Univ. of Mustansiriyah
College of Pharmacy
Branch of Clinical Laboratory Sciences

Medical Parasitology

Prof. Dr. Ahmed A. Mohammed

Lec. 7 Helminths

Introduction to Helminths

The term **"Helminths"** mean **"worms"** in parasitology. It refers to the parasitic worms, those comprises two large phyla: **Phylum Platyhelminths (flat worms)** and **Phylum Nemathelminths or Nematoda (true round worms)**, and two smaller ones: **Phylum Nematomorpha (hair snakes) and Phylum Acanthocephala (thorny-headed worms)**, in addition to one **class** group from **phylum Annelida**, the **class Hirudinea** (Leeches).

Special adaptations for the parasitic mode of life and for species survival are more apparent in the helminths than in the protozoa. The complete or partial loss of the digestive tract in certain parasitic helminths is presumed to be because of their location in the host's intestine or tissue, where predigested nutrients are abundant. It is greatly reduced or nearly absent in many trematodes, and although present and complete in most nematodes, it is much reduced in some. A related adaptation in the trematodes and cestodes is evident in the **tegument**, which on its outer surface has a coat of microvilli morphologically not unlike that of the intestinal mucosa of the vertebrates.

While most of the vital systems of the parasitic helminths have been modified toward simplification, the reproductive system has been modified toward increased capacity. However, with few exceptions, reproduction to increase the parasitic population within the same host (internal autoinfection) does not occur among helminths as a general rule, and the number of individuals in a worm population living within a given host does not exceed the number of the infective eggs or larva that entered from the outside. Moreover, under usual condition of host and environment, the number of worms that reach maturity in any given host is limited to levels that are tolerable to both host and people infected with helminths who are asymptomatic carriers; whereas the diseased individuals among the infected group are those with the heaviest worm burdens.

In some helminths, the life cycle is direct and relatively simple, involving only one host species and a brief period of development of an infective transfer stage as in the pinworm ***Enterobius vermicularis***. In a group referred to as **soil-transmitted helminths**, the life cycle involves only one host, man, but the infective transfer stage requires a period of development in the **soil** (larvae remaining in the eggs, as in the ***Ascaris lumbricoides*** and ***Trichuris trichiura***, or free in the soil, as in the **hookworm species**), the soil acts as an intermediate host. In others, the man-to-man cycle involves essential development in one intermediate host, as in the **filarial worms** and most **tapeworms**, or two intermediate hosts, as in most **trematodes**. The first being a snail or other mollusc; the second an animal or plant that is eaten by people (such as the larva of the **lung flukes** in crabs and the larva of the **liver flukes** in the fish or others on aquatic vegetation). In addition, certain nematodes, cestodes and trematodes include in their life cycles a special kind of transmission known as **paratenesis**, involving **paratenic hosts**. Intermediate hosts provide the parasite with support for essential development, protection and availability to its final host.

Worms and larvae that migrate through or reside in tissues generally produce **eosinophilia**, focally in the tissues, in the blood or in both. Persistent **hypereosinophilia** is the most widely recognized general sign of a helminthic infection. In addition to eosinophilia, common signals of occult helminthic infections are **hepatomegaly**, **pneumonitis**, **bronchial asthma**, **urticaria**, **subcutaneous cysts** or **swellings**, **neurologic disturbances** and **deviations in behavior**.

Groups of Helminths

I- Phylum: Platyhelminths

This phylum includes three classes:

1 Class: Turbellaria.
2 Class: Trematoda.
3 Class: Cestoda.

The class **Trematoda** has (3) recognized **subclasses**: **Monogenea, Digenea and Aspidogasterea**. Only **Digenea** (Digenetic Trematodes) produce infections in man. To simplify the study, Digenetic Trematodes are also classified to groups according to the location of the **adult fluke** (worm) in the host's body into:

1. Liver (or hepatic) flukes, ex: ***Fasciola hepatica***
Clonorchis sienensis
2. Intestinal flukes, ex: ***Fasciolopsis buski***
Heterophyes heterophyes
3. Blood flukes, ex: **Schistosomes**
4. Lung flukes, ex: ***Paragonimus westermani***

1. Class: Trematoda

Ex: Blood flukes or Schistosomes

The blood flukes referred to as family called **Schistosomatidae**. The name of the worm, ***Schistosoma***, is because of the split body on the ventral side of the male in which the female is held during insemination and egg laying. Human infection with blood flukes is often referred to as **schistosomiasis** or **Bilharziasis** in honor of **Theodor Bilharz** who in 1852 discovered the parasite ***Schistosoma haematobium*** at the postmortem of a man who died in Cairo, Egypt. He said that these worms causes the **haematuria** in the farmers, and it lays eggs with terminal spine discharges with urine.

Infections number is over 250 million people in 76 countries and, in spite of the efforts to control this disease, the level of incidence has shown no significant decrease. Egypt has one of the most heavily infected populations in the world, since not only *S. haematobium* endemic to that country, but *S. mansoni* also occurs with great frequency.

The genus ***Schistosoma*** has three species parasitized on man, they are:

1. *Schistosoma mansoni*, which causes intestinal Schistosomiasis.

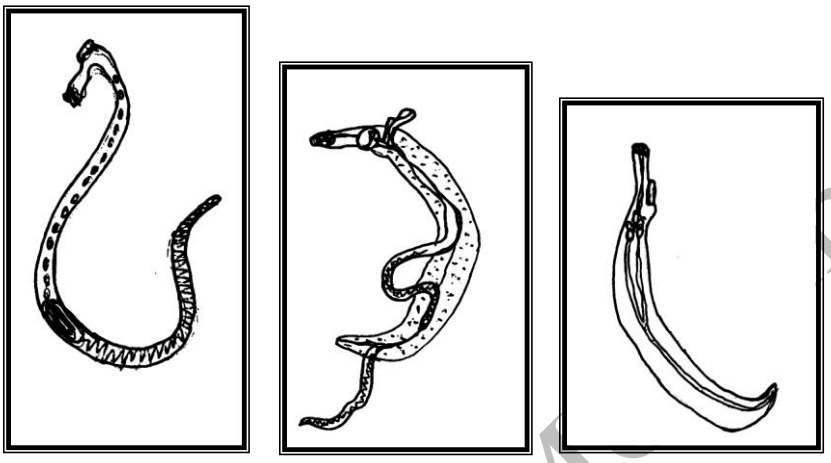
2. *Schistosoma haematobium*, which causes the vesicle Schistosomiasis or called urinary Bilharziasis.

3. *Schistosoma japonicum*, which causes the oriental intestinal Schistosomiasis.

The worms of the family Schistosomatidae characterized by:

1. They need one intermediate host to complete their life cycle.
2. They inhabit the circulatory system in their host's body where their bodies adapted to this environment.

3. They are dioecious (two sex).
4. The eggs are non-operculated, and fully embryonated when they discharged out of their host's body.
5. The cercaria characterized by its **forked tail**. They have the ability to penetrate the skin of the final host (the human).

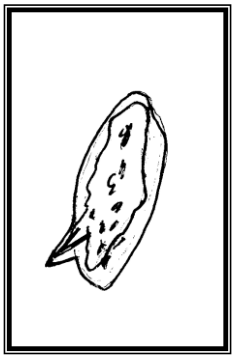


(♀) **(♂ & ♀) in copula** **(♂)**

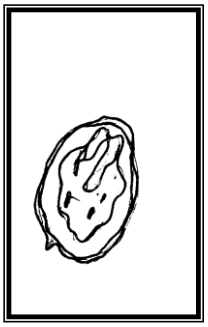
The mouth of the adult schistosome is surrounded by an oral sucker, and a ventral sucker is located immediately posterior to the level of bifurcation of the gut. The male body shorter and thicker than the female body, the outer surface of the male carrying tubercles different in size in the three species while the female body surface is smooth; there is a split like canal in the ventral side of the male, behind the ventral sucker, it is called gynecophoric canal or groove which is used to hold the female. The somewhat larger, more muscular male is attached by its suckers to the wall of the blood vessel, holding the threadlike female in its sex canal and thus enabling the female to extend its anterior extremity into the smaller venules in which it deposits its eggs.

The eggs large in size with relatively thin-shelled, non-operculated, covered with tubercles and have a spine different in position according to the species. The morphology of the egg is distinctive in each species and serves as a diagnostic criterion. The worms may live for 30 years in the human hosts, however, the average life span is possibly less than 5 years.

S. haematobium



S. mansoni



S. japonicum

"The eggs of *Schistosoma* sp.".

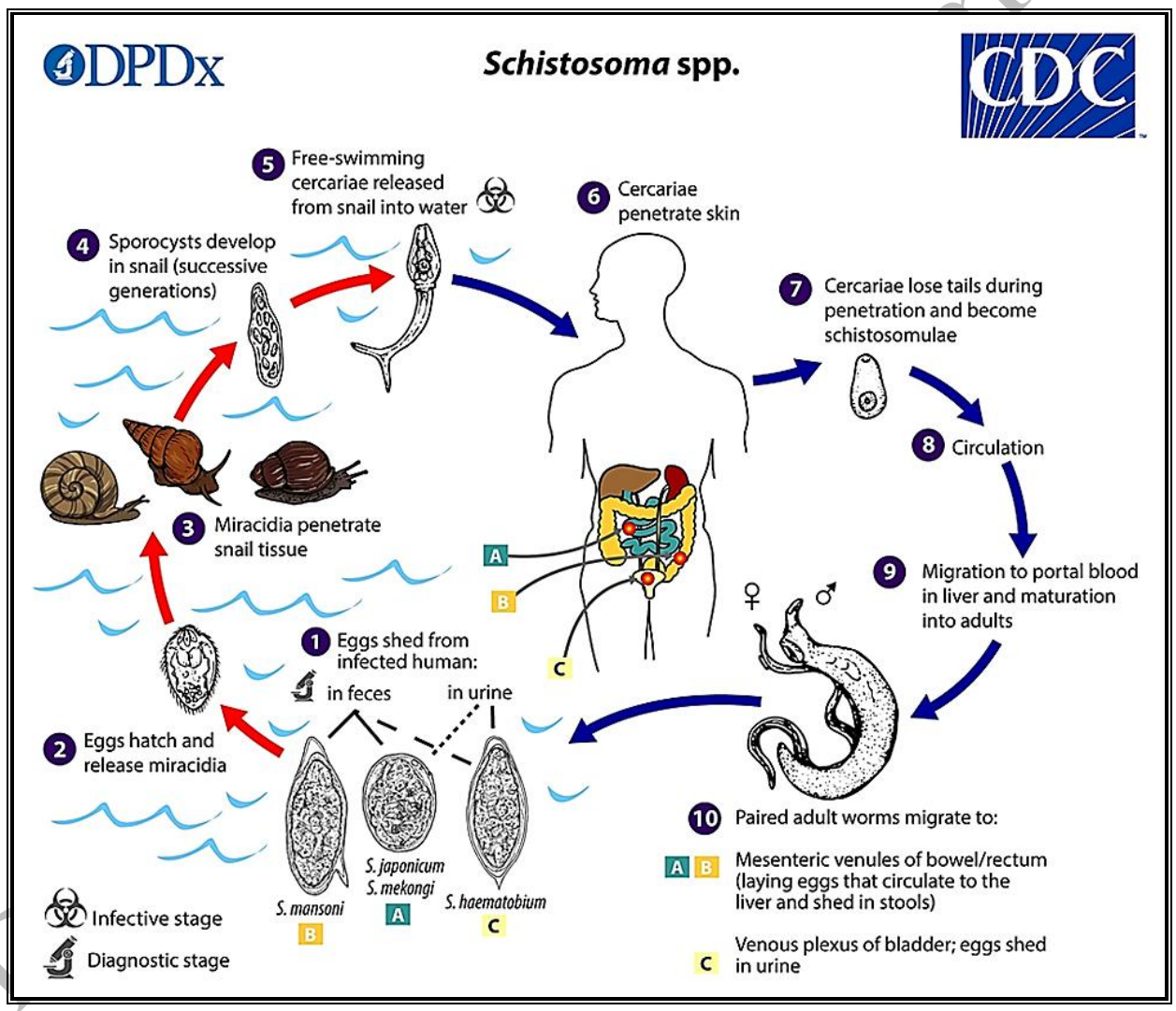
Life cycle

Adult schistosomes reside in the mesenteric veins that drain the intestine (*S. mansoni* and *S. japonicum*) or in the vesicular veins serving the urinary bladder (*S. haematobium*). The female usually migrates to the smaller venules before depositing eggs. The eggs of the Schistosomes are laid in the smaller venules, where they obstruct the normal flow of blood. Obstruction of the venules, pressure exerted by the worm, increase in size of the egg and hypermotility of the parasitized organ cause the blood vessel to rupture and discharge the eggs into surrounding tissues.

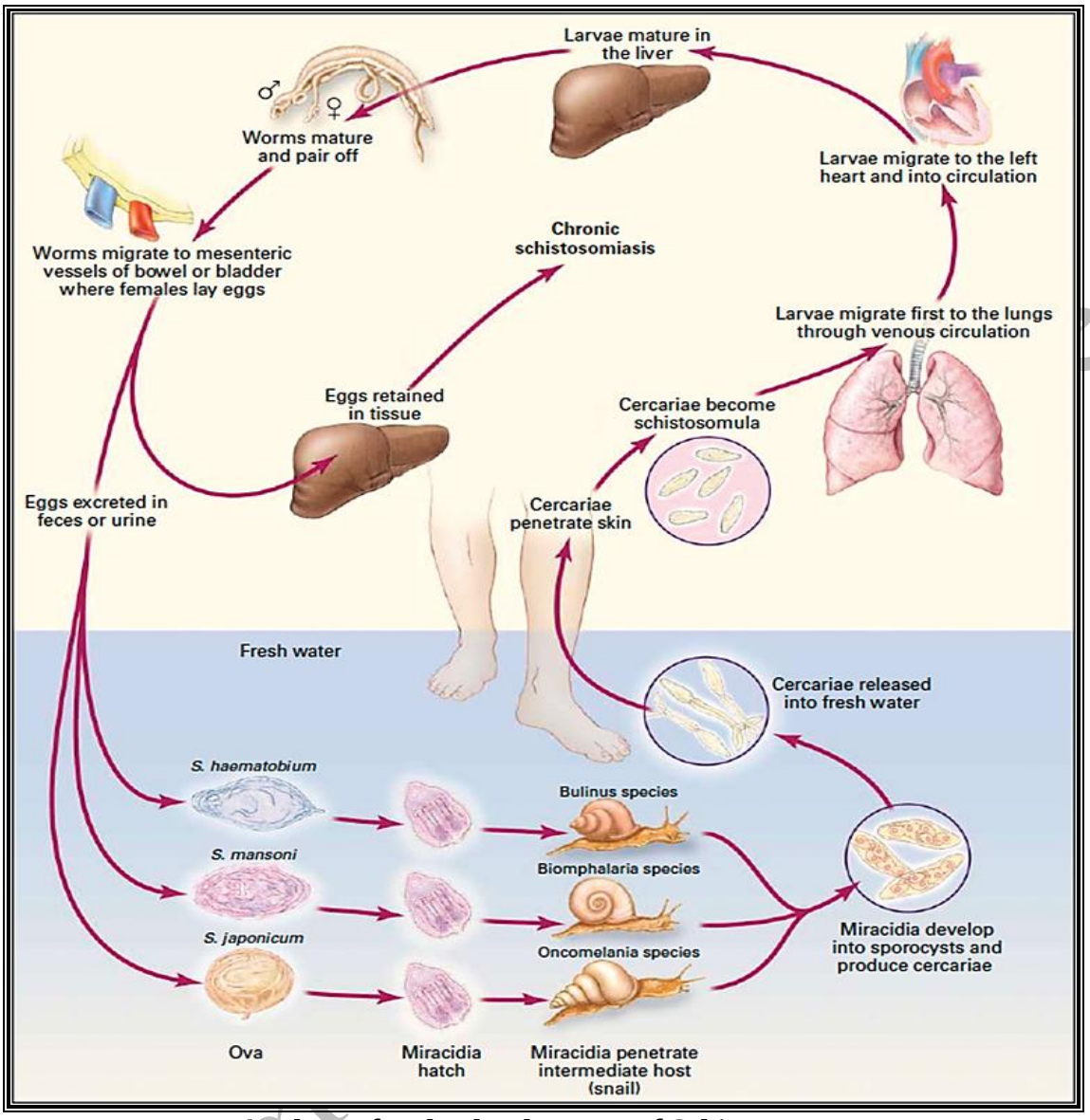
The enclosed miracidium in the egg is poorly developed at the time of oviposition but is well formed before it reaches the lumen of the infected organ. Maturation of the miracidium inside the egg while in the tissues takes place within about (1) week (***S. mansoni*** and ***S. haematobium***) or (12) days (***S. japonicum***), after which the egg sheds into the lumen of the organ and evacuated in the feces (intestinal type) or urine (vesicle type).

When the eggs reach fresh water, hatching occurs, and the miracidia become free-swimming. The miracidium penetrates an appropriate snail (the intermediate host) and develop into a **sporocyst**, then produce **secondary (daughter) sporocyst** which give rise to the cercarial generation. At that time, fork-tailed cercariae are produced over a period of several weeks (inside the snail tissues), when mature, the cercariae emerge from the snail by secretions from a pair of **escape glands** located in the cephalic region of the cercaria and swim about in the water.

Cercaria of Schistosomes



The life cycle of the three species of Schistosomes

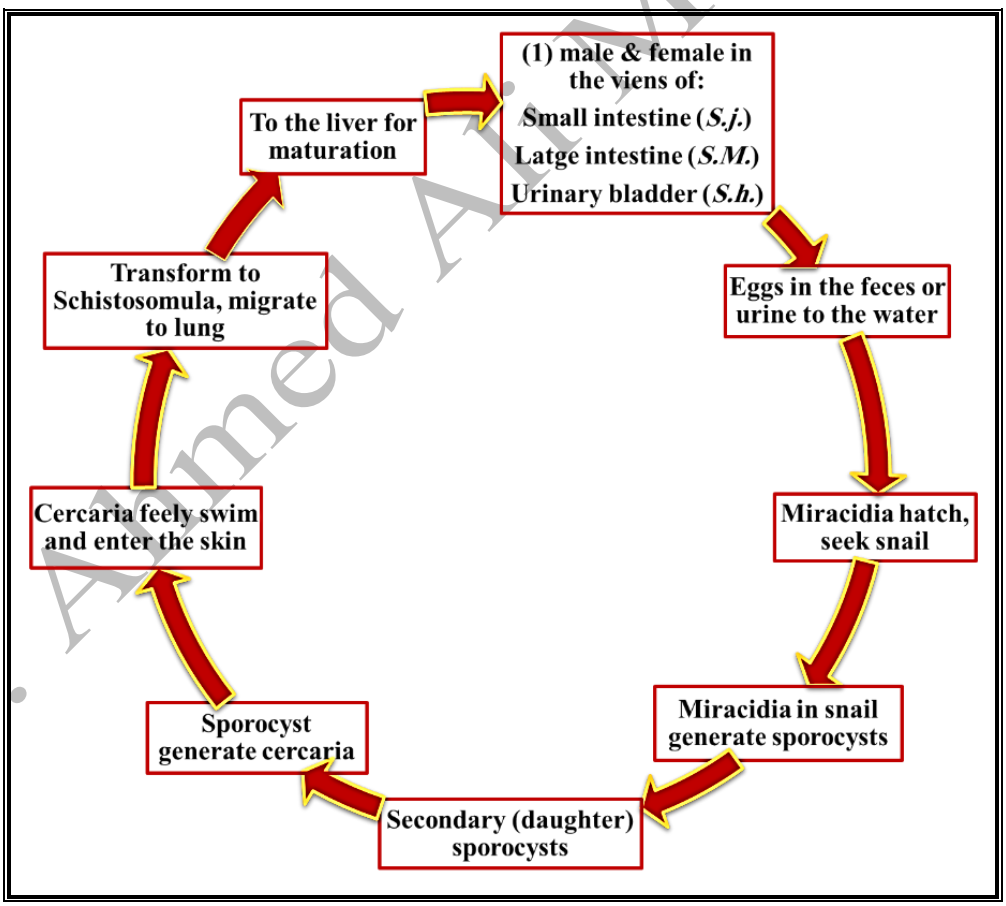


A scheme for the development of Schistosomes.

The cercariae are stimulated to attach and penetrate by the secretions of the mammalian skin. The cercaria adheres to the skin of the definitive host by means of both its muscular suckers and the mucoid secretions of its glands. On contact with the skin, the cercariae penetrate the outer layers of the skin by the secretion of the penetration glands. During the penetration process, three significant morphological changes occur in the cercaria: **they are shedding the tail, the surface coat become lost and the contents of the penetration glands are spent**; at this stage they called **Schistosomula**. On reaching the dermis they enters the peripheral capillary bed or the lymphatic system and migrates to the right side of the heart and then enters the lungs. Schistosomules appear in pulmonary capillaries by the third day post-penetration. On day 4, these juveniles begin feeding on host erythrocytes,

initiating a period of rapid growth and development. After growth and development in the parenchyma cell of the lungs, they may return to the heart by crawling against the blood stream along the walls of the pulmonary arteries and continue to move against the current through the atrium, posterior vena cava, and hepatic vein into the liver. An alternative theory is that the Schistosomula force their way through the pulmonary capillaries into the veins, where they are passively carried to the liver through the left side of the heart and arterial channels to the hepatic artery or through the intestinal arteries and intestinal capillaries to the portal vein and liver.

Approximately 3 weeks post-penetration, the worms reach the hepatic portal veins, where they reach sexual maturity and mate after 40 days. Each male embraces a female and migrates against the incoming portal blood stream to the venules at the definitive sites where egg-laying occurs primarily in the venules of the small intestine (***S. japonicum***), the venules of the colon (***S. mansoni***) and the urinary bladder (***S. haematobium***). The figure below clarifies the life cycle details.



"Scheme for the life cycle of *Schistosoma sp.*".

The stages of disease development

1. Incubation (or prepatent) period: it is starting from skin penetration to the appearance of eggs in the excreta (10-12) week, it includes slight bleeding, skin irritation in the penetration region appears as a rash, cell infiltration in the lungs, inflammatory reaction, infiltration of the eosinophils and sensitization in the liver.

2. Acute period (or stage): where the female is on its full activity of egg laying in the venules accompanied with the destruction of the tissues and bleeding which exit with the urine or feces, it is the most important symptom in the infection with **bilharzia**. There is also an inflammation around the eggs in the tissues.

3. Chronic period (or stage): this stage characterized by stable or decreased egg output, and more tissue fibrosis around the egg area, which forms pseudotubercles, and also tissue proliferation and repair.

Host immune response

The question may well be asked: **"If these worms produce immunogens to which the host responds, how do the worms evade this response?"**

While there is not yet a complete answer to this question, several significant factors provide clues. Perhaps the most remarkable of these is the ability of the worm to acquire protective host antigens on its surface. The antigens afford protection by disguising the worm's surface so that it escapes the detection by the host immune mediators. Antigen acquisition apparently begins during the early schistosomule stage and may be associated with the initiation of feeding on host blood. Therefore, an effective vaccine must target the larval stage before it attains this protection.

Pathology

The first symptom of schistosomiasis is localized dermatitis, often appear after cercariae penetrate the skin. The characteristic itching and local edema usually disappear after 4 days.

Hepatosplenomegaly (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 in ectopic regions, notably the liver and spleen, elicit inflammatory reactions due to leukocytic and fibroblastic infiltration, which produce cirrhosis, anemia, etc. Eventually, a granuloma (pseudotubercle) forms around each egg or cluster of eggs. The most severe

consequences result from an increase in portal blood pressure as the liver becomes fibrotic and filled with blood. Fluid accumulation in the peritoneal cavity and the formation of new blood vessels bypassing infected organs such as the liver are usually associated with these changes. The latter are subject to bursting, which may lead to life-threatening bleeding.

Symptomatology of the three species

1. *S. mansoni*:

The clinical signs include abdominal pain and diarrhea, the feces mixed with mucus and pus.

2. *S. haematobium*:

The symptoms during the incubation period is parallel those of the two intestinal types of the disease. When the cercaria reach to the heart and the lungs it may causes the jaundice and bleeding in the pulmonary capillaries that leads to eosinophilia especially around the small worms. When they reach the portal system, they continue in the growth and the discharge of the metabolic products which leads to toxic symptom and anorexia, headache and general malaise. During the period of egg laying the blood appears in the urine without pain in the beginning, but in the progressive case, burning sensation appears with urination and between the urination periods.

3. *S. japonicum*:

In the acute stage, diarrhea and eggs appearance in the feces occur, daily fever, epigastric pain and continued enlargement of the liver, the patient loses appetite and weight, the blood picture is one of anemia and increase in serum globulin levels with continued high eosinophilia.

Diagnosis

The surest means of diagnosis is finding and identifying the characteristic eggs in the excreta or in tissue biopsies, particularly rectal biopsies (in the 3 species). Radiology test to the calcified eggs in the urine (in ***S. haematobium***). Currently, the most promising diagnostic method utilizes immunodiagnostic techniques; however, positive results from these tests should be confirmed by identification of eggs since false positives sometimes result from concomitant infections with other parasites or exposure to various animal

schistosome cercariae. The latter sometimes produces a severe dermatitis called **swimmer's itch**.

During the prepatent period specific diagnosis is not possible. However, in the acute stage, eggs can usually be detected in the feces (***S. mansoni*** and ***S. japonicum***) and urine (***S. haematobium***) and sometimes in the feces; the recovery of the eggs could be carried out by the sedimentation method, acid-ether concentration method or by making thick smear.

Treatment

Treatment can't be expected to undo the chronic inflammatory lesions (fibrosis) that occur in the stages of healing and repair. ***Schistosoma japonicum***, the most pathogenic one, is the least responsive to treatment. ***Schistosoma haematobium*** the least pathogenic is the most responsive one. Treatment should only be given when eggs are demonstrated.

The chemotherapeutic agent recommended for all species of human schistosomes is **praziquantel**. In the schistosomes, this drug work on disrupting the integrity of the tegument and apparently exposes the inaccessible antigens which become as targets for host antibodies. **Niridazole** also effective in ***S. japonicum***.

Control

According to the World Health Organization (WHO), the key to eventual schistosomiasis control lies in a four-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; and education of the population.

Swimmer's Itch

An interesting phenomenon of schistosome biology is cercarial dermatitis, or swimmer's itch. While the condition is not life threatening, it can have a negative impact on the economy of regions where outbreaks occur, especially those popular with tourists. The condition is caused when cercariae of blood flukes that normally parasitize aquatic birds and mammals penetrate human skin, sensitizing points of entry 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 responses. Allergenic substances released from dead and dying cercariae produce a localized inflammatory reaction.