285 Blood Trematodes: Schistosomiasis

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Schistosomiasis (i.e., bilharzia or snail fever) is a parasitic infection caused by trematodes that reside in the circulatory system. More than 230 million people worldwide suffer from schistosomiasis, which causes a range of clinical disease from overt clinical manifestations to subtle hindrance of day-to-day activities. Infected children can have impaired growth and development. Infection occurs from exposure to freshwater into which snails, the intermediate host of the parasite, have shed cercariae that can penetrate skin.

The three main species of schistosomes that parasitize humans are *Schistosoma mansoni, S. japonicum,* and *S. haematobium.* Gastrointestinal and hepatic disease is caused by infection with *S. mansoni* or *S. japonicum*, and urogenital tract disease results from *S. haematobium* infection. Other schistosome species less commonly infect humans, including *S. intercalatum*, which is found in Cameroon and the Democratic Republic of Congo, and *S. mekongi,* which is found primarily in the Mekong River basin. Both species cause gastrointestinal disease.[1]

BIOLOGY

The complicated life cycle alternates between parasitic forms in the snail intermediate host and human definitive host and the free-living forms in water, the cercariae and the miracidia (Fig. 285.1). The cercariae are released from infected snails and penetrate intact human skin, where they transform into schistosomula that travel through the venous system to the lungs. From the lungs, schistosomula enter the arterial system; reach the liver, where they attain sexual maturity in 4 to 6 weeks; and then as adult worms descend against the blood flow of the portal venous system to the venules of the intestine (*S. mansoni* or *S. japonicum*) or bladder (*S. haematobium*).

Unlike other trematodes, schistosomes are not hermaphroditic. Males and females mate, and the females begin to deposit eggs. Eggs must pass through tissue to reach the lumen of the intestine or bladder and then on to the environment in feces or urine. About one half of the eggs are retained in intestinal or vesicular tissues, where they cause granulomatous inflammation and fibrosis. In the case of the intestinal *Schistosoma* species, eggs also can be swept by the portal blood system back to the liver, where they can cause similar pathologic changes.

Eggs that exit the body and reach freshwater hatch and release miracidia that infect certain genera of snails. *S. mansoni* infects snails of the *Biomphalaria* species, *S. haematobium* infects *Bulinus* species, and *S. japonicum* infects *Oncomelania* snails. In the receptive snail, a single miracidium forms sporocysts from which thousands of cercariae are released into the water over the lifetime of the infected snail, typically a period of 6 to 12 months.[1]

EPIDEMIOLOGY

Schistosomiasis is transmitted in 76 countries in tropical and subtropical areas, but 85% of infected people reside in Africa, where *S. mansoni* and *S. haematobium* occur and often are coendemic.[1–3] *S. mansoni* was

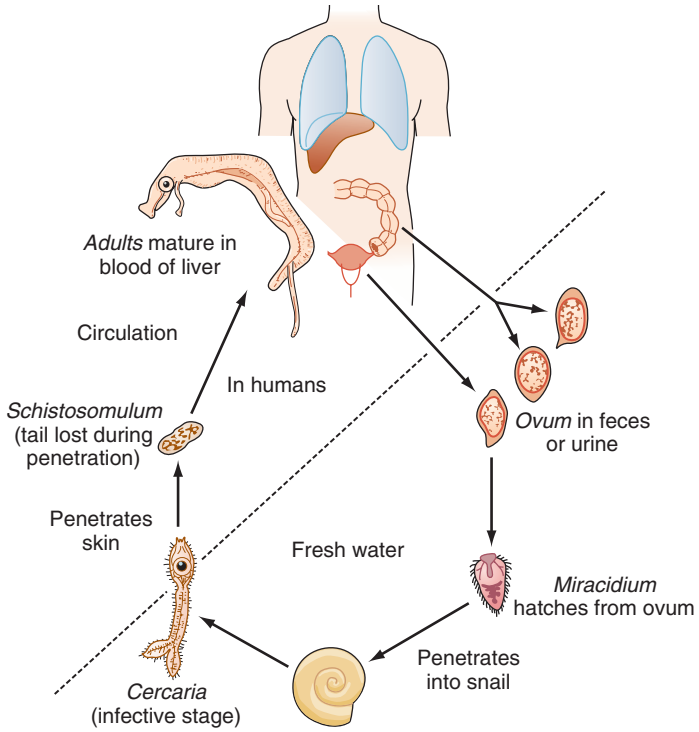

FIGURE 285.1 Life cycle of *Schistosoma* and occurrence of schistosomiasis.

transplanted, likely with the slave trade, to South America (especially Brazil, Venezuela, and Suriname) and several islands in the Caribbean (Antigua, Dominican Republic, Guadeloupe, Martinique, Montserrat, Puerto Rico, and Saint Lucia).[3] *S. haematobium* also occurs in a few countries of the Middle East, and a recent focus of transmission has been reported in Corsica, France.[4] *S. japonicum* is endemic in China, the Philippines, and Indonesia.[1–3]

People most heavily infected are responsible for most environmental contamination with parasite eggs. Cross-sectional studies of *S. haematobium* and *S. mansoni* show that the highest prevalence of infection occurs among school-aged children 10 to 14 years of age and that rates decrease in adulthood. Infants have been infected from being bathed in irrigation canals or in lake or river water.[5,6] Males are infected more often than females, and certain daily activities and occupations (e.g., fishing, doing laundry, washing cars) are important risk factors. Wide variations in community prevalence patterns and disease focality point to complex interactions with the environment and practices of human waste disposal, water contact, and acquired immunity. Hydraulic dams and irrigation projects often increase snail habitats and the risk of transmission.

Expatriates, missionaries, diplomats, Peace Corps volunteers, and other long-term residents of endemic areas are at particular risk. However, tourists also can become infected, particularly those who take part in adventure or ecotourism.[7]

PATHOGENESIS

The host immune response to schistosome egg antigens results in the major clinical and pathologic manifestations of schistosomiasis.[1] Cercarial penetration of skin can give rise to a local hypersensitivity reaction and papular dermatitis, usually within 72 hours of exposure.[7] This reaction typically is milder than the allergic rash associated with skin penetration of animal schistosome cercariae. Adult worm maturation and sudden exposure to antigens with the onset of egg laying by young female worms can result in an acute illness resembling serum sickness, which is more often reported in travelers than lifelong residents of endemic regions.[1,7,8]

Chronic organ damage and dysfunction are related to the number of eggs in tissues, which is related to the number of egg-laying female worms. People with a heavy worm load and the heaviest tissue egg load are at greatest risk of disease. The worm burden in humans grows only through repeated exposure to water containing cercariae. Some evidence suggests that humans acquire partial immunity to reinfection, but the mechanism of a protective immune response has not been defined.[1]

The eggs secrete antigenic materials that induce a host granulomatous response by macrophages, lymphocytes, giant cells, and eosinophils. Over time, granulomas decrease in size and are replaced by fibrosis. Fibrosis along the portal vein triads of the liver (i.e., periportal fibrosis or pipestem fibrosis) in intestinal schistosomiasis can be complicated by portal hypertension. Liver function remains intact unless there is concurrent insult, such as alcoholic or viral hepatitis. As portal hypertension advances and collateral blood flow channels increase, eggs can be shunted to the lungs, which can result in granulomatous pulmonary arteritis leading to pulmonary hypertension.

In urogenital schistosomiasis (caused by *S. haematobium*), chronic fibrosis of the urinary tract can lead to obstructive uropathy and hydronephrosis. Urogenital schistosomiasis can be complicated by pyelonephritis, calculi, and squamous cell carcinoma. Female genital schistosomiasis is characterized by inflammatory lesions of the genital tract, especially cervix, fallopian tubes, and vagina, including characteristic sandy patches associated with inflammation of the vaginal mucosa.[9]

Organs less commonly involved include skin, lungs, seminal vesicles, and central nervous system. *S haematobium* is associated with hematospermia (associated with seminal vesicle involvement) in males. Genital schistosomiasis in men and women can enhance transmission of human immunodeficiency virus (HIV) infection. *S. haematobium* also is associated with human papillomavirus (HPV) infection and infertility.[9]

Granulomatous reaction around ectopic eggs in the brain most often results from *S. japonicum* infection. Ectopic eggs in the spinal cord can cause transverse myelitis.[1,10]

CLINICAL FEATURES

Acute Schistosomiasis

An acute febrile illness resembling serum sickness can occur 4 to 7 weeks after the initial infection, concurrent with maturation of female worms and the first egg release. This syndrome has been named Katayama fever, after a village in Japan where the entity was first described in association with *S. japonicum* infections. Common signs and symptoms are sudden-onset fever, cough, abdominal pain, headache, lymphadenopathy, and mild hepatosplenomegaly. In contrast to chronic schistosomiasis, peripheral eosinophilia is prominent in acute schistosomiasis.[1,8]

Intestinal and Hepatosplenic Disease

Patients with intestinal schistosomiasis (*S. mansoni, S. japonicum, S. intercalatum,* and *S. mekongi* infections) can be asymptomatic, or they can have crampy abdominal pain, diarrhea, bloody stools, or colonic polyposis. Physical examination commonly reveals an enlarged, nontender liver and an enlarged spleen.

End-stage disease consists of portal hypertension, ascites, and portosystemic varices with an absence of jaundice. Esophageal varices can result in severe bleeding and death.

Urogenital Tract Disease

S. haematobium infections can cause microscopic or gross (often terminal) hematuria. In some endemic areas where transmission is intense, hematuria is so common among boys that it is considered a normal passage to manhood, locally described as male menstruation.[11] Other complaints can include dysuria and urinary frequency. Patients with obstructive uropathy or chronic or recurrent pyelonephritis can have hypertension or end-stage renal disease. Adults can have a suprapubic mass or urinary obstruction from squamous cell carcinoma of the bladder.

Growth and Development

Children, even those with modest and low intensity of infection, may have depressed growth and cognitive development.[11–14] Schistosomiasis

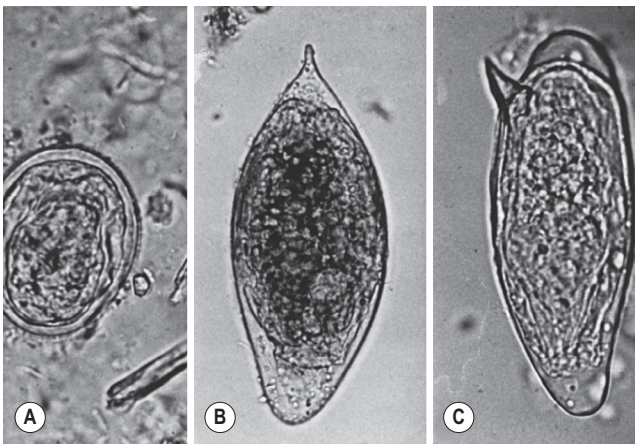

FIGURE 285.2 Ova of *Schistosoma japonicum* (A), *S. haematobium* (B), and *S. mansoni* (C) in stool or urine.

causes anemia. Physical findings in heavily infected children can include pallor and exercise intolerance.[14]

DIAGNOSIS

The history should focus on whether the person has been in an area endemic for schistosomiasis and has had contact with open and likely contaminated freshwater ponds, lakes, or streams. Ocean beaches and chlorinated swimming pools are not sources of infection. Depending on the stage of illness, the physical examination can show rash, fever, and hepatosplenomegaly. Eosinophilia characterizes acute schistosomiasis. People infected with *S. haematobium* can have hematuria.

A diagnosis is made by identifying distinctive eggs by microscopy of stool or urine specimens (Fig. 285.2). *S. mansoni* eggs are oval (measuring 60 × 150 µm) and have a distinctive lateral spine. *S. haematobium* and *S. intercalatum* eggs are a similar size and shape, but they have a large terminal spine. *S. japonicum* and *S. mekongi* eggs are smaller (75 µm) and round with small, inconspicuous spines.[3] The miracidia can be seen in living mature eggs.

A stool concentration technique (1-g fecal sample) or a Kato-Katz preparation (20- or 50-mg fecal sample) optimizes microscopic diagnosis. The sediment of at least 10 mL of urine should be examined for *S. haematobium* eggs; the optimal sample to examine is a midday, terminal urine specimen. Examining multiple samples collected on separate days increases the sensitivity of diagnostic testing based on microscopy. Some infections have been diagnosed by identification of viable ova in histologic examination of rectal biopsy samples.

Microscopic examination can be negative for patients with acute schistosomiasis or light-intensity infections, and serologic testing is more useful for these people. Antibody detection can be used to screen ecotourists, missionaries, and Peace Corps volunteers who have had freshwater exposure in endemic areas. Several specialty laboratories offer serologic testing for diagnosis of schistosomiasis; for patients with a complicated exposure history, species-specific antibody assays are available through the Centers for Disease Control and Prevention (phone: 404-718-4745).[3] Travelers with positive antibody results are treated presumptively with praziquantel, but serology cannot be used to monitor the success of treatment.[15] Interpretation of antibody test results is more difficult for patients who originate from endemic areas because parasite-specific antibody persists for years despite successful treatment.[15] A new test for the detection of antigen in urine appears to be useful for screening for *S. mansoni* infection in the setting of control programs, but its utility for patient diagnosis is not defined.[16]

Ultrasonography is useful for staging chronic schistosomiasis.[1,17] In cases of intestinal schistosomiasis, ultrasound can be used to describe characteristic hepatic findings and the degree of portal hypertension and splenomegaly. In cases of urinary schistosomiasis, ultrasound can show bladder wall thickening, dilation of the ureter and renal pelvis, and bladder calculi. Abdominal imaging can show bladder calcification in *S. haematobium* infections.

MANAGEMENT

Praziquantel is the drug of choice for therapy[1] (see Chapter 296, Appendix 296.1). For *S. mansoni* and *S. haematobium* infection, 40 mg/kg of praziquantel in 2 divided doses taken orally for 1 day is recommended. For *S. japonicum* infection, 60 mg/kg in 3 divided doses for 1 day is recommended. Side effects of praziquantel typically are mild, abdominal pain is most common in treatment of intestinal schistosomiasis, and severity correlates with the burden of infection.

Praziquantel results in parasitologic cure in approximately 80% of cases, but in people who are not cured, the egg burden is reduced by 95% to 99%. The efficacy of praziquantel treatment depends on a robust host immune response to the adult worms.[1] Oxamniquine is an alternative drug for *S. mansoni* that is used primarily in South America. Oxamniquine is not available in the United States.

Praziquantel is the primary drug periodically used in school-based or community-based mass treatment programs to reduce the egg burdens of infected people.[2] Treatment of children and young adults promptly results in reversal of much of the disease, cessation of hematuria in urinary schistosomiasis, and regression of hepatosplenomegaly in intestinal disease. Antiparasitic treatment does not reverse chronic fibrotic organ damage, and the prognosis is guarded for people with portal hypertension, esophageal varices, and hydronephrosis.

Prophylaxis with praziquantel shortly after water exposure is not effective because developing schistosomula are relatively resistant. Artemisinins (antimalarial drugs) appear to be effective against developing stages and may be useful when the timing of exposure is known.[1,18]

SPECIAL CONSIDERATIONS

Central nervous system schistosomiasis results from ectopic egg deposition after aberrant migration of adult worms to the venules draining the brain or spinal cord. The ensuing granulomatous inflammation gives rise to serious manifestations that include seizures, headache, and signs of transverse myelitis such as paralysis, lack of sensation, and bladder incontinence. Previously unexposed people (i.e., immunologically naïve) may be at greater risk for these presentations. Use of corticosteroids or extended courses of praziquantel, or both, in these patients is controversial.[8]

Cercarial dermatitis (i.e., swimmer's itch) is a pruritic macular, papular, or vesicular rash that occurs as a consequence of cercariae penetration of skin. Cercarial dermatitis can occur from exposure to animal (usually avian) schistosomes, often in countries nonendemic for human schistosomiasis, and after exposure to seawater and freshwater. The cercariae die in the skin, and the rash responds to symptomatic treatment and topical corticosteroids.

PREVENTION

People planning travel to regions where schistosomiasis may be endemic can consult the Centers for Disease Control and Prevention (CDC) travel health website for further information on endemic countries.[19] Travelers should avoid swimming, bathing, or wading in open freshwater in those areas.

Strategies for controlling schistosomiasis include mass chemotherapy, health education, behavioral modification, improved sewage and sanitation, and control of snails through environmental engineering or the use of molluscicides. Large-scale control programs using one or more of these strategies has had various degrees of success in several countries. Schistosomiasis was eliminated completely from Japan by environmental engineering and improved sanitation.[2] Despite prolonged use of mass praziquantel treatment in several country settings, there has been no broadly documented case of emergence of drug resistance.[1,2] Active research for a vaccine is ongoing.[1]

All references are available online at www.expertconsult.com.

Key Points: Characteristic Features of Schistosomiasis

MICROBIOLOGY

- Caused by trematodes that reside in the venules of the intestinal tract (*Schistosoma mansoni* and *S. japonicum*) or surrounding the bladder (*S. haematobium*). Female worms lay eggs that exit the body in feces or urine.
- If deposited in freshwater, miracidia emerge from eggs and infect specific snails. Cercariae later released from infected snails penetrate intact human skin and establish the infection, completing the life cycle.
- Eggs retained in tissue cause granulomatous inflammation that damages host tissues; patients with a heavy worm load are at greatest risk of disease.

EPIDEMIOLOGY

- More than 230 million people in 76 countries in tropical and subtropical areas are infected, but 85% of infected people reside in Africa, where *S. mansoni* and *S. haematobium* are the most common species and often are co-endemic.
- Schistosomiasis occurs in areas with poor sanitation where infected people deposit feces or urine containing eggs directly into freshwater containing the appropriate snails. Other people are later infected or reinfected when these same water bodies are used for swimming, bathing, washing of clothes and utensils, or agricultural purposes.

CLINICAL FEATURES

- An acute febrile illness resembling serum sickness can occur 4 to 7 weeks after the initial infection, concurrent with maturation of female worms and the first egg release (i.e., Katayama fever).
- *S. mansoni* and *S. japonicum* infections can cause crampy abdominal pain and an enlarged liver or spleen. End-stage disease can include portal hypertension, ascites, and portosystemic varices.
- *S. haematobium* infections can cause microscopic or gross hematuria, dysuria, and urinary frequency, and characteristic sandy patches in vaginal mucosa or the cervix. End-stage disease can include genital lesions, obstructive uropathy, and squamous cell carcinoma of the bladder.
- Even with light worm burdens, children may have depressed growth and learning ability and anemia.
- Dermatitis can occur within 72 hours of exposure to infected water as cercariae penetrate skin. Cercarial dermatitis (i.e., swimmer's itch) also is caused by animal (usually avian) schistosomes, occurring in countries nonendemic for human schistosomiasis and after exposure to seawater and freshwater.

DIAGNOSIS

- Detection of eggs in stool or urine
- Serologic testing

TREATMENT

- Praziquantel

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