CHAPTER 48

Trematodes

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The flukes, or trematodes, are long-lived parasites that can cause human disease by mechanical obstruction and by inciting local inflammatory responses in affected organs (**Table 48.1**). Blood flukes (*Schistosoma* spp.), hepatobiliary flukes (*Clonorchis sinensis*, *Opisthorchis* spp., and *Fasciola hepatica*), and lung flukes (*Paragonimus* spp.) can be associated with major systemic pathology, whereas intestinal flukes (*Metagonimus yokogawai*, *Heterophyes heterophyes*, *Fasciolopsis buski*, and *Echinostoma* spp.) usually cause gastrointestinal symptoms such as diarrhea, anorexia, and abdominal pain only in heavy infections.

SCHISTOSOMIASIS

Schistosomiasis is a trematode infection caused by blood flukes. In Africa, schistosomiasis is often called "Bilharzia" after Theodore Bilharz, the German physician who first described the parasitic origin of the clinical disease. Species pathogenic for man include *S. mansoni*, *S. japonicum*, *S. mekongi*, and *S. haematobium*. Acute infection of humans with nonpathogenic avian species of schistosomes can result in an allergic skin reaction called swimmers' itch (see below and Chapter 37).

Schistosomiasis affects approximately 200 million people worldwide and is an important cause of morbidity and mortality in rural tropical and semitropical areas. *S. japonicum* is endemic in the Philippines and the People's Republic of China (but no longer Japan, in spite of its name); *S. mekongi* along the Mekong River valley; *S. mansoni* in the Middle East, Africa, eastern South America, and parts of the Caribbean; and *S. haematobium* in the Middle East and Africa.

Transmission

Microscopic cercariae penetrate wet human skin during contact or immersion in fresh water inhabited by infected snails, the obligate intermediate host in the parasite lifecycle. After infection, the cercariae transform into schistosomula, which develop into adult worms over a 4- to 6-week period. During maturation, the schistosomula migrate through the patient's lungs to specific sites, depending on the species. Adult females find their way into the gynecophoric groove, or "schist," of a male, and the pair enters a lifelong state of copulation. The mated pair begin to produce hundreds to thousands of eggs per day. Migration in the patient appears to be a species-specific phenomenon. *S. japonicum* and *S. mekongi* worm pairs migrate to the superior mesenteric vein, *S. mansoni* to the inferior mesenteric vein, and *S. haematobium* to the venous plexus surrounding the bladder.

The eggs deposited by the female worms on the peritoneal side of the intestines or bladder work their way through the walls of these organs and are passed outside the body in the feces or urine. When stool or urine from infected humans is deposited into fresh water, the eggs hatch, and motile miracidia emerge and infect snails of certain species, thus completing the lifecycle.

TABLE 48.1 Location, Source of Infection, and Clinical Features of Trematode Infections

Species	Location	Source of Infection	Clinical Features
Blood flukes			
Schistosoma mansoni	Africa, Caribbean, South America, and Middle East	Fresh water, penetration of skin by cercaria from infected snails	Dermatitis, abdominal pain, hematochezia, and portal hypertension
S. japonicum	China and Southeast Asia		Same
S. mekongi	Cambodia and Laos		Same
S. haematobium	Africa and Middle East		Hematuria
Hepatobiliary flukes			
Opisthorchis viverrini	Thailand and Laos	Freshwater fish	Asymptomatic or abdominal pain
O. felineus	Eastern Europe and Vietnam		
Clonorchis sinensis	Far East		
Fasciola hepatica	Worldwide, sheep- and cattle-raising areas	Raw vegetables, especially watercress	Asymptomatic or abdominal pain, hepatomegaly, and fever
Lung flukes			
Paragonimus westermani	Worldwide	Freshwater crustaceans such as crabs or crawfish	Hemoptysis, cough, ± extrapulmonary involvement
P. heterotremus	Thailand, Laos, and China		
P. skrjabini (*P. szechuanensis*)	China	Same	Same but also with cutaneous nodules
Intestinal flukes			
Metagonimus yokogawai	Asia, Russia, and Spain	Freshwater fish	Asymptomatic or diarrhea with abdominal pain
Heterophyes heterophyes	Middle East, Egypt	Freshwater fish	
Echinostoma spp.	Asia	Freshwater snails, fish, or vegetables	
Fasciolopsis buski	Asia	Freshwater plants	

The adult worms can persist in the human host for decades; thus, infections acquired in endemic tropical areas can present as puzzling diagnostic problems years later if infected individuals emigrate to non-endemic areas where these infections are rarely encountered by clinicians.

Clinical Features

Asymptomatic Infections

Patients with a low worm burden (light infections) resulting from limited exposure to freshwater environments in areas of transmission may be completely asymptomatic.

Katayama Fever

At the time of initial parasite egg laying (oviposition), about 4-6 weeks after infection, the patient sometimes presents with a severe febrile illness called Katayama fever. The etiology of this systemic reaction is probably a hypersensitivity to egg-associated antigens; it has been

mainly associated with *S. mansoni* and *S. japonicum* infections. This febrile syndrome presents with fevers, headache, cough, urticaria, lymphadenopathy, tender hepatosplenomegaly, and hypereosinophilia of the peripheral blood. This syndrome typically settles spontaneously in a matter of days or weeks, although severe and even fatal cases have been reported.

Bloody Diarrhea and Obstipation

Eggs deposited by the female *S. mansoni*, *S. japonicum*, and *S. mekongi* worms on the peritoneal side of the colon work their way through the bowel wall and cause tissue inflammation and lesions on the luminal side. This acute process can produce cramping, abdominal pain, and bloody diarrhea.

As the infection progresses, some eggs are retained in the bowel wall, inciting a granulomatous response with eventual fibrosis. As increasing fibrosis displaces normal bowel wall tissue, the contractile dysfunction of the colon can result in obstipation.

Hepatosplenic Disease

In chronic infections, usually due to *S. mansoni*, *S. japonicum*, and *S. mekongi*, some eggs fail to penetrate the intestine walls but instead are carried via the portal blood to the liver. Egg granulomas in the portal triad area progress to extensive hepatic fibrosis (pipestem fibrosis). The result is development of portal hypertension and its sequelae of passive splenic congestion, ascites, and esophageal varices. In endemic areas, death by exsanguination from bleeding esophageal varices is not uncommon in heavily infected individuals in the second and third decades of life. Interestingly, hepatocellular function is usually preserved, so aminotransferase levels in the blood may be normal even during severe portal hypertension.

Urinary Tract Disease

The passage of eggs through the bladder wall in *S. haematobium* infections can result in microscopic or gross hematuria. Granulomatous lesions of the urinary bladder, especially in the trigone area, contribute to the development of ureteral obstruction, with subsequent reflux, hydroureter, and chronic bacterial pyelonephritis. In endemic areas, chronic *S. haematobium* infections are associated with the development of squamous cell carcinoma of the bladder. If eggs penetrate the seminal vesicles, hematospermia may develop; in women egg expulsion may lead to lesions of the vagina or Bartholin glands.

Lung Disease

Eosinophilic pneumonitis results when eggs reaching the general circulation are trapped in the alveolar capillaries.

Skin Disease

Acute penetration of the skin by cercarial forms may cause a short-lived pruritic rash. In chronic infections, *S. mansoni* eggs reaching the general circulation may lodge in the skin and cause chronic egg dermatitis. In northern regions, patients may develop a rash when they become infected with avian schistosomiasis. Here, species of *Schistosoma* that have evolved to infect birds accidentally enter the skin of human bathers in freshwater lakes or ponds; they elicit an intensely pruritic rash ("swimmer's itch"), a condition discussed in Chapter 37.

Central Nervous System (CNS) Disease

Cases of acute transverse myelitis occurring after the initial 4- to 6-week incubation period have been reported in patients infected with *S. mansoni* and *S. haematobium*. Presumably, eggs or worm pairs gain access to the spinal cord through the venous drainage system of the lower abdomen, resulting in an acute inflammatory reaction where they lodge in the spinal cord. *S. japonicum* eggs carried in the circulation to the brain may be a significant cause of seizure disorders in the Far East.

Bacteremia

For reasons that are unclear, patients with schistosomiasis are at increased risk of recurrent bloodstream infection with bacteria in the *Salmonella enterica* family. Thus, schistosomiasis

should always be considered in patients who present with this condition, starting with an exposure history.

Schistosomiasis in Pregnancy

Eggs lodging in the placenta may cause poor placental development and premature placental separation (Chapter 14).

Laboratory Studies

A definitive diagnosis can be made by identifying the schistosome eggs in samples of stool or urine submitted to the laboratory. The egg of each schistosome species has its own characteristic morphologic appearance and can be readily differentiated from the others. *S. mansoni* has a prominent lateral spine, *S. haematobium* has a terminal spine, and both *S. japonicum* and *S. mekongi* have a rudimentary lateral spine.

Eosinophilia of the peripheral blood may be present during the initial stages of clinical disease but is not a constant finding in late chronic infections.

Expatriates and travelers returning from schistosomiasis-endemic areas with CNS abnormalities should be studied by computed tomography (CT) or magnetic resonance imaging scan, and a diagnosis of neuroschistosomiasis should be considered, even in the absence of typical clinical features of acute schistosomiasis, and even if urine and stool examinations are negative.

Serologic testing with sensitive tests for schistosomiasis (Falcon assay screening test–enzyme-linked immunosorbent assay) and specific tests (immunoblot) for schistosomiasis is available from the Centers for Disease Control and Prevention (CDC) Parasitic Diseases Branch. Specimens for testing are submitted to the CDC through the state public health department, accompanied by a CDC medical history and request form (so that the correct immunoblot test can be performed based on the most likely species involved). The tests may be helpful to detect low-intensity infections in travelers, expatriates, and immigrants with a history of freshwater exposure in schistosomiasis-endemic areas who have negative stool and urine examinations. If the clinical picture and geographic history are strongly suggestive of schistosomiasis, but the stool or urine samples are negative for eggs, biopsies of inflamed areas of rectum or colon (via sigmoidoscopy or colonoscopy) or bladder (via cystoscopy) may reveal schistosome eggs retained in the tissues. The eggs may be seen in wet mounts of crushed tissue or histologically stained preparations of the biopsy specimens.

Treatment

Praziquantel is an oral drug and the only drug that is efficacious against all forms of schistosomiasis. Oxamniquine is an oral drug that has efficacy against *S. mansoni* infections only. It is contraindicated in patients with a history of seizures. Metrifonate is an oral drug that has efficacy against *S. haematobium* infections. Neither oxamniquine nor metrifonate is available in the United States.

Artemesinins exhibit antischistosomal properties as well as antimalarial activity. In preclinical studies, artemether administered at therapeutic doses for malaria in research mice infected with *S. mansoni* showed significantly lower worm burdens. Further epidemiologic studies in areas where malaria and schistosomiasis co-exist, and where artemisinin-based combination therapy (ACT) is being used for malaria control, may show that ACT has ancillary benefits against schistosomiasis and other trematode infections in humans.

Treatment of acute hypersensitivity syndromes (Katayama fever, acute transverse myelitis) is directed toward general systemic support of severely ill patients. Corticosteroids to decrease the inflammatory reaction to parasite antigens may be indicated.

Potentially exposed individuals should be counseled to watch for influenza-like symptoms 4-6 weeks following water exposure, because this could represent Katayama fever and should trigger prompt medical evaluation. Some travelers choose to treat themselves presumptively following return from endemic regions. If this is considered, it should be limited to those with symptoms or those who had a true freshwater exposure (swimming, rafting) and should

be administered at least 6 weeks after the last exposure, because praziquantel is most effective against the adult worms, not their immature forms.

Prevention

Prevention consists of avoiding water contact or immersion in areas known to be endemic for schistosomiasis. If accidental water contact occurs, travelers should be counseled that rapid toweling to dry the skin may prevent parasite penetration but that this technique is far from perfect.

In endemic areas where water contact is unavoidable, annual mass drug administration (MDA) programs using praziquantel combined with environmental measures to control the snails and promote sanitary disposal of human waste must proceed concurrently to decrease the incidence and prevalence of the disease. In areas of overlapping disease endemicity, efforts to integrate schistosomiasis into other MDA programs against onchocerciasis and lymphatic filariasis by simultaneous administration of safe oral antihelminthic drugs (praziquantel, ivermectin, and albendazole) will promote optimal use of health services infrastructure in resource-poor economies.

For travelers, as noted above, a vaccine against schistosomiasis in humans is not available at the time of writing, although an irradiated cercarial vaccine against a bovine strain of schistosomiasis has been used in cattle in Africa with some success.

HEPATOBILIARY FLUKES: *CLONORCHIS* AND *OPISTHORCHIS*

Biliary fluke infections with *Clonorchis sinensis* or *Opisthorchis* species are common among people from Laos, Cambodia, Thailand, the southern People's Republic of China, Hong Kong, Korea, Japan, and the far-eastern regions of the Soviet Union.

Transmission

Humans acquire liver fluke infections from eating raw, undercooked, pickled, or smoked fish. Parasite eggs, passed in the feces, hatch in fresh water. The first intermediate hosts, snails, become infected and shed free-swimming cercariae into the water, which then infect fish and encyst in the muscles. After humans eat infected undercooked fish, the larvae (metacercariae) migrate up the bile duct and mature into adult worms. In addition to humans, definitive hosts for the liver flukes may be dogs, cats, pigs, badgers, and ducks, thus serving as reservoirs of infection in endemic areas.

Liver flukes mature in the hepatic biliary radicles, and the infection may be silent, although parasite adults induce ductal hyperplasia and fibrosis. The eggs in the bile exit the body via the fecal stream.

Clinical Features

The majority of chronically infected individuals are asymptomatic. For patients with heavy worm burdens, right upper quadrant abdominal pain and jaundice may be present.

Acute Biliary Obstruction

This is a surgical emergency occurring in late infections characterized by heavy parasite loads. Physical obstruction by numerous flukes and narrowed bile duct lumen secondary to fibrosis probably contribute to the condition. As with all kinds of acute biliary obstruction, restoration of bile flow may be important. However, in minor cases where acute surgical or endoscopic decompression is not necessary, treatment with praziquantel may be effective.

Acute Pancreatitis

Occasionally, the flukes migrate into the pancreatic ducts and cause obstruction and inflammation.

Recurrent Pyogenic Cholangitis

This is a clinical syndrome with fever, right upper quadrant pain, jaundice, and intrahepatic biliary gallstones. This infectious process is thought to be secondary to bacterial infection

in the presence of fibrosis and foreign bodies in the biliary tree. While recurrent pyogenic cholangitis has not conclusively been shown to be caused by *C. sinensis* or *Opisthorchis* species, there is some epidemiologic and anatomic evidence to suggest that these flukes may be associated with this syndrome.

Cholangiocarcinoma

Primary biliary carcinoma is a relatively rare form of malignancy. However, an increased incidence has been found among people living in endemic areas for biliary fluke infection and may be related to chronic inflammation of the biliary tree.

Laboratory Studies

Infections are detected by finding the characteristic eggs in stool specimens. The eggs are among the smallest of parasite eggs and are more easily detected by stool concentration techniques.

The eggs of intestinal flukes *Metagonimus* and *Heterophyes* are relatively difficult to differentiate from the *Clonorchis* and *Opisthorchis* eggs. Fortunately, the drug of choice for biliary fluke infections is also the recommended treatment for intestinal fluke infections (**Table 48.2**).

In difficult cases of biliary obstruction, endoscopic retrograde cholangiopancreatography may be performed, with adult flukes and eggs recovered directly from the bile during the procedure.

TABLE 48.2 Drug Treatment of Human Fluke Infections

Parasite	Drug of Choice	Alternative Drugs
Blood flukes		
S. japonicum	Praziquantel: 60 mg/kg given orally in three divided doses 4-6 h apart on a single day	
S. mansoni	Praziquantel: 40 mg/kg given in two divided doses on a single day	
S. haematobium	Praziquantel: 40 mg/kg in two divided doses on a single day	
Hepatobiliary flukes		
Clonorchis sinensis, *Opisthorchis viverrini*	Praziquantel: 75 mg/kg given orally in three divided doses 4-6 h apart	Albendazole: 10 mg/kg × 7 days
Fasciola hepatica	Bithionol: 30-50 mg/kg per day given orally alternate days for 10-15 total doses	Triclabendazole: 10 mg/kg once or twice[a]
Lung flukes		
Paragonimus spp. (*P. westermani*, *P. heterotremus*, *P. skrjabini*)	Praziquantel: 75 mg/kg per day given orally in three divided doses 4-6 h apart on two consecutive days	
Intestinal flukes		
Metagonimus yokogawai, *Heterophyes heterophyes*, *Echinostoma* spp., *Fasciolopsis buski*	Praziquantel: 75 mg/kg given orally in three divided doses 4-6 h apart on a single day[b]	

[a]Not available for human use in the United States.
[b]Considered an investigational drug for this purpose.

Treatment

In light of the potentially serious consequences of long-term infection with liver flukes, even asymptomatic infections should be treated when they are detected. Praziquantel is the drug of choice and has been known to cure over 90% of infections after a single therapeutic dose (**Table 48.2**). Acute biliary obstruction due to liver flukes requires surgical decompression and drainage. Prevention of infection consists of eating only well-cooked fish. No vaccine is available, and reinfection is possible.

HEPATOBILIARY FLUKES: *FASCIOLA HEPATICA*

Fasciola hepatica is a large liver fluke that lives in the bile ducts of its mammalian hosts, which commonly include sheep and cattle. It is endemic in more than 40 countries, including those in Europe, North Africa, Asia, South America, and the Western Pacific.

Transmission

Parasite eggs passed in the feces hatch into miracidia, which infect freshwater snails. Cercaria emerge from the snails after 6-7 weeks and attach to aquatic plants where they encyst as metacercaria. Humans become infected from ingestion of contaminated aquatic plants, such as watercress, in sheep- and cattle-raising areas. After ingestion, the metacercaria penetrate the intestinal wall, enter the peritoneal cavity, and then penetrate through Glisson capsule into the liver.

Clinical Features

Acute Phase

This phase occurs during parasite migration from the duodenum to the liver via the peritoneal cavity. The classic symptoms and signs include right upper quadrant abdominal pain, fever, and hepatomegaly.

Chronic Phase

After reaching the hepatobiliary system, the chronic phase of the disease begins. Patients can develop cholangitis and cholecystitis, although it is not clear what percentage of patients progress to these complications. There is no association of *F. hepatica* with cholangiocarcinoma, as there is with *Clonorchis* and *Opisthorchis*, presumably because its smooth tegument elicits less inflammation of the biliary lining, but this is not certain.

Laboratory Studies

Diagnosis is made by finding the characteristic eggs in stool or duodenal aspirates. The sensitivity ranges widely depending on the microscopy technique, intensity of infection, and phase of infection (no egg secretion during the acute migration phase). Serologic tests are also available. Ultrasound and CT scan findings include linear hepatic tracks and a subcapsular location.

Treatment

Bithionol has been the first-line agent for fascioliasis at a dose of 30-50 mg/kg on alternate days for 10-15 doses (**Table 48.2**). It is considered an investigational drug in the United States and must be obtained from the CDC. Unfortunately, it is no longer manufactured, and only limited supplies are currently available. While praziquantel is effective for most trematode infections, treatment of fascioliasis has been only partially successful. Investigational alternatives to bithionol include triclabendazole, nitazoxanide, emetine (cardiac toxicity), niclofolan, metronidazole, and albendazole. Triclabendazole has become the drug of choice in many regions of the world but is not commercially available in the United States.

LUNG FLUKES

Chronic pulmonary infection with *Paragonimus westermani* and related species can mimic pulmonary tuberculosis, and the diagnosis should be considered in "atypical" cases of tuberculosis that do not seem to respond to standard chemotherapy (Chapter 25).

Paragonimiasis is endemic in areas where freshwater crab, crawfish, or shrimp are eaten raw, pickled, or undercooked. The infection is worldwide in distribution, with cases reported from Asia, South America, and Africa. A lung fluke infection acquired in California was documented in a man who ate "drunken" crab (dunked live in alcohol then swallowed); however, most cases seen in North America are imported infections among immigrant and refugee populations from Asia and Southeast Asia.

Transmission

Adult flukes live in the lungs of humans and other mammals, such as cats, dogs, minks, and opossums. The worms lay eggs that are coughed up in the sputum or swallowed and then passed in the feces. The eggs hatch in fresh water and develop into miracidia that infect freshwater snails. The infection in snails produces cercariae, which then infect freshwater crabs, crawfish, or prawns. The encysted parasites at this stage are called metacercariae and are in the muscle, viscera, and gills. When raw or inadequately cooked crabs, crawfish, or prawns are eaten by humans and other mammals, the parasites excyst in the small intestine, penetrate the bowel wall, and migrate through the peritoneum, diaphragm, and pleura until they reach the lung parenchyma. In the lungs, the larvae mature into adult flukes and start the lifecycle over again.

Clinical Features

Pulmonary Paragonimiasis

While hemoptysis, dyspnea, and chest pain are the classic presenting symptoms, light pulmonary infections may be completely asymptomatic. Symptoms often develop 6 months to several years after infection. On chest radiography, parenchymal lesions of the lung, including segmental or diffuse infiltrates, nodules, cavities, or "ring" cysts, may be seen. Less frequently, the radiographic appearance is that of a pleural effusion. Peripheral eosinophilia is commonly present.

Extrapulmonary Paragonimiasis

Around 30% of patients present with extrapulmonary features thought to result from ectopic migration of excysted larvae from the bowel. Involved locations include the skin, liver, kidney, peritoneum, epididymis, spinal cord, and brain. The most serious complications from lesions involving the brain include seizures, headache, motor deficits, and visual disturbances. Subcutaneous nodules are a distinct feature of *Paragonimus skrjabini* infections found in China. The nodules range in size from a few millimeters to several centimeters and are often migratory.

Laboratory Studies

The diagnosis of paragonimiasis can be made by identification of the characteristic operculated eggs in specimens of sputum or stool. Sputum concentration techniques on 24-hour sputum specimen collections may be helpful in recovering eggs when random sputum specimens are negative. Eggs present in sputum specimens may be destroyed by Gram stain or acid-fast staining techniques, so the microbiology laboratory must be alerted when specimens are being submitted for parasitologic examination.

If the sputum or stool specimen is submitted to a laboratory that does not regularly do parasitologic examinations, the eggs of *Paragonimus* species may be misinterpreted as *Diphyllobothrium latum* eggs. If *D. latum* is reported in a specimen from an immigrant or refugee patient, the clinician should ask for a review of the specimen by a consulting parasitologist. Complement fixation and immunoblot tests are available and may be helpful in establishing the diagnosis in patients from endemic areas with radiographic lesions and nondiagnostic sputum studies.

Treatment

The drug of choice in the treatment of this infection is praziquantel, a total of 150 mg/kg given orally in divided doses over two consecutive days (75 mg/kg per day) (**Table 48.1**).

Adverse effects associated with drug treatment include nausea on the days of medication and urticaria during the week following medication (presumed to be a hypersensitivity reaction to antigen released by dead and dying parasites). Bithionol was previously used for the treatment of paragonimiasis (**Table 48.2**) but is considered an investigational drug in the United States and can be obtained only from the CDC. In addition, bithionol treatment failures have been noted in Southeast Asians with lung fluke infections.

INTESTINAL FLUKES

Endemic areas for the intestinal flukes *Metagonimus yokogawai* and *Heterophyes heterophyes* include countries in the Far East (Japan, China, Taiwan, eastern Siberia, Korea, the Philippines, and Thailand), where humans acquire infections from eating raw or undercooked fish. *Metagonimus* infections have also been reported from Israel, Romania, and Spain, and *Heterophyes* infections from India, Egypt, and Tunisia. The lifecycle of the organism is similar to that of *Clonorchis sinensis* and *Opisthorchis* species, except for the anatomic residence of the adult flukes in the intestines instead of the biliary tract.

Fasciolopsis buski is a relatively large intestinal fluke that is acquired in the Far East from ingestion of parasite cysts attached to aquatic plants, such as water chestnuts, contaminated by feces from infected mammals (pigs, humans). Human infection with *Echinostoma* species can be found in Indonesia, the Philippines, Taiwan, and Thailand. Transmission occurs via ingestion of infected snails, fish, or vegetables.

Clinical Features

Light infections with intestinal flukes are often asymptomatic. Persons with heavy infections may present with abdominal pain, chronic diarrhea, anorexia, nausea, and weight loss. Rarely, extraintestinal lesions may result from ectopic migration of larvae or from eggs gaining access to the circulation and being deposited in ectopic sites.

Laboratory Studies

Diagnosis can be made by finding the characteristic parasite eggs in submitted stool samples. No diagnostic serologic tests are available.

Treatment

The treatment of choice is praziquantel (**Table 48.2**). Tetrachloroethylene, a drug not available for human use in the United States, is often used in developing countries because of its low cost.

FURTHER READING

Harinasatu, T., Pungpak, S., Keystone, J., 1993. Trematode infections: opisthorchiasis, clonorchiasis, fascioliasis, and paragonimiasis. Inf. Dis. Clin. N. Am. 7, 699–716.
A comprehensive review of liver and lung fluke infections by authors with extensive clinical experience.

Kilpatrick, M.E., Farid, Z., Bassily, S., et al., 1981. Treatment of *Schistosomiasis mansoni* with oxamniquine—five years' experience. Am. J. Trop. Med. Hyg. 30, 1219–1222.
Oxamniquine is a drug that is not commonly used outside schistosomiasis-endemic areas.

Nagayasu, E., Yoshida, A., Hombu, A., et al., 2015. Paragonimiasis in Japan: a twelve year retrospective case review (2001–2012). Intern. Med. 54, 179–186.
Paragonimiasis in Japan decreased in the 1970s, possibly as a result of increased public awareness of food-borne risks, but reemerged in the 1980s. Immigrants from other parts of Asia (China, Thailand, Korea) accounted for one-fourth of the cases in this retrospective case review and acquired their infections from eating raw freshwater crabs. Cases in resident Japanese citizens tended to be from one region and were acquired by eating fresh wild boar meat or freshwater crabs.

Olsen, A., 2007. Efficacy and safety of drug combinations in the treatment of schistosomiasis, soil-transmitted helminthiasis, lymphatic filariasis and onchocerciasis. Trans. R. Soc. Trop. Med. Hyg. 101, 747–758.
Co-infection with multiple parasites is common in tropical rural environments; efficacy and safety of drug combinations against multiple parasites is an important consideration for treatment programs where access to health care is limited.

Schwartz, D.A., 1986. Cholangiocarcinoma associated with liver fluke infection: a preventable source of morbidity in Asian immigrants. Am. J. Gastroenterol. 81, 76–79.
Liver flukes can live for a decade or two (or more) in human hosts, so it is worthwhile to screen for liver fluke infection among Asian immigrants from endemic areas, even if they left years before, and to treat all infections detected.

Sharma, O.P., 1989. The man who loved drunken crabs: a case of pulmonary paragonimiasis. Chest 953, 670–672.
Paragonimiasis acquired in the United States by a Los Angeles dock worker who loved to eat drunken crabs with his international co-workers.

Utzinger, J., Xiao, S.H., Tanner, M., et al., 2007. Artemesinins for schistosomiasis and beyond. Curr. Opin. Investig. Drugs 8, 105–116.
A relatively limited menu of drugs available to treat parasitic infections and emerging drug resistance among parasites fuels the search for new combinations and new uses for antiparasitic drugs already in use. This article explores the use of artemesinins in the treatment of malaria and schistosomiasis.

Wright, R.S., Jean, M., Rochelle, K., et al., 2011. Chylothorax caused by *Paragonimus westermani* in a native Californian. Chest 140, 1064–1066.
The patient acquired P. westermani *by eating imported live raw crabs from Asia in California sushi restaurants. Food-borne trematode infections in non-endemic areas will become an increasing problem in the future due to the growth of international seafood markets.*