All life cycle diagrams in this section are courtesy of the DPDx Parasite Image Library
Centers for Disease Control (CDC)

PARASITOLOGY - CHAPTER SIX

TREMATODES (FLUKES)

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The most significant trematodes from a clinical point of view are blood flukes, *Schistosoma mansoni*, *S. japonicum* and *S. hematobium*. Other trematodes of significance are intestinal fluke, *Fasciolopsis buski*, liver fluke, *Clonorchis sinensis* and lung fluke, *Paragonimus westermani*.

SCHISTOSOMIASIS (BILHARZIASIS)

The three species of Schistosoma have different geographic distributions. *S. hematobium* is prevalent in Africa, *S. mansoni* is found in Africa and America and *S. japonicum* is common in the far east.

Epidemiology
Approximately 250 million people are infected with schistosomes and 600 million are at risk.

Morphology
Adult worms are 10 to 20 mm long; the male has an unusual lamelliform shape with marginal folds forming a canal in which the slender female worm resides. Unlike other trematodes, schistosomes have separate sexes (figure 1).

Life cycle
Man is infected by cercaria in fresh water by skin penetration. The cercaria travel through the venous circulation to the heart, lungs and portal circulation. In about 3 weeks, they mature and reach the mesenteric (*S. japonicum* and *S. mansoni*) or the bladder (*S. hematobium*) vessels where they live and ovulate for the duration of the host's life. Eggs germinate as they pass through the vessel wall into the intestine or bladder and are excreted in feces (*S. japonicum* and *S. mansoni*) or urine (*S. hematobium*). In fresh water, the larval miracidium hatches out of the egg and swims about until it finds an appropriate snail. After two generations of multiplication in the snail, the fork-tailed cercariae emerge into the water and infect another human (figure 2).

Symptoms
Penetration of cercariae causes transient dermatitis (swimmers' itch). The symptoms of schistosomiasis are primarily due to a reaction against the eggs and include splenomegaly, lymphadenopathy and diarrhea. In the bladder, they produce granulomatous lesions, hematuria and sometimes urethral occlusion. Most bladder cancers in endemic areas are associated with chronic infection. In the intestine, they cause polyp formation which, in severe cases, may result in life threatening dysentery. In the liver, the eggs cause periportal fibrosis and portal hypertension resulting in hepatomegaly, splenomegaly and ascites. A gross enlargement of the esophageal and gastric veins may result in their rupture. *S. japonicum* eggs are sometimes carried to the central nervous system and cause headache, disorientation, amnesia and coma. Eggs carried to the heart produce arteriolitis and fibrosis resulting in enlargement and failure of the right ventricle (figure 2a).

Pathology and Immunology
The 'swimmers' itch is due to physical damage to the skin by proteases and other toxic substances secreted by the cercaria. The host develops both type I and type IV hypersensitivity reactions to schistomal secretions and egg constituents. Embryonated eggs cause collagenase-mediated damage to the vascular endothelium. Host immune

responses, both humoral and cell mediated, have been shown to be of some protective value. IgE and eosinophil mediated cytotoxicity has been suggested as a mechanism of killing the adult worm.

Diagnosis

Diagnosis is based on a history of residence in an endemic area, swimmers' itch and other symptoms. The eggs are very characteristic and confirm diagnosis. *S. hematobium* eggs in urine (55 to 65 by 110 to 170 micrometers) have an apical spine or knob. *S. mansoni* eggs in feces (45 to 70 by 115-175 micrometers) have a spine on the side. *S. japonicum* eggs (55 to 65 by 70 to 100 micrometers) are more round with a vague spine on the side.

Treatment and control

Praziquantel is effective against all species. Contaminated water should be avoided. Control measures include sanitary disposal of sewage and destruction of snails. No vaccine is available.

 Figure 1A
Schistosomes. WHO

 Figure 1B
Male and female schistosomes. (Drawn by Sylvia Treadgold) WHO

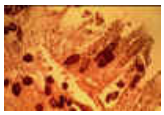 Figure 1C
Intestinal schistosomiasis: eggs in the wall of the gut. WHO

 Figure 1D
Schistosoma haematobium egg © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

 Figure 1E
Eggs of Schistosoma haematobium (A). In this species, the eggs are large and have a prominent terminal spine at the posterior end. Length 112-170 µm. In (B), a greater magnification shows the miracidium inside the egg. CDC

 Figure 1F
Schistosoma haematobium adult male © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

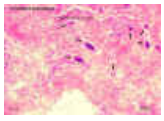 Figure 1G
Schistosoma haematobium eggs in section of bladder (H&E) © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

 Figure 1H
Schistosoma japonicum adult male and female, in copula © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

A  B  Figure 1I
Egg of Schistosoma japonicum (A). The egg is typically oval or subspherical, and has a vestigial spine, which is better shown in (B). Schistosoma japonicum eggs are smaller (68 - 100 µm by 45 - 80 µm) than those of the other species. CDC


Figure 1J
Schistosoma japonicum egg © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission


Figure 1K
Schistosoma japonicum adult male and female © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

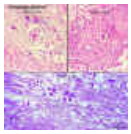
Figure 1L
Schistosoma japonicum eggs in tissue section (H&E) © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

A  B  Figure 1M
Eggs of Schistosoma mansoni in a patient from Egypt. These eggs are large (length 114 - 180 µm) and have a characteristic shape, with a prominent lateral spine near the posterior end. The anterior end is tapered and slightly curved. When the eggs are excreted, they contain a mature miracidium (visible especially in A). CDC


Figure 1N
Schistosoma mansoni adult male and female © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission


Figure 1O
Schistosoma mansoni adult male and female, in copulo © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

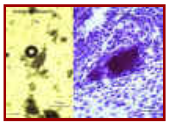
Figure 1P
Schistosoma mansoni egg, whole and in section (H&E) © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

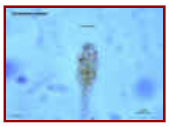
Figure 1Q
Schistosoma mansoni miracidium © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission


Figure 1R
Schistosoma mansoni in section of snail tissue (H&E) © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission


Figure 1S
Schistosoma mansoni cercaria © Dr Peter Darben, Queensland University of Technology clinical parasitology collection. Used with permission

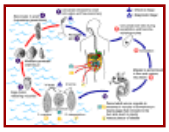
Figure 1T
Life cycle of schistosomes

Eggs are eliminated with feces or urine (1). Under optimal conditions the eggs hatch and release miracidia (2), which swim and penetrate specific snail intermediate hosts (3). The stages in the snail include 2 generations of sporocysts (4) and the production of cercariae (5). Upon release from the snail, the infective cercariae swim, penetrate the skin of the human host (6), and shed their forked tail, becoming schistosomulae (7). The schistosomulae migrate through several tissues and stages to their residence in the veins ((8), (9)). Adult worms in humans reside in the mesenteric venules in various locations, which at times seem to be specific for each species (10). For instance, *S. japonicum* is more frequently found in the superior mesenteric veins draining the small intestine (A), and *S. mansoni* occurs more often in the superior mesenteric veins draining the large intestine (B). However, both species can occupy either location, and they are capable of moving between sites, so it is not possible to state unequivocally that one species only occurs in one location. *S. haematobium* most often occurs in the venous plexus of bladder (C), but it can also be found in the rectal venules. The females (size 7 to 20 mm; males slightly smaller) deposit eggs in the small venules of the portal and perivesical systems. The eggs are moved progressively toward the lumen of the intestine (*S. mansoni* and *S. japonicum*) and of the bladder and ureters (*S. haematobium*), and are eliminated with feces or urine, respectively (1). Pathology of *S. mansoni* and *S. japonicum* schistosomiasis includes: Katayama fever, presinusoidal egg granulomas, Symmers' pipe stem periportal fibrosis, portal hypertension, and occasional embolic egg granulomas in brain or spinal cord. Pathology of *S. haematobium* schistosomiasis includes: hematuria, scarring, calcification, squamous cell carcinoma, and occasional embolic egg granulomas in brain or spinal cord.

Human contact with water is thus necessary for infection by schistosomes. Various animals, such as dogs, cats, rodents, pigs, hourse and goats, serve as reservoirs for *S. japonicum*, and dogs for *S. mekongi*.


Figure 2A
The abdomen of an 11-year-old boy with intestinal schistosomiasis with the size and extent of the liver and spleen marked. Both are well below the midline, indicating the severity of infection. The disease has caused a stunting of the boy's growth, he is only 120cms tall and weighs 22 kg. WHO/TDR/Crump


Figure 2B
Two boys, victims of schistosomiasis showing typical distension of the abdomen. WHO


Figure 2C
A 13-year-old boy with schistosomiasis (bilharziasis). Hepatosplenomegaly, ascites, muscle atrophy, pyrexia, anaemia and haemorrhage from the gastrointestinal tract. WHO/TDR/Vogel

FASCIOLOPSIS BUSKI (GIANT INTESTINAL FLUKE)

Epidemiology
This is a parasite of central and southeast Asia.

Morphology
The elongate oval fluke is 2 to 7 cm long and lives in the small intestine of man (figure 3).

Life cycle
Man is infected by ingesting water chestnuts contaminated with metacercaria which find access to the small intestine, attach themselves to the mucosa and mature in 25 to 30 days. The fluke eggs are passed in the feces and hatch in fresh water producing miracidia which must penetrate a suitable snail within hours. The miracidia in the snail develop into cercaria and enter fresh water where they attach themselves to water plants (water chestnut) and encyst to become metacercaria (figure 4).

Symptoms
Epigastric pain, nausea and diarrhea are experienced, especially in the morning. In heavier infections, generalized edema and ascites occur.

Pathology
The fluke attaches itself to the intestinal mucosa where inflammation, ulceration and abscesses occur.

Diagnosis
Diagnosis is based on clinical symptoms in endemic areas. Eggs in feces (75 to 100 by 130 to 150 micrometers) provide the final diagnosis.

Treatment and control
Praziquantel has proven effective. Water chestnuts from contaminated waters should be avoided. Sewage should be treated before disposal.

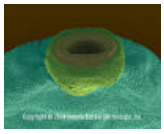
Figure 3A
Liver fluke, a trematode liver parasite - helminth (*Fasciola* spp.) Mouth and pharynx of the adult liver fluke. Humans are infected by ingestion of uncooked aquatic vegetation on which the metacercariae stage is encysted. Metacercariae excyst in the duodenum and migrate through the intestinal wall in to the peritoneal cavity. The larvae enter the liver by penetrating the capsule and wander through the liver parenchyma for up to 9 weeks. Most damage is done in the liver parenchyma by physical irritation and metabolic by products.


Figure 3B
Fasciolopsis buski adult, carmine stain


Figure 3C
Fasciolopsis buski egg

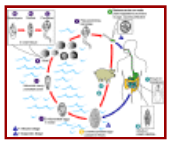
Figure 4
Life cycle of *Fasciolopsis buski*

Immature eggs are discharged into the intestine and stool 1. Eggs become embryonated in water 2, eggs release miracidia 3, which invade a suitable snail intermediate host 4. In the snail the parasites undergo several developmental stages (sporocysts 4a, rediae 4b, and cercariae 4c). The cercariae are released from the snail 5 and encyst as metacercariae on aquatic plants 6. The mammalian hosts become infected by ingesting metacercariae on the aquatic plants. After ingestion, the metacercariae excyst in the duodenum 7 and attach to the intestinal wall. There they develop into adult flukes (20 to 75 mm by 8 to 20 mm) in approximately 3 months, attached to the intestinal wall of the mammalian hosts (humans and pigs) 8. The adults have a life span of about one year.

LIVER FLUKES

Epidemiology

Fasciola hepatica, *Opisthorchis* (previously named Chlonorchis) *sinensis*, *O. felineus* and *O. viverini* affect humans in various parts of the world. *F. hepatica* is distributed worldwide and is a parasite of grazing animals (sheep and cattle) and man. *O. sinensis* is a widespread parasite of man, dogs and cats in southeast Asia. It is extraordinarily common in China and is also found in Korea and Japan. Related *Opisthorchis* species parasitizing European cats (*Opisthorchis felinus*) and SE Asian dogs (*O. viverini*) infect humans in the endemic areas. Liver fluke cases are rare in the United States, although snails harboring *F. hepatica* are present in the western and southern parts of the US.

FASCIOLA HEPATICA

Morphology
F hepatica is leaf shaped and measures approximately 1 x 3 cm. The eggs measure 80 x 150 µm.

Life cycle
Humans are infected by the consumption of improperly cooked watercress that harbors encysted larval metacercariae. The larval fluke penetrates the duodenal wall and migrates to the peritoneal cavity, penetrates the

liver capsule and migrates into the bile duct where it matures. The adult fluke passes its eggs in stool that hatch in water to produce miracidia. The miracidium must find an appropriate snail to continue the life cycle. In the snail, the miracidium divides and gives rise to cercariae which exit the snail and encyst as metacercariae attached to watercress leaves.

Symptoms
Passage of the larva through the liver produces tenderness and hepatomegaly. The infection results in upper quadrant pain, chills and fever accompanied with eosinophilia. The toxic secretions cause hepatitis. The presence of the worm in the bile duct causes irritation resulting in hyperplasia of the epithelium and bile obstruction. Adult worms may invade the liver and cause necrotic foci (liver rot).

Diagnosis
Diagnosis is based on symptoms and history. The eggs in the stool are indistinguishable from those of *F. buski*.

Treatment
In contrast with *F. buski*, *F. hepatica* is not responsive to praziquantel. However, Triclabendazole is effective.

OPISTHORCHIS SINENSIS, *O. FELINEUS* AND *O. VIVERINI*

Morphology
These are spindloid flukes measuring about 16x4 mm. The eggs measure 29 x 16 µm.

Life cycle
Man is infected by eating raw or improperly cooked fish that carries the infective metacercaria in a cyst. The cyst is digested and the larval worm migrates up the bile duct to liver where it matures into an adult. The eggs deposited in the biliary duct pass in the feces and find their way to fresh water. Upon ingestion by a suitable fresh water operculate snail, the egg hatches to produce a miracidium. The miracidium in the snail develops into cercaria that break out in water to penetrate under scales of fish. In fish, the cercaria encysts in the muscle and forms the metacercaria that are infectious to man.

Symptoms
The worm causes irritation of the bile ducts that become dilated and deviated. The liver may become enlarged (hepatomegaly), necrotic and tender and liver function may be impaired. Modest infections result in indigestion, epigastric discomfort, weakness and loss of weight. Heavier infections produce anemia, hepatomegaly, slight jaundice, edema, ascites and diarrhea.

Diagnosis
Diagnosis is based on symptoms and presence of endemic infection in the area. Definitive diagnosis is dependent on finding the characteristic eggs in the feces or biliary drainage.

Treatment and control
Praziquantel has proven to be of value. Fish should be cooked well before consumption. Sewage must be treated before disposal.

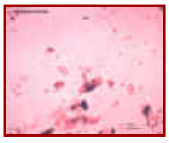
Figure 5A
Clonorchis sinensis egg

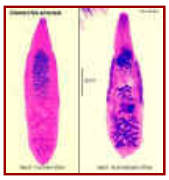
Figure 5B
Clonorchis sinensis adult, carmine and haematoxylin stain


Figure 5C
Clonorchis sinensis adults in section of liver (H&E)

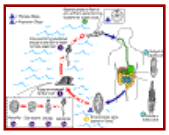
Figure 6

Embryonated eggs are discharged in the biliary ducts and in the stool 1. Eggs are ingested by a suitable snail intermediate host 2; there are more than 100 species of snails that can serve as intermediate hosts. Each egg releases a miracidia 2a, which go through several developmental stages (sporocysts 2b, rediae 2c, and cercariae 2d). The cercariae are released from the snail and after a short period of free-swimming time in water, they come in contact and penetrate the flesh of freshwater fish, where they encyst as metacercariae 3. Infection of humans occurs by ingestion of undercooked, salted, pickled, or smoked freshwater fish 4. After ingestion, the metacercariae excyst in the duodenum 5 and ascend the biliary tract through the ampulla of Vater 6. Maturation takes approximately 1 month. The adult flukes (measuring 10 to 25 mm by 3 to 5 mm) reside in small and medium sized biliary ducts. In addition to humans, carnivorous animals can serve as reservoir hosts.

PARAGONIMUS WESTERMANI (LUNG FLUKE)

Epidemiology
Lung fluke is most commonly encountered in parts of Asia, Africa and South America.

Morphology
It is a plump reddish brown oval worm measuring 10 by 4 mm. The ovum measures 85 by 55 micrometers (figure 7).

Life cycle
Lung fluke infects man (and domestic carnivores) when crabmeat infested with encysted metacercaria is consumed. The metacercaria reach the small intestine, exit their shell and bore their way, as young flukes, through the intestinal wall, through the thoracic diaphragm and penetrate the lung. There, they become enclosed in 1 to 2 cm cysts and reach maturity. The eggs are found in the sputum or, if swallowed, in the feces, 2 to 3 months after infection. The eggs, when introduced in fresh water produce a miracidia which penetrates the suitable snail. In the snail they develop into cercaria which break out in water and penetrate gills, muscle or viscera of fresh water crabs and become encysted in flesh as metacercaria (figure 8).

Symptoms
The fluke provokes the development of a fibrous tissue capsule with bloody purulent material containing eggs. There is inflammatory infiltrate around the capsule. The symptoms include a dry cough, followed by production of blood stained rusty brown sputum. Pulmonary pain and pleurisy may develop. Worms may migrate to the brain where they lay eggs and cause a granulomatous abscess resulting in symptoms similar to epilepsy.

Diagnosis
Diagnosis is based on history and symptoms. Eggs are found in rust colored sputum, often being examined for tuberculosis.

Treatment and control
Praziquantel taken orally is quite effective. Adequate cooking of crustaceans is a preventive measure. Improved sanitary conditions have lowered the infection rate in endemic areas.


Figure 7A

Paragonimus westermani egg


Figure 7B

Paragonimus westermani adult, carmine stain


Figure 7C

Paragonimus westermani adult in section of lung (H&E)

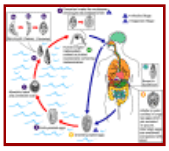

Figure 8
Paragonimus westermani (Lung Fluke) Life Cycle
The eggs are excreted unembryonated in the sputum, or alternately they are swallowed and passed with stool ❶. In the external environment, the eggs become embryonated ❷, and miracidia hatch and seek the first intermediate host, a snail, and penetrate its soft tissues ❸. Miracidia go through several developmental stages inside the snail ❹: sporocysts ❹a, rediae ❹b, with the latter giving rise to many cercariae ❹c, which emerge from the snail. The cercariae invade the second intermediate host, a crustacean such as a crab or crayfish, where they encyst and become metacercariae. This is the infective stage for the mammalian host ❺. Human infection with *P. westermani* occurs by eating inadequately cooked or pickled crab or crayfish that harbor metacercariae of the parasite ❻. The metacercariae excyst in the duodenum ❼, penetrate through the intestinal wall into the peritoneal cavity, then through the abdominal wall and diaphragm into the lungs, where they become encapsulated and develop into adults ❽ (7.5 to 12 mm by 4 to 6 mm). The worms can also reach other organs and tissues, such as the brain and striated muscles, respectively. However, when this takes place completion of the life cycles is not achieved, because the eggs laid cannot exit these sites. Time from infection to oviposition is 65 to 90 days. Infections may persist for 20 years in humans. Animals such as pigs, dogs, and a variety of feline species can also harbor *P. westermani*.

Summary

Organism	Transmission	Symptoms	Diagnosis	Treatment
S. mansoni *S. japonicum*	skin penetration by cercaria	Dermatitis, abdominal pain, bloody stool, peri-portal fibrosis, hepato-splenomegaly, ascites, CNS	Eggs in stool	Praziquantel
Schistosoma hematobium	skin penetration by cercaria	Dermatitis, urogenital cystitis, urethritis and bladder carcinoma	Eggs in urine	Praziquantel
Fasciolopsis buski	Metacercaria on water chestnut	Epigastric pain, nausea, diarrhea, edema, ascites	Eggs in stool	Praziquantel,
C. sinensis *O. felinus* *O. viverini*	Cysts in fish	Inflammation and deformation of bile duct, hepatitis, anemia and edema	Eggs in stool	Praziquantel
Paragonimus westermani	Cyst in crab meat	Cough (dry / rusty brown sputum), pulmonary pain, pleurisy, tuberculosis-like	Eggs in sputum	Praziquantel

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