigrant; ankle swelling, dyspnea, abnormal liver functions, 14% eos followed by jaundice, stricture of common bile duct
46	Ona and Dytoc 1991	*C. sinensis*	Rochester, NY (I)	A 37-year-old Laotian male in USA for 2+ years, and 58-year-old Laotian male in USA for 10 months; both with cholangiocarcioma; symptoms include epigastric pain, 3–11% eos, hepatic abscesses and lobe atrophy, dilated pancreatic duct; both with history of *Clonorchis*; infection treated with praziquantel
47	Balthazar and Lamb 1993	*C. sinensis*	New York, NY (I)	A 56-year-old Chinese male in USA for 20 years; severe abdominal pain, jaundice, epigastric tenderness, 15% eos, pancreatic; gallbladder removed previously
48	Buchwald et al. 1995	*C. sinensis*	Seattle, WA (I)	Survey of stool specimens from 201 SEA refugees screened in 1990, 64% female, 55% Cambodian, 7% Laotian, 89% in USA for 1+ year; 2% prevalence (4 cases)
49	Kitchen 1999	*C. sinensis*	St Paul, MN (I)	An 18-year-old Vietnamese female in USA for 8 months; nausea, vomiting, upper right quadrant and epigastric pain, bile duct disorder
50	Lewin and Weinert 1999	*C. sinensis*	Houston, TX ([a])	An 84-year-old male from SE China in USA for 30 years; fever, chills, cough, painless jaundice, decreased appetite, weight loss, hepatomegaly, bile duct disorder
51	Lai et al. 2001	*C. sinensis*	Minneapolis, MN (I[a])	A 48-year-old Laotian male, in USA for 25 years; 2 day history of epigastric pain, nausea, vomiting, pancreatic duct obstruction; prior rt upper quadrant pain, bile duct obstruction
52	Stauffer et al. 2004	*Opisthorchis* sp. and *C. sinensis*	St Paul and Minneapolis, MN (I)	Survey of stool specimens from 1291 international patients from SEA, Former Soviet Union and Ecuador, during 1993–98, 4–79 years: 1.3% prevalence (17 cases); many with mild eosinophilia
53	Papachristou et al. 2005	*C. sinensis*	Pittsburg, PA (I)	A 35-year-old Thai male immigrant in USA for 20 years, with frequent visits to Thailand; epigastric pain, rt upper quadrant pain, decreased appetite, fatigue, weight loss, 4% eos, mass in porta hepatica, advanced metastatic cholangiocarcioma

eos eosinophilia, *rt* right, *SEA* Southeast Asian(s)

[a] Uncertain as to location where infection was acquired

[b] Some cases may have been included in Catanzaro and Moser 1982

[c] Some cases may have been included in Jones et al. 1980

The earliest case of *Paragonimus* in the USA was reported by Abend (1910) of a German male residing in the USA for 20 years, who worked on railroad construction in Texas, Colorado, and Missouri. He probably acquired the infection from eating undercooked or raw crayfish prepared by Chinese cooks while in camp (see entry number 1 in Table 2, Ameel 1934). Most local cases acquired in the continental USA have been reported since 1986. In general, these cases tend to be of male outdoor adventurers who consumed infected undercooked crayfish while on river trips in the midwest USA (see entry numbers 20, 25, 28, 33, 35 in Table 2). Suspected locations for acquiring infections in the USA include tributaries of the Arkansas River in Ohio and northeast Oklahoma (see entry numbers 25 and 28 in Table 2), the Current and Jacks Fork Rivers in Missouri (see entry numbers 20 and 35 in Table 2), and the Meramec River in Southeast Missouri (see entry number 35 in Table 2). Impaired judgment due to alcohol intoxication was suggested as a factor along with eating raw crayfish in three recent cases (see entry number 35 in Table 2). Two recent cases suggest infected imported crabmeat or other crustaceans as a possible local source (see entry numbers 27 and 30 in Table 2), one of which included acquiring infection through occupational exposure as a sushi chef (see entry number 30 in Table 2).

The earliest imported case of infection with *Paragonimus* was noted by Fehleisen and Cooper (1910), of a 35-year-old Japanese male who emigrated to the USA 6 years earlier (see entry number 2 in Table 2). Throughout the 1970s and early 1980s, most cases were imported to the USA by Southeast Asian refugees (see entry numbers 6, 7, 9–14, 16–19, 22, 24 in Table 2) or immigrants from Korea or the Philippines (see entry numbers 3–5, 8, 17 in Table 2). As noted for *Clonorchis* infections, many of the Southeast Asian refugees during this period were originally from Laos, Cambodia, and Vietnam and spent time in refugee camps in Thailand, where they may have acquired the infection (see entry numbers 6, 7, 11–14, 18, 22, 24 in Table 2). More recently, several cases have been noted in immigrants from El Salvador (see entry numbers 21, 29, 34 in Table 2), with another case most likely acquired in Mexico or Costa Rica (see entry number 31 in Table 2). There have been two reported cases in Hawaii (see entry numbers 3 and 4 in Table 2), both of which are thought to be imported with some question as to certainty. Several case reports or surveys indicated that patients infected with *Paragonimus* were often coinfected with other helminths, including *Clonorchis* (e.g., entry numbers 6, 7, 18 in Table 2).

The overriding symptoms associated with paragonimiasis are cough, hemoptysis or dyspnea (see entry numbers 1, 2, 4–6, 8–11, 13–16, 18–22, 24–30, 32–35 in Table 2), some of which overlap with tuberculosis and other pulmonary disorders. Pulmonary infiltrates, effusion, nodules, or lesions were also very common (e.g., entry numbers 6, 8, 10, 13–18, 20–22, 26–30, 32–35 in Table 2). A number of cases reported an eosinophilia of 20% or higher (see entry numbers 6, 12, 14, 16, 21, 26, 30, 35 in Table 2), though cases of 3% and lower were also reported (see entry numbers 2, 8, 24, 29 in Table 2). Some cases also have fever, headache, weight loss, or empyema (see entry numbers 2, 11, 20, 24–26, 29, 31, 33–35 in Table 2). Unusual presentations as a result of infection with *Paragonimus* include two females with breast involvement (see entry numbers 15 and 23 in Table 2) and a child with brain and CNS disturbances (see entry numbers 29 and 34 in Table 2). Most cases do not show all of the above symptoms. Diagnosis is based on a history of eating raw or undercooked shellfish, characteristic eggs in the stool or sputum, and whenever possible, immunological and molecular diagnostic tests. Diagnosis may be further complicated when paragonimiasis is extrapulmonary and worms locate in foreign sites such as muscles, and numerous vital organs including the brain. Differential diagnosis of paragonimiasis from tuberculosis and other non-helminthic pulmonary infections is important. Recommended treatment for lung fluke infections is 25 mg/kg body weight of praziquantel 3× a day for two consecutive days (Keiser and Utzinger 2009). Prevention is accomplished by eating properly cooked shellfish.

Fasciola

We have only included information on *F. hepatica* since this is the single fasciolid reported as a human FBT in the USA. For global consideration of *F. hepatica* and other fasciolids, see Keiser and Utzinger (2009) and Mas-Coma et al. (2007).

F. hepatica is a parasite of the liver and bile ducts of human and non-human definitive hosts. This fluke may induce considerable pathology in the liver and biliary system. Acquisition of this fluke by humans occurs when subjects inadvertently swallow cysts attached to tainted vegetation. One of the numerous plants associated with infection is watercress. As reviewed by Mas-Coma et al. (2007), numerous other plants may become infected with the cercariae of *F. hepatica*. Infection may also occur by drinking contaminated water containing free-floating cysts (Mas-Coma et al. 2007). The first intermediate hosts of *F. hepatica* are numerous lymnaeid and related pulmonates. Since lymnaeids and their relatives occur in the USA, reports of endemic life cycles mainly involving herbivores as definitive hosts do occur locally. Because the *F. hepatica* cycle does exist in the USA involving lymnaeid snails, vegetation, and herbivores, it is likely that additional reports of endemic human fascioliasis will occur in the

Table 2 A summary of studies of *Paragonimus* in the USA

Entry #	Reference	Species	Reporting locale for presumed local (L) or imported (I) infections	Case reports, survey and medical presentation
1	Abend 1910	*Paragonimus* sp.	Germany[a] (L)	A German male residing in USA for 20 years, including TX, CO and MO; hemoptysis
2	Fehleisen and Cooper 1910	*Paragonimus* sp.	San Francisco, CA (I)	A 35-year-old Japanese male in USA for 6 years; difficulty swallowing, history of hemoptysis, weight loss, chronic headache, 2% eos
3	Alicata 1964	*P. westermani*	Honolulu, HI (I[a])	Patient had resided in Korea, reported in HI during 1949; no other details provided
4	Peroff 1974	*P. westermani*	Honolulu, HI (I[a])	A 15-year-old Korean male immigrant in USA for 1 year; hemoptysis, pulmonary inflammation or mass
5	Willie and Snyder 1977	*P. westermani*	Los Angeles, CA (I)	A 40-year-old Korean male in CA for 3 years, previously in HI for 5 years, regular trips to Korea; chronic cough and hemoptysis, 5–18% eos, lobe infiltration
6	Mayer 1979	*P. westermani*	Bronx, NY (I)	A 3-year-old Laotian female refugee in USA for 1 month; cough, 23% eos, pulmonary infiltrates and cystic lesions, prior treatment for pneuomonitis,
7	Erickson and Hoang 1980	*P. westermani*	Hartford, CT (I)	Survey including stool specimen of 194 SEA refugees, 61% Vietnamese, screened 1979–1980 shortly after arrival in USA, ages 0–79; prevalence: <1% (1 cases, 0–19 years)
8	Fischer et al. 1980	*P. westermani*	Honolulu, HI (I)	A 4-year-old Filipino female immigrant in US for <3 weeks; chronic cough for several months, recent history or hemoptysis, anorexia, and fever; pulmonary infiltrates, 3% eos
9	Hart 1980	*P. westermani*	Hartford, CT (I)	An 11.5-year-old Laotian male refugee in USA for <6 months; cough, pain and swelling in ankle, 11% eos, consolidation involving rt lobe and adenopathy
10	Coleman and Root 1981; Coleman and Barry 1982	*P. westermani*	New Haven, CT (I)	A male and a female Laotian (married) refugees, 31–32 years, in USA for <2 months; both with pleural infiltrates, cough; female: pleuritic chest pain, subcutaneous inflammation in left breast; male: cavitation, 8% eos, relapsed 4 months after apparent eradication
11	Collins et al. 1981	*P. westermani*	Charlottesville, VA (I)	A 15-year-old Laotian male refugee in USA for 1 year; cough, hemoptysis, dyspnea, wheezing, weight loss, pulmonary infiltrates, 17% eos
12	Minh et al. 1981	*Paragonimus* sp.	Orange Co., CA (I)	A 25-year-old Laotian male refugee in USA for <2 months; pleural effusion, 33% eos; three additional cases briefly mentioned
13	Burton et al. 1982	*P. westermani*	Chicago, IL (I)	Three 8 to 11-year-old Laotian refugees, all recent arrivals; symptoms vary but include chronic cough, hemoptysis in two patients, fever, pleural infiltrates and eosinophilia (5–13%) in all
14	Johnson et al. 1982; Johnson and Johnson 1983	*P. westermani*, *Paragonimus* sp.	Minneapolis, MN and Seattle, WA (I)	25 SEA refugees examined 1980–1982 (MN: 17 Hmong refugees; WA: 7 Laotians and 1 Vietnamese), 80% male, 80% ages 10–35; cough in most, many with hemoptysis, 7–52% eos, pleural effusion or lesions
15	Rangdaeng et al. 1982	*P. westermani*	Houston, TX (I)	A 19-year-old Nigerian female in USA for medical treatment; with fatigue, myalgia, enlargement of right breast, 15.4% eos, history of hemoptysis, pulmonary lesions, lymphoma of right breast
16	Taylor and Swett 1982[b]	*P. westermani*	New Haven, CT (I)	A 31-year-old Laotian female refugee in USA; cough, chest pain, pleural infiltrates, 36% eos, coinfected with *Opistorchis sinensis*; a 32-year-old Laotian male refugee; pleural mass and infiltrates
17	Wall and McGhee 1982	*P. westermani*	Portland, OR (I)	A 17-year-old Korean female immigrant in USA for 4 months; acute epigastric pain localizing to right lower quadrant, vomiting, 0% eos; a 15-year-old Laotian male, recent immigrant; pulmonary lesion, 10% eos
18	Johnson et al. 1983	*P. westermani*	Seattle, WA (I)	A 34-year-old Laotian male refugee in USA for <1 month.; history of intermittent productive cough, pulmonary infiltrate, 7–8% eos

19	Johnson et al. 1985	*Paragonimus* sp.	Seattle, WA (I)	8 SEA refugees, ages 7–66 years in USA for 10–40 months, 75% male; five with symptoms including cough, chest pain, history of hemoptysis; seven with abnormal chest roentgenogram
20	Pachucki et al. 1984; Mariano et al. 1986	*P. kellicotti*	Fulton, IL (L)	A 19-year-old American male, no international travel, float trip on Current River, MO; fever, malaise, fatigue, dyspnea, chest pain, 6–13% eos; followed by pleural effusion and infiltrate
21	Sharma 1989	*P. westermani*	Los Angeles, CA (I)	A 46-year-old El Salvador male in USA for 13 years; pneumothorax, infiltrates, followed by hemoptysis, 33% eos
22	Yee et al. 1992	*P. westermani*	San Joaquin Valley, CA (I)	Three Laotian males, age 13–39 year, in USA for 1–2 years; a 40-year-old Laotian female in USA for 1 month; all with hemoptysis, two with cystic areas in pulmonary lobes, two with pulmonary infiltrates
23	Fogel and Chandrasoma 1994	*Paragonimus* sp.	Los Angeles, CA (I)	Middle aged Korean female immigrant, with cystic breast mass as only reported symptom; aspiration detected eggs in fluid
24	Heath and Marshall 1997	*P. westermani*	Seattle, WA (I)	An 11.5-year-old Hmong Laotian male in USA for 16 months; 2–3 months history of increasing weakness, dyspnea, cough, weight loss, 2% eos, pleural effusion
25	Procop et al. 2000	*P. kellicotti*	Cleveland, OH (L)	A 21-year-old American male, no international travel, float trip on tributary of Arkansas river; fever, hemoptysis
26	DeFrain and Hooker 2002	*P. kellicotti*	Grand Rapids, MI (L)	An 18-year-old American male; diarrhea, recent history of headache, fatigue, dyspnea, weight loss; 25% eos, pleural effusion and infiltrate
27	Meehan et al. 2002	*P. westermani*	Rochester, MN (L)	A 86-year-old Laotian male in USA for 8 years; severe dyspnea, chest pain, pneumothoraces, lung and liver nodules, 12% eos
28	Castilla et al. 2003	*P. kellicotti*	Cleveland, OH and Tulsa, OK (L)	A 35-year-old American male, no international travel, trip on tributary of Arkansas river; hemoptysis, followed by persistent cough, pulmonary lesion, dyspnea
29	Bartlett et al. 2005	*Paragonimus* sp.	Houston, TX (I)	A 13-year-old El Salvadoran male in USA for 14 months; seizure, headaches, hemoptysis, brain lesion, 2% eos, lung nodules
30	Robertson et al. 2006	*Paragonimus* sp.	Denver, CO (L)	A 21-year-old American male of Korean ancestry, working as sushi chef; pain in rt lower quadrant, exertional dyspnea, cough, subcutaneous nodule, 56% eos, pleural effusions
31	Vincent et al. 2006	*Paragonimus* sp.	Tampa, Fl (I)	A 63-year-old Korean female, international travel in the past 7 years including Mexico and Costa Rica; diarrhea, vomiting, weight loss, lt upper quadrant pain, mass in colon and chest
32	Boe and Schwarz 2007	*Paragonimus* sp.	Denver, CO (L)	A 31-year-old American male, no international travel; chronic cough, hemoptysis, dyspnea, nausea, 13% eos, pulmonary cavitation and nodules
33	Madariaga et al. 2007	*P. kellicotti*	Omaha, NE (L)	A 71-year-old American male Caucasian; dyspnea, followed by septic shock, fever, hypotensive, pleural effusion, resulting in death
34	Zarrin-Khameh et al. 2008[c]	*P. mexicanus*	Houston, TX (I)	A 12-year-old El Salvadorean male in USA for 14 months; seizures, headaches, intermittent hemoptysis, weight loss; multiple nodules, encephalomalacia
35	Lane et al. 2009	*P. kellicotti*	St. Louis, MO(L)	A 26-year-old female and two males 31–32 years in USA, with trips on Meramec, Current and Jacks Fork rivers; common presentation include malaise, cough, fever, pleural effusion, 20–30% eos; other symptoms include headache, night sweats, vomiting, chest pain, dyspnea, weight loss, nodular lesion on lip, lobe infiltrates, atypical pleural mass

eos eosinophilia, *rt* right, *SEA* Southeast Asian(s)

[a] Acquired in the USA, reported in Germany

[b] Uncertain as to location where infection was acquired

[c] Appears to be same case described by Coleman and Root 1981

[d] Those identified as *Paragonimus* sp. were not identified to species

Table 3 A summary of studies on *Fasciola hepatica* in the USA

Entry #	Reference	Reporting locale for local (L) or imported (I) infections	Case reports, survey and medical presentation
1	Adams 1934	Almeda County, CA (I)	A 38-year-old Portuguese female immigrant in USA for 5 years, including residence in Hawaii; severe abdominal pain, fever, 2% eos, acute cholecystitis; history of pain in upper abdomen
2	Ortiz 1935	New York, NY (I)	A 29-year-old Puerto Rican male in USA for medical treatment; history of weight loss, weakness, jaundice, anorexia, and malaise, problems with vision, 3% eos, followed by paralysis of left face, abdominal pain
3	Alicata 1953; Stemmermann 1953[a]	Honolulu, HI (L[b])	21 cases in Hawaiian islands during 1906–1952, length of residency unknown, age 7–66 years; symptoms include pain in abdomen, chest, and epigastric area; weight loss, fever; some with nausea or vomiting, jaundice; liver lesions; 24–60% eos noted in later cases,
4	Clay and Straight 1961	Miami, FL (I)	A 54-year-old Haitian male visitor; epigastric and rt upper quadrant pain, severe nausea, jaundice, 12% eos, cholecystitis
5	Norton and Monroe 1961	La Jolla, CA (L)	A 50-year-old American female; abdominal pain, vomiting, diarrhea, epigastric and rt upper quadrant pain, cholecystitis, 1% eos; prior history of epigastric pain, fever, 40% eos after likely infection 9 years earlier; three neighbors also likely infected
6	Hadden and Pascarelli 1967	New York, NY (I)	A 53-year-old Puerto Rican male immigrant in USA for 5+ years; fever, headache, nausea, vomiting, 11% eos, enlarged liver, cholecystitis; prior episodes include jaundice
7	Knodell et al. 1972	San Francisco, CA (I)	A 55-year-old Mexican American male with recent trip to Mexico, in USA for 1 month; rt upper quadrant pain, occasional diarrhea, malaise, fever, weight loss, 64–68% eos, raised liver enzymes
8	Belgraier 1976	New York, NY (I)	A 53-year-old Puerto Rican female in USA for 18 years; rt upper quadrant pain, bloating, nausea, 10% eos, biliary obstruction
9	DeGirolami and Kimber 1983	Boston, MA (I)	Stool specimens from 1,478 SEA refugees (80% Cambodian, 10% Laotian, 10% Vietnamese) screened during 1981–82: <1% prevalence (2 cases)
10	Hauser and Bynum 1984	Boston, MA (L)	A 42-year-old American Caucasian female with little foreign travel; jaundice, fatigue, nausea, vomiting, abdominal pain, biliary cirrhosis, apparent sclerosing cholangitis; history of bloody diarrhea, rt upper quadrant pain, pancreatitis
11	Schiappacasse et al. 1985	Warren, MI (I)	A 28-year-old Yemenite female in USA for >10 years with regular return trips to Yemen; recurrent abdominal pain and nausea; cholecystitis, 16% eos
12	Wong et al. 1985	Washington, DC and Bethesda, MD (I)	A 27-year-old Thai female in USA for 2 months; abdominal pain, fever, jaundice, upper GI bleeding, hemobilia, 14–22% eos; coinfected with *O. viverini*
13	Nutman et al. 1987	Washington, DC (I)	Survey of 128 SEA refuges (87% Cambodian) between 1981 and 1984 with eosinophilia, 53% male: 7% prevalence (9 cases)
14	Price et al. 1993	Washington, DC (I)	A 56-year-old American male, with travel to Africa and Puerto Rico, and a 52-year-old American female with foreign residence in Cape Verde; both with epigastric or rt upper quadrant pain, 19–25% eos, liver abscess; female: weight loss, fever, decreased appetite, cholecysitis
15	Stark et al. 1993	Winston-Salem, NC (I)	A 63-year-old American female with history of international residences including Egypt; fever, abdominal pain, 29% eos, liver lesion
16	Danilewitz et al. 1996	Sacramento, CA (I)	A 49-year-old American male with extensive foreign travel to far east, esp. Taiwan; upper abdominal pain, nausea, vomiting, jaundice, biliary obstruction
17	LaPook et al. 2000	New York, NY (I)	A 65-year-old American male and 61-year-old American female couple, recently back from trip to Ireland; male: fever, anorexia, weight loss, 15% eos, hepatic necrosis, cholangiolitis; female: 45% eos, raised liver enzymes
18	Graham et al. 2001	Boston, MA (I)	A 67-year-old Cape Verdean male in USA for >5 years with subsequent return trip; rt upper quadrant pain, nausea, anorexia, weight loss, weakness, diarrhea, 35% eos, liver lesions; a 33-year-old Cape Verdean male in US for 2 months; mild abdominal pain, diarrhea, 7% eos, liver lesions

19	Neff et al. 2001	Miami, FL (L)	51-year-old American male without foreign travel for 20 years; nasal/skin rash, fever, rt upper quadrant pain, liver lesions, 30% eos
20	Noyer et al. 2002	Bronx, NY (I)	A 26-year-old Dominican female immigrant in USA for 1 month; rt upper quadrant pain, fever, 27–46% eos, mass in liver
21	Clark et al. 2005	San Antonio, TX (I)	A 28-year-old Peruvian male; fever, jaundice, 2 months history of anorexia, nausea, weight loss, rt upper quadrant pain, biliary obstruction
22	Fullerton et al. 2006	Louisville, KY (I)	A 25-year-old Mexican male in USA for 3 years; abdominal pain, nausea, vomiting, 1% eos, raised liver enzymes, biliary obstruction
23	Alatoom et al. 2008	Dallas, TX (I)	A 28-year-old pregnant Hispanic female with frequent visits to north central Mexico; nausea, vomiting, rt upper quadrant pain, biliary obstruction

eos eosinophilia, *rt* right, *SEA* Southeast Asian(s)

[a] Includes cases reported by Herbert (1907), Hall (1936), and Swanson (1939)

[b] Uncertain as to location where infection was acquired

future. The relative scarcity of human cases acquired in the continental USA is surprising. Currently, the reports indicate only one human case acquired in the continental USA, with most local cases reported in Hawaii (see Table 3).

Metacercarial cysts of *F. hepatica* excyst in the small intestine following ingestion of tainted vegetation by humans and the excysted metacercariae actively penetrate the intestinal lining, gain access to the peritoneal cavity, penetrate the liver capsule, and then enter the biliary system. These parasites reach sexual maturity in the biliary system and produce eggs which enter the intestine via the bile ducts. Eggs released into the stool are characteristic of *F. hepatica* infection and can be helpful in diagnosing the infection. Infection in the liver and bile ducts may lead to severe pathology associated with mechanical and chemical damage. Fasciolids secrete elaborate excretory–secretory (ES) products including potent proteases which exacerbate the infection.

Diagnosis of this fluke is usually based on finding typical fasciolid eggs in the stool, although numerous immunological and molecular tests are also available, especially in chronic cases where eggs in the stool may not be present. It is important to distinguish this infection from other liver and bile duct disorders of helminthic and non-helminthic origins.

In regard to prevention, avoidance of uncooked tainted vegetation such as watercress and related plants is suggested, especially from areas where known infections of *F. hepatica* occur in cattle, sheep, and other herbivores. Although numerous treatments have been used in the past on humans and animals, the drug of choice is triclabendazole administered in two separate treatments of 10 mg/kg per treatment (Mas-Coma et al. 2007; Keiser and Utzinger 2009).

The 23 cases in Table 3 provide an overview of *F. hepatica* infections in the USA. *F. hepatica* is largely imported (see entry numbers 1, 2, 4, 6–9,11–18, 20–23 in Table 3), with several locally acquired cases (see entry numbers 3, 5, 10, 19 in Table 3). Countries spanning a wide geographic range are sources of the imported cases and include: Cape Verde, the Dominican Republic, Egypt, Haiti, Ireland, Mexico, Peru, Portugal, Puerto Rico, and Yemen (see entry numbers 1, 2, 4, 6–8, 11, 14,15,17,18, 20–23 in Table 3). As with the *Clonorchis*, *Opisthorchis*, and *Paragonimus* infections, cases of *F. hepatica* originating from East Asia and Southeast Asia have also been reported (see entry numbers 9, 12, 13, 16 in Table 3). Most locally acquired cases have been reported from the Hawaiian Islands (see entry number 3 in Table 3) but also include cases acquired from locally grown watercress in California and Florida (see entry numbers 5 and 19 in Table 3, respectively).

Transmission is often attributed to the consumption of watercress or other aquatic plants (see entry numbers 3, 5, 7, 12, 14, 16–21 in Table 3), but contaminated water (see

Table 4 Miscellaneous FBT infections in the USA

Entry #	Reference	Species	Reporting locale of presumed local (L) or imported (I) infections	Case reports, survey and medical presentation
Diplostomidae				
1	Beaver et al. 1977	*Alaria* sp.	New Orleans and Baton Rouge, LA (L)	A 43-year-old Caucasian American male; small inter-dermal mass on upper thigh close to groin; later similar mass on left lumbar area
2	McDonald et al. 1994	*Alaria* sp.	San Francisco, CA (L)	A 35-year-old American male of Chinese ancestry, never out of CA; A 38-year-old Chinese male immigrant in CA for 10 years; unilateral decreased/blurred vision
3	Kramer et al. 1996	*Alaria* sp.	Northern CA (I)	A 38-year-old American male, with travel to Manitoba, Canada; intermittent hives, brocheospasms, 15% eos; followed by subcutaneous nodule on chest
Echinostomidae				
4	Vogel 1933	*Himasthla muhlense*	Germany[a] (L)	German patient who traveled to New York, USA; previous resident of Colombia
5	DeGirolami and Kimber 1983	*Echinostoma* sp.	Boston, MA (I)	Survey of 1,478 SEA refugees (80% Cambodian, 10% Laotian) screened 1981–82: <1% prevalence (4 cases)
6	Poland et al. 1985	*Echinostoma* sp.	Minneapolis, MN (I)	18 American tourists (in tour group of 20), recently back from Kenya/Tanzania; symptoms vary and include minimal flatulence, abdominal discomfort, abdominal pain, loose stools, epigastric pain/tenderness, eos
Heterophyidae				
7	Alicata and Schattenburg 1938	*Stellantchasmus* sp.	Honolulu, HI (L)	A 26-year-old Hawaiian male of Japanese ancestry, born and raised in Oahu, never traveled; diarrhea, weight loss, lack of strength, followed by nervousness, upper right quadrant discomfort
8	Coleman et al. 1958	*Heterophyes heterophyes*	Chicago, IL (I)	A 36-year-old Chinese male immigrant in USA for 5 years; increasing abdominal distention, epigastric and right upper quadrant pain; followed by severe diarrhea, 8% eos; hepatic failure and severe cholangitis resulting in death; coinfected with *C. sinensis*
9	Ching 1961	*Heterophyes* sp.	Honolulu, HI (L and I[b])	Survey of stool samples from 1,380 Hilo and Honolulu residents during 1959–60; primarily of Hawaiian or Filipino decent, some with Chinese ancestry: 3% prevalence (41 cases)
10	Tittle et al. 1982	*Metagonimus yokagawaii*	Oakland, CA (I)	Survey of medical records and stool samples from 98 SEA children, aged 2 weeks to 17 years; 3% prevalence (3 cases, in Laotians and Cambodians only)
11	Goldsmith 1978	*M. yokagawaii*	San Francisco, CA (I)	A 60-year-old Caucasian American female with extensive travel through far east; episodic diarrhea characterized by watery stools, mild cramping; 4% eos
12	Sutherland et al. 1983	*M. yokagawaii*	Mayo Clinic, MN (I)	Survey of 426 SEA refugees (50% Vietnamese, 25% Laotian) seeking care during 1975–81, aged 6 months–72 years, 55.2% male: 0.2% prevalence (8 cases)
13	Adams et al. 1986	*H. heterophyes*	Philadelphia, PA (L)	A 48-year-old American female never traveled out of the country; history of diarrhea, 5% eos
14	Nutman et al. 1987	*M. yokogawai*; *H. heterophyes*	Washington, DC (I)	Survey of 128 SEA refugees (87% Cambodian) refuges between 1981 and 1984 with eos, 53% male: *M. yokogawai* <1% prevalence (1 case); *H. heterophes*: 3% prevalence (4 cases)
Plagiorchiidae				
15	McMullen 1937	*Plagiorchis muris*	Pelston, MI (L)	Self-inflicted case; swallowed *P. muris* cysts

Troglotrematidae				
16	Phillip 1958	*Nanophyetus salmincola*	Hamilton, MT (L)	Self-inflicted case; consumed infected trout and experienced mild intestinal discomfort
17	Eastburn et al. 1987	*N. salmincola*	Corvallis, OR, and Seattle, WA (L)	10 USA cases 1974–1985, 60% male, all Caucasian, age 6–55 years; symptoms vary and include diarrhea, 2–43% eos, abdominal discomfort, nausea, vomiting, weight loss and fatigue.
18	Fritsche et al. 1989	*N. salmincola*	Seattle, WA and Corvallis, OR (L)	10 cases 1982, plus 1986–1987 from west central Oregon; includes three American Caucasian and 7 Laotian immigrants, most in USA for >7 years; various symptoms included abdominal pain and discomfort, gas, loose stools, diarrhea, 0–43% eos
19	Harrell and Deardorff 1990	*N. salmincola*	Manchester, WA (L)	A 19-year-old American male biology technician; malaise, intermittent diarrhea, abdominal discomfort, nausea, vomiting

eos eosinophilia, *SEA* Southeast Asian(s)

[a] Reported in Germany, acquired in the USA

[b] Uncertain as to location where infection was acquired

entry numbers 3, 11, 12 in Table 3) has also been implicated. Other less common transmission routes include home-grown lettuce (see entry number 6 in Table 3) and the consumption of the "water morning glory" plant in Thailand (see entry number 12 in Table 3). An equal number of male and female cases have been reported, with no clear pattern in terms of age. Reports of cases among 20–60-year-old subjects predominate in our review. Common symptoms include a combination of right upper quadrant or more diffuse abdominal pain, fever, jaundice, malaise, diarrhea, vomiting, or nausea (see entry numbers 1–8, 10–12, 14–23 in Table 3). A number of subjects also reported anorexia or substantial weight loss (see entry numbers 2, 3, 7, 14, 17, 18, 21 in Table 3). Other common clinical findings include cholecystitis, cholangitis, or other biliary disorders, as well as elevated liver enzymes, liver lesions, or pancreatitis (see entry numbers 1, 3–8, 10–12, 14, 16–23 in Table 3). Eosinophil counts vary considerably, up as high as 45% or 68% in recently acquired cases (e.g., entry numbers 7 and 17 in Table 3) to 3% or less in those with a history of relevant symptoms (e.g., entry numbers 1, 2, 5 in Table 3).

Miscellaneous FBT infections in the USA

Here we consider miscellaneous FBT reported in the USA. The trematodes considered in this section are not well-known to most American health care providers. Reports of the involvement of these FBT with humans in the USA are from both the clinical and non-clinical literatures. Salient information about these cases is summarized in Table 4. Most of these miscellaneous trematodes are only mildly pathogenic in humans when they infect the intestinal tract. Some of them in extraintestinal sites, especially heterophyids and alariids, can affect vital organs and cause pathogenesis in humans. For further discussion of this topic, see Fried et al (2004).

The trematodes included here are in the families Diplostomatidae, Echinostomatdiae, Heterophyidae, Plagiorchiidae, and Troglotrematidae. Details of the biology and life cycles of representative species that are important as global FBT are in Fried et al. (2004). The major species in these families reported from the USA, either of local or non-local origin are: for the diplostomids, species of *Alaria*; for the echinostomatids, species of *Echinostoma* and *Himasthla*; for the heterophyids, species of *Stellanchasmus*, *Heterophyes*, and *Metagonimus*; for the plagiorchids, species of *Plagiorchis*. As for most digenetic trematodes, the first intermediate hosts of the flukes mentioned in Table 4 are either pulmonate or prosobranch snails. Specific first intermediate hosts for selected trematodes in these taxa have been given in Fried et al. (2004).

Transmission of the FBT considered in this section occurs when humans eat tainted food infected with either the metacercaria stage (cyst) or in *Alaria* sp., a unique unencysted larval stage known as a mesocercaria. Thus, the alarids are mainly transmitted with tainted game or frog meat (eaten raw or undercooked). The echinostomatids are transmitted by the ingestion of cysts in raw or undercooked frogs, snakes, fish, clams, and snails. For instance, in the case of infection by *Himasthla muhlense* in a human (see entry number 4 in Table 4), transmission occurred by the ingestion of raw *Mercenaria* quohogs (clams on the half shell). In cases involving heterophyids and troglotrematids, human infection occurs following the ingestion of contaminated fish (either raw or undercooked) containing the infective metacercariae. For instance, in entry 13, the infective agent was sushi containing heterophyid cysts. Transmission of plagiorchiids occurs following the ingestion of tainted fish or insect larvae containing the metacercariae; the only known human case in the USA resulted from a self-inflicted infection by the author of the study who swallowed plagiorchiid metacercariae (see entry number 15 in Table 4).

Table 4 provides a survey of our remaining FBT, and includes *Alaria americana*, *H. muhlense*, *Heterophyes heterophyes*, *Metagonimus yokagawaii*, and *Nanophyetus salmincola*. Many of these were locally acquired (see entry numbers 1, 2, 4, 7, 9,13,17–19 in Table 4), with the greatest number of cases due to the consumption of raw, undercooked, or smoked salmon or steelhead trout or steelhead eggs infected with *N. salmincola* in the Pacific northwest (see entry numbers 17 and 18 in Table 4). At least three local cases were due to consuming tainted Asian food in restaurants, most likely from ingesting raw oysters, undercooked wild duck, or frog legs infected with *Alaria*, or sushi made with imported fish infected with *Heterophyes* (see entry numbers 2 and 13 in Table 4, respectively). Consumption of raw or undercooked mullet, or another local freshwater fish infected with *Heterophyes* is largely responsible for the infections reported in the Hawaiian Islands (see entry numbers 7 and 9 in Table 4). Cases resulting from the home preparation of smoked salmon infected with *Nanophyetes* and undercooked game animals including raccoon, deer, rabbit, and squirrel infected with *Alaria* have been documented (see entry numbers 18 and 1 in Table 4, respectively). Three cases among biologists were reported: McMullen (1937) infected himself by drinking a solution containing *Plagiorchis muris* cysts (see entry number 15 in Table 4), and Phillip (1958) infected himself by consuming raw trout infected with *Nanophyetes* (see entry number 16 in Table 4). A biological laboratory worker became infected with *Nanophyetes* through accidental ingestion of this parasite after handling coho salmon (see entry number 19 in Table 4).

The imported cases reflect a number of countries previously mentioned in this review for other trematode infections, particularly countries in the far east and Southeast Asia for *Echinostoma* and *Heterophyes* infections (see entry numbers 5, 10–12, 14 in Table 4). One case of *Alaria* was imported from Canada, from the consumption of undercooked wild goose meat (see entry number 3 in Table 4). Eighteen cases of *Echinostoma* infection were imported by a tourist group visiting Kenya and Tanzania, which were attributed to the consumption of tainted salads or local water (see entry number 6 in Table 4). The echinostome species were not indentified in these cases (see entry number 6 in Table 4).

The symptoms reported for the miscellaneous infections noted in this table tend to be more general and less severe when compared to the other FBT discussed in this review. For *Alaria* infections, symptoms vary and depend on where the trematode was located; they include a mass/nodules on the upper thigh (see entry number 1 in Table 4) and chest (see entry number 3 in Table 4) and decreased/blurred vision (see entry number 2 in Table 4) from location in the eye. Diarrhea is a main symptom for *Heterophyes* infection (see entry numbers 7, 8, 11, 13 in Table 4), with other possible symptoms including weight loss or right upper quadrant discomfort (see entry number 7 in Table 4). The *Nanophyetus* cases reported a somewhat wider range of symptoms including abdominal pain, loose stools or diarrhea, weight loss, nausea, vomiting, and fatigue (see entry numbers 17–19 in Table 4). As for most FBT, prevention is best achieved by avoiding raw or undercooked food products. Praziquantel is an effective treatment for the above FBT, but the dosage regimen varies according to the infective species of trematode. See Fried et al. (2004) for more information on treatments of the miscellaneous trematodes reported in this section.

Concluding remarks

We have examined the salient literature on FBT in the USA from 1890 to 2009 and provided information on these flukes in 4 tables and in the text. The number of entries in the tables is as follows: 53 on the opisthorchiids in Table 1; 35 on the paragonimids in Table 2; 23 on *F. hepatica* in Table 3; and 19 on miscellaneous trematodes in Table 4. The miscellaneous trematodes are of relatively minor public health concerns, are not well-known to most health care providers, and are not addressed further here. The opisthorchiid cases listed in Table 1 and discussed in the text are imported into the continental USA. They are serious pathogens of the liver and biliary system and cause considerable harm to humans. They are preventable infections that can be avoided by not eating raw or

improperly cooked freshwater fish tainted with cysts. Moreover, in chronic cases, these FBT infections can induce cancer of the liver and/or bile ducts. Since these FBT infections can be avoided by proper health measures, i.e., the avoidance of infected fish products, cancer cases resulting from opisthorchiid infections are in the category of preventable cancers.

The paragonimids can be acquired in the USA. Local snails and freshwater crustaceans serve as intermediate hosts along with vertebrate reservoirs as definitive hosts for these flukes. Therefore, as noted in Table 2, a number of cases have been acquired locally. Humans who eat tainted crustaceans can become infected with these lung flukes; infection can lead to severe pulmonary complications that mimic tuberculosis and other non-helminthic pulmonary disorders. Because of the general unfamiliarity with *Paragonimus* and paragonimiasis in the USA, diagnosis of this infection in humans may be missed.

As discussed by Mas-Coma et al. (2007), fascioliasis is on the rise globally. In the USA, the disease in humans can result from local or imported infections. The presence of local infected snails and vegetation compatible with the cercarial infection plus susceptible herbivore definitive hosts guarantees the continuance of this cycle in the USA. This fluke is a serious human pathogen of the liver and biliary system. As with other FBT, fascioliasis is preventable if care is taken to avoid tainted raw or improperly cooked vegetation.

Lastly, we note the rise of interest in exotic foods eaten raw or improperly cooked in the USA; increased attention should be emphasized by public health workers of the importance of consuming properly cooked shellfish, fish, and vegetation to avoid acquiring FBT.

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