

## **Schistosomiasis (*Schistosoma mansoni*, *S. haematobium*, *S. japonicum* and others) (Pathogen – Intestinal Trematode)**

### **Organism:**

Schistosomes belong to the phylum Platyhelminthes, family Schistosomatidae, and are a group of digenetic, dioecious trematodes requiring definitive and intermediate hosts to complete their life cycles. Four species are important agents of human disease: *Schistosoma mansoni*, *S. japonicum*, *S. mekongi*, and *S. haematobium*. *S. intercalatum* is of less epidemiologic importance. *S. malayensis* is a member of the *S. japonicum* complex and is found in Peninsular Malaysia; however, the number of cases is small (1). Schistosomiasis affects between 200 million and 300 million people in 77 countries throughout the world and is a significant cause of disease in areas of endemic infections. In Egypt, approximately 20% of the population is infected; prevalence rates in some villages have been estimated to be 85%. The number of infected individuals in China is estimated to be 1.52 million. Although only about 10% of infected people have serious disease, this represents 20 million to 30 million individuals worldwide. Approximately half of the remaining 180 million to 270 million infected individuals have symptoms.

Schistosomes (i) have two sexes, (ii) live in the blood vessels, (iii) have nonoperculated eggs, and (iv) have no encysted metacercarial stage in the life cycle. The human is the definitive host for *S. mansoni*, *S. japonicum*, and *S. haematobium*; for *S. mekongi* and *S. malayensis* (both similar to *S. japonicum*); and for *S. intercalatum*. *S. mattheei*, which causes infections in sheep, cattle, and horses, also infects humans and can cause disease. Other schistosomes have been found in humans but do not tend to cause any pathology. Also, cercariae from birds and mammals can penetrate human skin but cannot complete the life cycle and tend to die without migrating or maturing; however, they do cause cercarial dermatitis.

### **Life Cycle:**

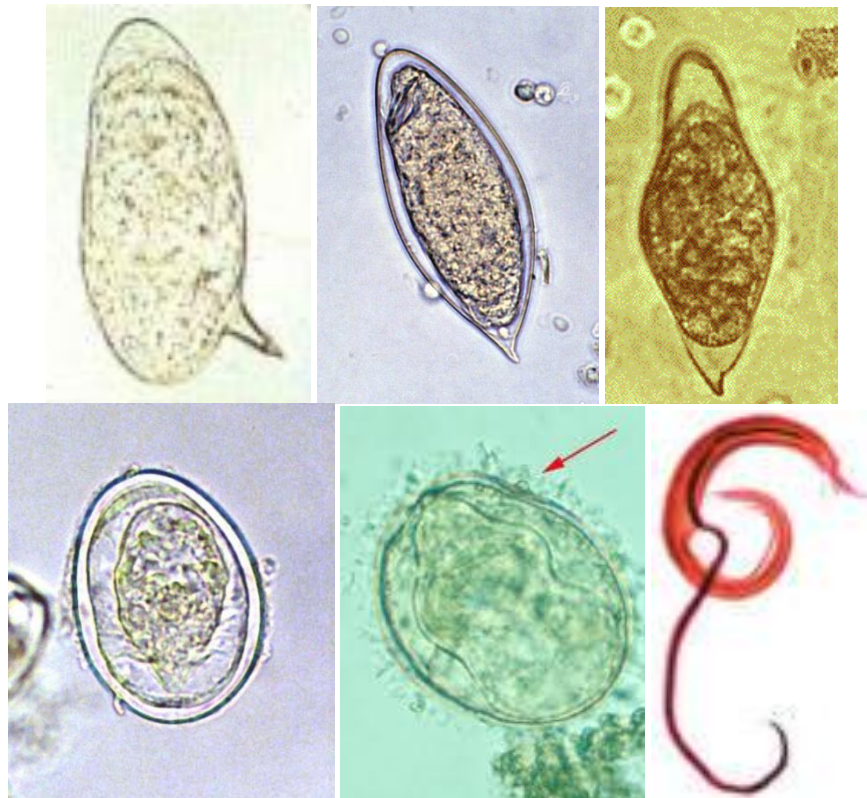
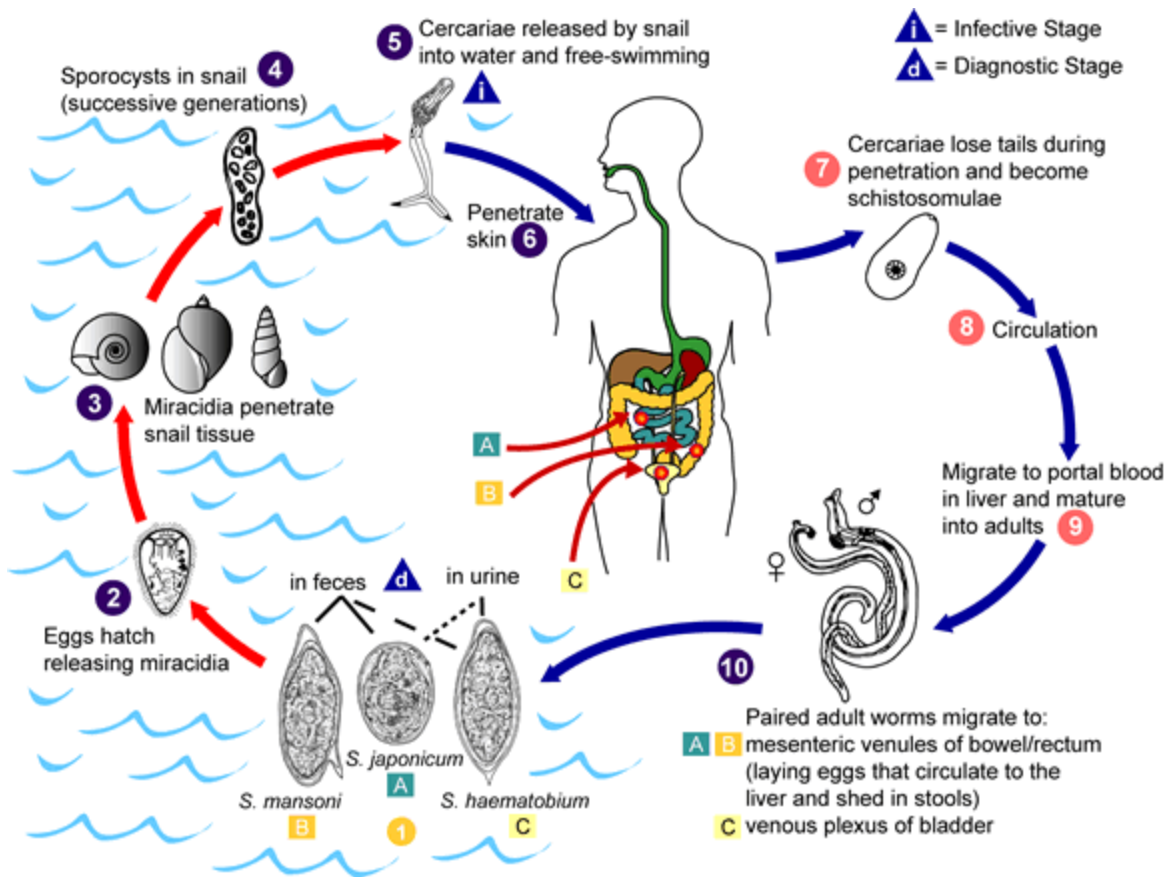
Humans become infected by penetration of cercariae through intact skin; penetration can occur within as little as 5 min after initial skin contact. Cercariae consist of a body with glands containing a proteolytic enzyme (elastase), which is used to penetrate skin, and a bifurcated tail that is lost when the cercariae penetrate the skin. Once the cercariae have successfully entered the host, the organism is termed a schistosomulum. After about 48 h, the schistosomulum migrates through the tissues and finally invades a blood vessel. On entry into the blood vessels, the schistosomulum is carried to the lungs and then the liver. Once within the liver sinusoids, the worms begin to mature into adults. The adults of *S. mansoni* are found in the inferior mesenteric veins. *S. japonicum* adults are found in the radicles of the superior mesenteric vein draining the small intestine. *S. haematobium* adults reside in the vesical and pelvic plexuses of the venous circulation of the bladder. The worms form pairs (male and female), with the female lying in the gynecophoral canal of the male. Sexual maturity of female schistosomes depends on the presence of mature male worms. The female worm has selective gene expression in the reproductive tract in the presence of male worms, whereas females separated from male worms lose this capability. Prior to egg production, migration and maturation generally require about 4 to 6 weeks.

### **Acquired:**

Humans become infected by penetration of cercariae through intact skin; penetration can occur within as little as 5 min after initial skin contact.

### **Epidemiology:**

The geographic distribution of the disease depends on the distribution of the intermediate snail hosts and the opportunity to infect humans and snails. Schistosomiasis is transmitted from infected people defecating or urinating in or near water where the appropriate snail host resides. Infections can persist indefinitely in humans. Most infected individuals have low worm burdens, but a few have very heavy infections. It is the latter group that probably makes the greatest contribution to the dissemination of schistosomiasis. The highest rates of infection have been found in children; the greatest cercarial exposure usually occurs in boys aged 5 to 10 years. Older children may have less recreational exposure but are more likely to be exposed while performing chores such as agricultural activities, washing dishes and clothes, and bathing younger siblings. Although adults also have less recreational exposure to water, they also have partial acquired immunity.



*Schistosoma* spp: Top Row Left, *S. mansoni* egg (note lateral spine); Middle, *S. haematobium* egg (note terminal spine); Right, *S. intercalatum* egg (note bulge in middle); Bottom Row Left, *S. japonicum* egg (note the very tiny lateral spine on lower/left side of egg); Middle, *S. mekongi* egg (note tiny lateral spine similar to that seen in *S. japonicum*); Right adult worms (note the slender female lying in the gonochophoral canal of the larger male worm).

### Clinical Features:

Disease syndromes associated with schistosomiasis are related to the stage of infection, previous host exposure, worm burden, and host response. Syndromes include cercarial dermatitis, acute schistosomiasis (Katayama syndrome), and related tissue changes resulting from egg deposition. It has been noted that schistosomiasis exerts disruptive influences on the nutritional reserves and growth of humans from middle childhood through adolescence.

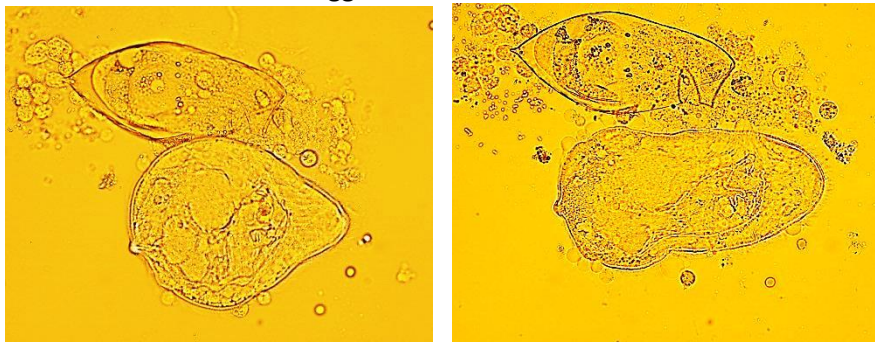
**Schistosome Cercarial Dermatitis.** Cercarial dermatitis follows skin penetration by cercariae, and the reaction may be due partly to previous host sensitization. Few clinical manifestations are associated with primary exposure, but both humoral and cellular immune responses are elicited on subsequent exposure. After cercarial skin penetration, petechial hemorrhages with edema and pruritus occur. The subsequent maculopapular rash, which may become vesicular, may last 36 h or more. Cercarial dermatitis is common with *S. mansoni* infections. Dermatitis is a constant feature of human infection with avian schistosomes, with cercarial death occurring in the subcutaneous tissues and immediate hypersensitivity reactions occurring at the invasion sites. This condition is known as swimmer's itch. Avian schistosomiasis can be found in the Great Lakes and Delaware Bay regions in the United States and in Lake Geneva. Any body of water, typical of bay regions with freshwater or saltwater, where infected snails are found can be linked to nonhuman cercarial dermatitis. Previous contact with cercariae will lead to a more immediate intense immune response. Schistosomiasis must be included in the list of differential diagnosis of skin lesions, especially in endemic areas, due to the potential sequelae in cases in which the diagnosis and treatment are delayed.

**Acute Disease: Katayama Syndrome.** Acute schistosomiasis (Katayama syndrome) is an early clinical manifestation of schistosomiasis that occurs several weeks post-infection with *Schistosoma* spp (trematode) worms and is associated with heavy primary infections and the initiation of egg production throughout areas of high transmission risk. Because of this time delay and its non-specific presentation, it is most likely to be misdiagnosed by travel medicine physicians and infectious disease specialists in non-endemic countries. The signs and symptoms resemble those of serum sickness. Characteristic symptoms include high fever, hepatosplenomegaly, lymphadenopathy, eosinophilia, and dysentery. Diffuse pulmonary infiltrates are seen radiologically, and almost all patients have eosinophilia and a history of water contact 14-84 days before presentation of symptoms.

**Chronic Schistosomiasis (All species).** After production of eggs by the adult worms, the eggs become trapped in the fine venules and are able to pass through the tissues, escaping into the intestine or the bladder. The eggs liberate a number of soluble antigens, evoking minute abscesses, which facilitate their passage into the lumen. The passage of eggs through the wall of the intestine or bladder leads to symptoms that correlate with the worm burden of the host, including fever, abdominal pain, liver tenderness, urticaria, and general malaise. In *S. mansoni* infection, blood and mucus are detected in the stools and the patient may have diarrhea or dysentery. In the case of schistosomiasis with *S. haematobium*, urogenital disease and bladder carcinoma are also serious sequelae of the infection. Patients with schistosomiasis caused by *S. japonicum* also tend to have hepatosplenic and/or CNS disease, as well as colorectal cancer and inflammatory bowel symptoms.

### Clinical Specimen:

**Stool and urine:** Since adult worms occasionally get into venules that are not their normal site, it is always recommended to examine both FRESH stool and UNPRESERVED urine if schistosomiasis is suspected. Occasionally, *S. mansoni* eggs are detected in the urine; adult worms may be found in vessels that are not their normal habitat, and this finding is known as "crossover." If eggs are found, they should be carefully examined for viability (visible cilia on the excretory cells in the miracidium larva within the egg shell).

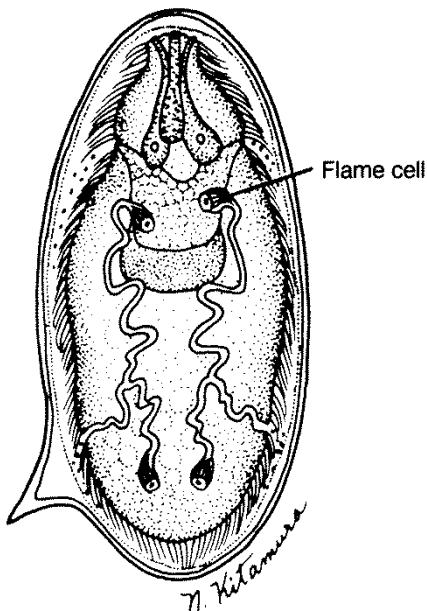


*Schistosoma haematobium* eggs: Left and Right, *S. haematobium* egg shells (upper) and hatched miracidia larvae (lower). This was from a urine with probably a low specific gravity (more like water) and the eggs hatched on their own. Note also how large the miracidia larvae are compared with the egg shell.

#### Laboratory Diagnosis:

**Stool:** The routine sedimentation concentration is recommended. The eggs are too heavy to be recovered using the zinc sulfate flotation method. In chronic infections in which the worm burden is light, hatching tests can be performed. Fresh stool specimens are diluted with nonchlorinated water in a sedimentation flask or a beaker. The sides of the flask or beaker are covered with aluminum foil to prevent light from passing through. A light source is used to project a perpendicular light beam through the water at the top. Miracidia that hatch from the live eggs will concentrate in the light and can be detected swimming around. This motility can easily be observed with a hand lens. Aliquots of the surface water can be transferred to a small petri dish and observed under a dissecting microscope for miracidia. Observation periods should be frequent because of the limited life span of the miracidia. Ideally, observations should be made every 30 min over a period of 4 h.

**Biopsy Specimens:** Rectal and bladder biopsy specimens have been particularly useful in detecting eggs in patients with light, chronic, or inactive infections. The biopsy tissue can be crushed between two glass slides; the tissue can also be stained without routine sectioning. This technique is more effective than histologic examination and allows assessment of the species and viability of the eggs prior to staining. The viability of the eggs can be determined by closely observing the miracidium for flame cell activity. Each miracidium contains two pairs of flame cells, and these are actively beating in live miracidia (see diagram below)



Note the location of the flame cells within the miracidium larva.

**Antibody and Antigen Detection:** A large number of **serologic tests** have been used in the diagnosis of schistosomiasis; however, many have not been particularly useful because of cross-reactions with other helminth infections, continuation of elevated titers long after successful treatment, and slow immunologic response of the host. The most commonly and widely used methods that have been validated in large-scale field trials include ELISA, the circumoval precipitin test, the indirect hemagglutination test, the indirect immunofluorescence test, and the skin reaction test. ELISA has also been used to detect **circulating schistosome antigens** in the serum and urine of infected patients and may be one of the preferred methods of diagnosis. The **role of PCR-based assays** in schistosomiasis diagnosis outside of research settings remains poorly defined, despite their significant potential in low transmission settings and in situations where high sensitivity and specificity are required.

**Laboratory Report:**

*Schistosoma mansoni* viable eggs recovered.

**Treatment:**

**Praziquantel.** Praziquantel, a pyrazinoquinolone, is the drug of choice for treating schistosome infections. The current recommendation is 40 mg/kg/day in two doses for 1 day. Praziquantel can also be taken orally in a single dose and is well tolerated by the host. Side effects, which are usually mild and transient, include abdominal discomfort, dizziness, drowsiness, headache, fever, and loose stools. These effects usually disappear within 48 h. In heavily infected individuals, the side effects, although transient, may be very severe. Split doses have been recommended for treating heavy infections, but this may be a concern for population-based therapy, where individuals may not present themselves for follow-up therapy. Data suggest that a single dose of praziquantel (40 mg/kg of body weight) may have a longer-lasting effect than previously thought, possibly more than 2.5 years. Praziquantel has little effect on immature stages of the parasite, and this affects the cure rates as the immature parasites develop to maturity and egg production. The mechanism of action may involve glutathione *S*-transferase, a detoxifying enzyme found in many helminths. Cure rates have been reported to be from 70 to 95%. Praziquantel damages the tegument of the worm, thereby exposing the antigens to parasite-specific antibodies. The use of immunoglobulins along with praziquantel has been proposed to increase the efficacy of treatment.

**Garcia, L.S.** 2015. *Diagnostic Medical Parasitology*, 6<sup>th</sup> ed., ASM Press, Washington, D.C.

**Control:**

Water resource development projects involving the construction of artificial bodies of water and canals for irrigation have contributed to the extension of the disease. The migration of infected persons into virgin areas where suitable snail hosts reside also contributes to the spread of schistosomiasis. These two important factors make control programs difficult.