Chapter 16 - Digeneans: Strigeiformes

Taxonomy

C. Trematoda
  S.C. Digenea
    O. Strigeiformes
      F. Diplostomatidae
        G. Alaria, Uvulifer
      F. Schistosomatidae
        G. Schistosoma

Super Family Strigeoidea

The bodies of the strigeoidea are divided into 2 parts
The anterior spoon-shaped portion that usually bears pseudosuckers on each side of the oral sucker
Also located in this area is a tribocytic organ, that secretes proteolytic enzymes that digest the mucosa of the host; it may also serve as a hold-fast
The posterior part of the body is cylindrical and contains the reproductive organs

The strigeoids are parasites of fish-eating vertebrates, and they occur mostly in the digestive tracts of these hosts

Family Diplostomidae

Alaria americiana

They have a complex life cycle involving 4 hosts
Adults reside in the small intestine of carnivorous mammals, especially canines
Eggs are shed with the feces and hatch into miracidia in the water
Miriacidia then penetrate a host snail (planorbid)
Mother sporocysts produce daughter sporocysts
Eventually daughter sporocysts give rise to cercariae

Cercariae leave the host and swim to the surface of the water
They are stimulated by the water currents of a passing tadpole and will chase down and penetrate one that passes by
Cercariae transforms into a mesocercaria
This stage is infective to the definitive host (and also to a paratenic host)
If a canine eats an infected tadpole or frog, the mesocercariae penetrate into the coelom and move to the lungs. Here it transforms to the diplostomula stage. These migrate to the tracheae and ultimately end up in the intestinal tract.

Note: Snakes can eat infected tadpoles and then carry mesocarirae thus serving as paratenic hosts.

Adult *Alaria* are considered pathogenic and cause severe enteritis that may ultimately kill the definitive host.

**Uvulifer ambloplitis**

This is one of several species of strigeoides that cause “black spot” disease in the skin of FW fishes in NA.

The adults are parasites of kingfishers. Eggs hatch out into miracidia which then penetrate snails of the genus *Helisoma*. This is followed by the production of sporocysts and daughter sporocysts that in turn produce cercariae. Cercariae penetrate fish and once in the dermis they metamorphose into neascus *metacercariae* and secrete a cyst around themselves. Subsequent melanization of the host results in a black spot. Kingfishers becomes infected when it eats infected fish.

**Superfamily Schistosomatoidea**

The schistosomes cause serious disease to man - *shistosomiasi*) Animals (e.g. fishes, reptiles, birds, and mammals) also serve as hosts for these worms.

This is a peculiar group for a number of reasons:

- members of this group do not have a second intermediate host
- adults reside in the blood vascular system of the definitive host
- most species are dioecious
Family Schistosomatidae

Genus Schistosoma

General

The human disease complex known as schistosomiasis is primarily caused by 3 members of the genus Schistosoma: *S. haematobium*, *S. mansoni*, and *S. japonicum*. Human infections by these flukes are in excess of 250 million worldwide.

Morphology

The mouth of the adult schistosome is surrounded by an oral sucker, and a ventral sucker is located immediately posterior to the level of bifurcation of the gut.

While no pharynx is present, there is an esophagus with prominent esophageal glands. The paired ceca reunite posteriorly, forming a single cecum that extends along the remaining length of the body.

The adult male is larger in circumference than the female, with a ventral fold or groove called the gynaecephoral canal. The female is longer and more slender than the male; she is held in the canal, permitting almost continuous mating.

The male possesses 5-9 testes and the male genital pore opens ventrally, immediately posterior to the ventral sucker. There is no cirrus.

Females have a single ovary.

Life Cycle

For the most part, the life cycles of the 3 species are almost identical. Adult schistosomes reside in veins that drain certain organs of their host's abdomen. The 3 species that we are focusing on have distinct preferences:

- *S. haematobium* live primarily in veins of the urinary bladder.
- *S. mansoni* prefers the portal veins that drain the large intestine.
- *S. japonicum* more concentrated in the veins of the small intestine.

The female usually migrates to smaller venules before depositing eggs. The morphology of the egg is distinctive in each species and serves as a criterion for diagnosis.
The egg must penetrate the venuole endothelium and then traverse the intervening tissues and the mucosal lining before entering the lumen of the gut or the bladder to escape to the outside. The method by which the egg passes through tissues probably involves hydrolytic secretions emitted through the porous shell. The process is inefficient since only about 1/3 of the eggs produced reach the exterior. The remaining eggs are either trapped in the urinary bladder or intestinal walls or are swept back by the blood flow to become lodged in ectopic sites such as the liver or spleen. After reaching the lumen, the egg passes out in either feces or urine.

Upon reaching FW, the miracidium hatches from the egg. The free-swimming miracidium must penetrate a suitable snail intermediate host within a few hours after hatching or it dies.

After transforming into a sporocyst stage in the head-foot of the snail, it produces a second generation of migratory sporocysts, which move to the digestive gland or gonads where they produce either additional generations of sporocysts or the cercarial generation.

The cercaria leave the sporocyst in which they have developed via a birth pore and pass through the tissues of the snail to the exterior. This passage is facilitated by secretions from a pair of escape glands located in the cephalic region of the cercaria.

The cercaria swim upward to the surface of the water and then sink slowly toward the bottom. Or, they may adhere to the surface film and come to rest, awaiting contact with their next host. The cercaria are stimulated to attach and penetrate by the secretions of mammalian skin.

The cercariae adheres its body to the skin of the definitive host using both its muscular suckers and the mucoid secretions of the acetabular glands.

Once the cercaria enters the skin (10-30 secs), it burrows to the peripheral capillary bed or enters the lymphatic system. In either case, the worms reach the right side of the heart and then enter the pulmonary capillaries of the lungs.

During the penetration process 3 significant morphological changes occur in the cercaria:

- the tail is lost
- the surface coat is lost
- contents of the penetration gland is spent

Following these changes, the transformed cercaria is called a schistosomule. Schistosomes appear in pulmonary capillaries by the 3rd day of post penetration.
On the 4th day juveniles begin feeding on host RBCs, undergoing rapid growth and development. After about a week, the schistosomules move through the pulmonary vein to the left side of the heart and then into the systemic circulation. It appears that only those schistosomules that enter the mesenteric arteries, traverse the intestinal capillary bed, and reach the liver by the hepatic portal system can continue to grow. About 3 weeks post penetration the worms reach the hepatic portal veins (S. mansoni), veins of the small intestine (S. japonicum), or those of the urinary bladder (S. haematobium) where they reach sexual maturity and mate.

**Life Cycle Variations**

<table>
<thead>
<tr>
<th>Feature</th>
<th><strong>S. haematobium</strong></th>
<th><strong>S. mansoni</strong></th>
<th><strong>S. japonicum</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Locality</td>
<td>Africa, Middle East</td>
<td>Africa, South America</td>
<td>Far East</td>
</tr>
<tr>
<td>Host</td>
<td><em>Balinus</em></td>
<td><em>Biomphalaria</em></td>
<td><em>Oncomelania</em></td>
</tr>
<tr>
<td>Testes</td>
<td>4-5</td>
<td>6-9</td>
<td>7</td>
</tr>
<tr>
<td>Ovary</td>
<td>middle</td>
<td>anterior half</td>
<td>Posterior half</td>
</tr>
<tr>
<td>Male tegument</td>
<td>tubercules</td>
<td>tubercules</td>
<td>smooth</td>
</tr>
<tr>
<td>Eggs</td>
<td>terminal spine</td>
<td>lateral spine</td>
<td>no spine, clusters</td>
</tr>
</tbody>
</table>

**Symptomology and Diagnosis**

The first symptom is a localized dermatitis, often observed following cercarial penetration of the skin. It is characterized by itching and local edema, which usually disappear after 4 days.
Following skin penetration, the symptoms of human schistosomiasis appear in 3 phases

1. The migration phase (from penetration to egg production)

It can be characterized by toxic reactions and pulmonary congestion accompanied by fever.
This phase may last 4-10 weeks, during which the worms migrate from the lungs to the liver where they reach sexual maturity and mate.

2. The acute phase (begins at egg production)

This phase is considerably longer, lasting 2 months to several years.
Symptoms such as blood stools (S. mansoni and S. japonicum) and hematuria (S. hematobium) are caused by passage of eggs through the intestinal and urinary bladder walls.

3. The chronic phase

Usually there is mild, chronic bloody diarrhea, with mild abdominal pain and lethargy, or with S. haematobium there is pain during urination.
It is also characterized by severe intestinal, renal, and hepatic pathology, caused by the reaction of the host to schistosome eggs.
Enlargement of the liver and spleen is a common symptom of advanced schistosomiasis.

Eggs trapped in the walls of the intestine and urinary bladder as well as ectopic regions, notably the liver and the spleen, elicit inflammatory reactions resulting from leucocystic and fibroblastic infiltration and producing cirrhosis, anemia, etc.

Eventually, a granuloma or pseudotubercle forms around each egg or cluster of eggs.
Essentially there is leukocyte infiltration and secretion of fibroblast growth factors.

Small abcesses, accompanied by occlusion of small blood vessels, lead to necrosis and ulceration.

In endemic areas, where re-infection is common, repeated penetration of the intestinal and urinary bladder walls by migrating eggs results in extensive scar tissue formation, which impedes the normal functioning of the organs.
Because formation of scar tissue also blocks the migration of eggs through infected organs, more eggs are swept back to other sites, producing organ enlargement (e.g. the liver and spleen).
Treatment

Treatment varies according to species
No reliable prophylactic regimen is presently available other than the observance of proper sanitation procedures, avoidance of cercarial infested waters, and the prevention of water contamination by human excreta

There are a number of chemotherapeutic agents on the market many of which have toxic side effects

According to WHO, the key to future schistosomiasis control lies in a 4-pronged attack:

- population-based chemotherapy, with repeated drug administration to infected individuals
- use of molluscicides
- introduction of biological controls, such as carnivorous snails and fish
- education of the population

Immunity

It is known that animals experimentally infected with schistosomes that normally infect humans develop immunity and that infected humans develop at least partial immunity

The life span of adult schistosomes in the human host can be longer than 30 years and during much of this time the worms are producing vast numbers of eggs
This ability, augmented with their longevity, elicits a wide range of immune responses, both humoral and cell mediated

Actually, such responses can be correlated with several parasitic stages in the human host
The first, or skin penetration stage, is characterized by a response to the penetrating cercaria’s glycocalyx and penetration gland secretions, both released in the host’s tissues

The second, or early development stage produces 2 responses

1. One is caused by tegumental changes of the migrating schistosomule
2. The other is a response to immunogens released from either migrating or trapped eggs

The third, or adult worm, stage is a response to immunogens released from the adult worm’s intestine, tegument and excretory system
The question may be asked. “If worms produce immunogens to which the host responds, how do the worms evade the host response?”

The parasites appear to have the ability of the adult worm to acquire protective host antigens on its surface. The antigens afford protection by disguising the worm’s surface so that it escapes detection by the host immune mediators.

Antigen acquisition apparently begins during the early schistosomule stage. Logically, therefore, the target for an effective vaccine must be the larval stage before such acquisition has occurred.

**Swimmers Itch**

An interesting aspect of schistosome biology concerns cercarial dermatitis or swimmer’s itch. The condition is caused when cercariae of blood flukes that normally parasitize aquatic birds and mammals penetrate the human skin, sensitizing the areas of attack and causing pustules and an itchy rash. Since humans are not suitable definitive hosts for these flukes, the cercariae do not normally enter the blood stream and mature. Instead, after penetrating the skin, they are destroyed by the victim’s immune response. Allergenic material released from dead and dying cercariae produce a localized inflammatory reaction.