Class Digenea (Trematoda)
The Flukes

Lecture 8
Medical Parasitology Course (MLAB 362)

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Class Digenea (Trematoda)

- Adult trematodes are parasites of vertebrates.
- All have complex life cycles requiring one or more intermediate hosts.
- Most are hermaphroditic, many capable of self-fertilization.
- Eggs shed by the adult worm within the vertebrate host pass outside to the environment, and a larva (called a miracidium) may hatch and swim away or (depending on species) the egg may have to be ingested by the next host.
- Every species of trematode requires a certain species of molluscan (snail, clam, etc) as an intermediate host.
- A complex series of generations occurs in the mollusk, resulting ultimately in the liberation of large numbers of larvae known as cercariae.
General adult's appearance

1. Body is non-segmented, flattened dorsal-ventrally, leaf-shaped, and covered with a cuticle which may be smooth or spiny.

2. Attachment organs are two cup-shaped suckers, two cup-shaped suckers, - oral and ventral.

Oral cavity leads to muscular esophagus, from which intestines branch to form 2 ceca, which run parallel to each other ending blindly near the posterior end of the worm.

4. Simple digestive system, no anus - waste products are regurgitated.

5. Reproductive system

a. Uterus is usually the largest organ with a single ovary, two testes & a series of glandular structures that produce shell material that covers the ovum.

b. Uterus may be filled with thousands of eggs.

TREMATODES STAGES

• EGG:
Excreted in the urine or stool from definitive host. If the egg reaches fresh water, it hatches to release the free swimming larvae, the miracidium.

• MIRACIDIUM:
Ciliated, bullet-shaped, larva which penetrates the intermediate host (snail/mollusc) where asexual reproduction to cercaria takes place.

• CERCARIA:
This stage encysts in or on aquatic plants or animals and metamorphoses into metacercariae.

• METACERCARIAE:
Definitive hosts (humans) ingest these forms and are thus infected (Paragonimus, Clonorchis). In another trematode pattern, the metacercariae leave the mollusc host and directly penetrate the definitive host (Schistosoma).
### Members classification

1. **Intestinal**
   - a. *Fasciolopsis buski*
   - b. *Heterophyes heterophyes*
   - c. *Echinostoma ilocanum*
   - d. *Metagonimus yokogawai*

2. **Liver / Lung**
   - a. *Clonorchis sinensis*
   - b. *Opisthorchis viverrini*
   - c. *Fasciola hepatica*
   - d. *Paragonimus westermani*

3. **Blood**
   - a. *Schistosoma mansoni*
   - b. *Schistosoma haematobium*
   - c. *Schistosoma japonicum*

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**Fasciola hepatica**
Fascioliasis

- **Causal Agents:**
  - The trematodes *Fasciola hepatica* (the sheep liver fluke) and *Fasciola gigantica*, parasites of herbivores that can infect humans accidentally.

- **Geographic Distribution:**
  - Fascioliasis occurs **worldwide**. Human infections with *F. hepatica* are found in areas where sheep and cattle are raised, and where humans consume raw watercress, including Europe, the Middle East, and Asia. Infections with *F. gigantica* have been reported, more rarely, in Asia, Africa, and Hawaii.

Life Cycle

- Immature eggs are discharged in the biliary ducts and in the stool.
- Eggs become embryonated in water, eggs release miracidia, which invade a suitable snail intermediate host, including many species of the genus *Lymnae*.
- In the snail the parasites undergo several developmental stages (sporocysts, rediae, and cercariae).
- The cercariae are released from the snail and encyst as metacercariae on aquatic vegetation or other surfaces.
- Mammals acquire the infection by eating vegetation containing metacercariae.
- Humans can become infected by ingesting metacercariae-containing freshwater plants, especially watercress.
• After ingestion, the metacercariae excyst in the duodenum and migrate through the intestinal wall, the peritoneal cavity, and the liver parenchyma into the biliary ducts, where they develop into adults.

• In humans, maturation from metacercariae into adult flukes takes approximately 3 to 4 months.

• The adult flukes (Fasciola hepatica: up to 30 mm by 13 mm; F. gigantica: up to 75 mm)

• reside in the large biliary ducts of the mammalian host.

• Fasciola hepatica infect various animal species, mostly herbivores.
Clinical Features:

- **During the acute phase** (caused by the migration of the immature fluke),
- manifestations include abdominal pain, hepatomegaly, fever, vomiting, diarrhea, urticaria and eosinophilia, and can last for months.

- **In the chronic phase** (caused by the adult fluke within the bile ducts), the symptoms are more discrete and reflect intermittent biliary obstruction and inflammation.
Laboratory Diagnosis:

- Microscopic identification of eggs is useful in the chronic (adult) stage.
- Eggs can be recovered in the stools or in material obtained by duodenal or biliary drainage.
- They are morphologically indistinguishable from those of *Fasciolopsis buski*.
- **False fascioliasis (pseudofascioliasis)** refers to the presence of eggs in the stool resulting not from an actual infection but from recent ingestion of infected livers containing eggs. This situation (with its potential for misdiagnosis) can be avoided by having the patient follow a liver-free diet several days before a repeat stool examination.

- Antibody detection tests are useful especially in the early invasive stages, when the eggs are not yet apparent in the stools, or in ectopic fascioliasis.
Fasciola hepatica adult (anterior)

Eggs of F. hepatica

Fasciola (adult)
Egg of *Fasciola*

![Egg of Fasciola](image)

Cercaria of *Fasciola*

![Cercaria of Fasciola](image)
Shell of *Lymnaea* snail

*Heterophyes heterophyes*
The Life Cycle of Heterophyes Heterophyes

Eggs are passed in the host's feces.

The eggs are ingested by the first intermediate host.

The parasite reproduces asexually, and cercariae are liberated.

The cercariae penetrate the skin of the second intermediate host.

Cercariae "encyst" to form metacercariae.

The definitive host is infected when raw or undercooked fish is ingested.

The adult worms are found in the host's small intestine.

(Parasites and Parasitological Resources)
Life Cycle of *Heterophyes heterophyes*

- Adults release embryonated eggs each with a fully-developed miracidium, and eggs are passed in the host's feces.
- After ingestion by a suitable snail (first intermediate host), the eggs hatch and release miracidia which penetrate the snail’s intestine.
- The miracidia undergo several developmental stages in the snail, i.e. sporocysts, rediae, and cercariae.
- The cercariae are released from the snail and encyst as metacercariae in the tissues of a suitable fresh/brackish water fish (second intermediate host).

- The definitive host becomes infected by ingesting undercooked or salted fish containing metacercariae.
- After ingestion, the metacercariae excyst, attach to the mucosa of the small intestine and mature into adults (measuring 1.0 to 1.7 mm by 0.3 to 0.4 mm).
- In addition to humans, various fish-eating mammals (e.g., cats and dogs) and birds can be infected by *Heterophyes heterophyes*.
**Geographic Distribution:**
Egypt, Asia, the Middle East, and Far East.

**Clinical Features:**
- These are **intestinal flukes, therefore, no liver involvement** and symptoms would be expected.
- The main symptoms are diarrhea and colicky abdominal pain. Migration of the eggs to the heart, resulting in potentially fatal myocardial and valvular damage, has been reported from the Philippines.
- Migration to other organs (e.g., brain) has also been reported.

**Laboratory Diagnosis:**
- The diagnosis is based on the microscopic identification of eggs in the stool.
- However, the eggs are indistinguishable from those of *Metagonimus yokogawai*
- Adults are found in the small intestine.
- Adults not found in feces until after treatment.
**Heterophyes heterophyes egg**

![Image of Heterophyes heterophyes egg]

**Schistosomiasis**

*Schistosoma mansoni* Pair

![Image of Schistosoma mansoni Pair]

Fig. The threadlike female is enclosed in a groove in the body of the male.

1 mm
Schistosomiasis

- Schistosomiasis is also known as bilharzia after Theodor Bilharz, a German pathologist, who first identified the parasite in Egypt in 1851. Infection is widespread with a relatively low mortality rate, but a high morbidity rate, causing severe debilitating illness in millions of people. The disease is often associated with water resource development projects, such as
  - irrigation schemes,
  - fresh water reservoirs,
  - artificial lakes,
  - cultivation of rice,
  - where the snail intermediate hosts of the parasite breed.

Schistosomiasis

- **Causal Agents:**
  - Schistosomiasis is caused by digenetic blood trematodes.
  - The three main species infecting humans are *Schistosoma haematobium*, *S. japonicum*, and *S. mansoni*.
  - Two other species, more localized geographically, are *S. mekongi* and *S. intercalatum*.
  - In addition, other species of schistosomes, which parasitize birds and mammals, can cause cercarial dermatitis in humans.
Causative agent

- Trematode flatworms (flukes) of the genus Schistosoma.
  - *S. haematobium* is the most prevalent and widespread species in Africa and the Middle East
  - *S. mansoni* is found in Africa and is the only species seen in Latin America
  - *S. japonicum* is restricted to the Pacific region including China and the Philippines
  - *S. intercalatum* occurs in 10 countries in the rainforest belt of Africa
  - *S. mekongi* is found in limited areas of Laos and Cambodia.

- *S. mansoni* adult female worms have a very long longevity of between 10 and 30 years
- male worms are 10-15 mm long and 1 mm large
- female worms are 15-18 mm long and less than 1 mm large

Distribution

<table>
<thead>
<tr>
<th>Responsible organisms</th>
<th>Regions</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Schistosoma haematobium</em></td>
<td>Africa, East Mediterranean</td>
</tr>
<tr>
<td><em>Schistosoma mansoni</em></td>
<td>Africa, South America</td>
</tr>
<tr>
<td><em>Schistosoma japonicum</em></td>
<td>Asia</td>
</tr>
</tbody>
</table>

600 million people are exposed to the risks of schistosomiasis of whom 200 million are infected. Schistosomiasis is after malaria the most important parasitic disease of mankind.
Life Cycle:

- Eggs are eliminated with feces or urine.
- Under optimal conditions the eggs hatch and release miracidia
- Miracidia swim and penetrate specific snail intermediate hosts
- The stages in the snail include 2 generations of sporocysts and the production of cercariae.
- The infective cercariae swim, penetrate the skin of the human host, and shed their forked tail, becoming schistosomulae.
- The schistosomulae migrate through several tissues and stages to their residence in the veins.
- Adult worms in humans reside in the mesenteric venules in various locations, which at times seem to be specific for each species.

- *S. japonicum* is more frequently found in the superior mesenteric veins draining the small intestine, and
- *S. mansoni* occurs more often in the superior mesenteric veins draining the large intestine.
- However, both species can occupy either location, and they are capable of moving between sites,
- *S. haematobium* most often occurs in the venous of bladder, 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.
Pathology of *S. mansoni* and *S. japonicum* schistosomiasis includes:
Katayama fever, hepatic perisinusoidal 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, horse and goats, serve as reservoirs for *S. japonicum*, and dogs for *S. mekongi*. 
Life cycle

• Schistosomula

• Adult worms in:
  – blood vessel around rectum (mansoni)
  – bladder (haematobium)
  – mesenteric veins and pulmonary arteries (japonicum)

• Egg production (10-30 per day)

• Cercaria (500 per year per snail)

• Sporocysts (several per miracidium)

• Miracidium in water

Transmission

• Occurs in freshwater when intermediate snail hosts release infective forms of the parasite. People are infected by contact with water where infected snails live.

  Intermediate hosts are molluscs  schistosome
  • Bullinus globosus  S. haematobium
  • Bullinus truncatus
  • Biomphalaria pfeifferi  S. mansoni
  • Biomphalaria glabratta

• Larval forms of the parasites (known as cercariae), released by the snails, penetrate the skin of people in the water. The snails themselves become infected by another larval stage of the parasite, known as a miracidium, which develops from eggs passed out in the urine or faeces of infected people.
Symptoms

- Adult male and female schistosomes pair and live together in human blood vessels. The females release eggs, some of which are passed out in the urine (in S. haematobium infection) or stools (S. mansoni, S. japonicum), but some eggs are trapped in body tissues. Immune reactions to eggs lodged in tissues are the cause of disease.
Clinical Features:

- Many infections are asymptomatic.
- **Acute schistosomiasis may occur weeks after the initial infection**, especially by *S. mansoni* and *S. japonicum*.
- Manifestations include **fever, cough, abdominal pain, diarrhea, hepatosplenomegaly**, and eosinophilia.
- Occasionally **central nervous system lesions** occur: cerebral granulomatous disease may be caused by ectopic *S. japonicum* eggs in the brain, and granulomatous lesions around ectopic eggs in the spinal cord from *S. mansoni* and *S. haematobium* infections may result in a transverse myelitis with flaccid paraplegia.

Continuing infection may cause granulomatous reactions and **fibrosis in the affected organs**, which may result in manifestations that include:

- colonic polyposis with **bloody diarrhea** (*Schistosoma mansoni* mostly);
- **portal hypertension** with hematemesis and splenomegaly (*S. mansoni*, *S. japonicum*, *S. mansoni*);
- **cystitis and ureteritis** (*S. haematobium*) with **hematuria**, which can progress to bladder cancer;
- **pulmonary hypertension** (*S. mansoni*, *S. japonicum*, more rarely *S. haematobium*); glomerulonephritis; and **central nervous system lesions**.
Types of disease

- *S. haematobium* (urogenital)
- In urinary schistosomiasis damage to the urinary tract is revealed by blood and schistosome eggs in the urine. Eggs which get stuck in the tissues may calcify and lead to the formation of granulomas and superinfections. Urination becomes painful and is accompanied by progressive damage to the bladder, ureters and then the kidneys. Bladder cancer is common in advanced cases.

Types of disease (2)

- In intestinal schistosomiasis (infection with *S. mansoni*, *S. japonicum*, *S. mekongi*) disease is slower to develop.
- There is progressive enlargement of the liver and spleen, intestinal damage due to fibrotic lesions around eggs lodged in these tissues, and hypertension of the abdominal blood vessels. Bleeding from these vessels leads to blood in stools, and can be fatal. Sufferers become seriously weakened by the disease and, in some cases, the functioning of organs such as spleen and kidneys becomes impaired.
- Death is mostly due to bladder cancer associated with urinary schistosomiasis and to bleeding from varicose veins in the oesophagus associated with intestinal schistosomiasis. Children are especially vulnerable to infection, which develops into chronic disease if not treated.
Laboratory Diagnosis:

- Microscopic identification of eggs in stool or urine is the most practical method for diagnosis.
- Stool examination should be performed when infection with *S. mansoni* or *S. japonicum* is suspected,
- urine examination should be performed if *S. haematobium* is suspected.
- Eggs can be present in the stool in infections with all *Schistosoma* species.
- The examination can be performed on a simple smear (1 to 2 mg of fecal material).
- Since eggs may be passed intermittently or in small amounts, their detection will be enhanced by repeated examinations and/or concentration procedures (such as the formalin - ethyl acetate technique).

- Kato-Katz technique (20 to 50 mg of fecal material) or the Ritchie technique.
- Eggs can be found in the urine in infections with *S. haematobium* (recommended time for collection: between noon and 3 PM) and with *S. japonicum*.
- Detection will be enhanced by centrifugation and examination of the sediment.
- Tissue biopsy (rectal biopsy for all species and biopsy of the bladder for *S. haematobium*) may demonstrate eggs when stool or urine examinations are negative.
- Antibody detection can be useful in both in clinical management (e.g., recent infections) and for epidemiologic surveys.
Diagnosis

Diagnosis using urine filtration and faecal smear techniques:
- Haematobium: search for eggs in urine
- Mansoni: search for eggs in stool

Antigen detection in endemic areas
Antibody tests in non-endemic areas

Schistosoma sp. cercaria

Fig. The threadlike female is enclosed in a groove in the body of the male.
Schistosoma mansoni egg

Schistosoma japonicum egg

Schistosoma haematobium egg

Egg of *S. mansoni* with lateral spine.

Egg of *S. intercalatum* with terminal spine.
Schistosoma

Schistosoma mansoni

Female

Male

Schistosoma (copula)

female
Egg of *Schistosoma mansoni*  
Egg of *Schistosoma haematobium*

Uncalcified and calcified (black) eggs of *S. mansoni* in rectal biopsy.
Cercaria of *Schistosoma*

*Bulinus* snail
Biomphalaria snail

Egg of *S. japonicum*. Rudimentary spine is not visible.

Uncalcified and calcified (black) eggs of *S. mansoni* in rectal biopsy.
Snail control through focal mollusciciding

China: Molluscide (niclosamide) to kill intermediate host snails (Oncomelania) involved in the transmission of Schistosoma japonicum, being sprayed over riverbank and flood-prone land using a high-pressure hose.

An irrigation canal can create ideal habitats for the freshwater snails that are intermediate hosts of schistosomes.

Other measures of prophylaxis

- Health education
Provision of safe, adequate water supply and sanitation

A researcher using a scoop to search for freshwater snails which are intermediate hosts in the schistosomiasis cycle.

Drug treatment

- Drug treatment is the only way to reduce disease symptoms and improve the situation of the patients. Drugs available are:
  - praziquantel: effective in a single dose against all species
  - oxamniquine: effective in a single dose, but only against S. mansoni
Eggs and Larvae of Important Helminths

- **Schistosoma mansoni**
  - Size: 112-175 x 45-70 μm

- **S. haematobium**
  - Size: 83-187 x 60-70 μm

- **Fasciola hepatica**
  - Size: 130-150 x 63-90 μm

- **Fasciolopsis buski**
  - Size: 130-154 x 78-98 μm

- **Dicrocoelium dendriticum**
  - Size: 38-49 x 22-33 μm

- **Opisthorchis felineus**
  - Size: 26-32 x 11-15 μm

Fig. Differential diagnosis of the eggs of important helminths (trematodes, cestodes, and nematodes) and of the larvae of Strongyloides stercoralis. Note: images are not to the same scale! (Images of Hymenolepis and Enterobius: H. Mehlhorn, Düsseldorf.)

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Eggs and Larvae of Important Helminths

- **Clonorchis**
  - Size: 27-35 x 11-20 μm

- **Paragonimus africanus**
  - Size: 70-110 x 40-65 μm

- **Diphyllobothrium latum**
  - Size: 58-70 x 40-50 μm

- **Toxocara spp.**
  - Size: 30-43 x 29-38 μm

- **Hymenolepis nana**
  - Size: 44-62 x 30-53 μm

- **Ascaris lumbricoides**
  - Size: 55-75 x 35-50 μm

- **Trichuris trichiura**
  - Size: 50-55 x 22-24 μm

- **Ancylostomes**
  - Size: 60-75 x 36-40 μm

- **Enterocephalus vermicularis**
  - Size: 50-60 x 20-32 μm

**Strongyloides stercoralis**

Length: 180-380 μm