Schistosomiasis

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KEYWORDS

• Schistosomiasis • Bilharzia • *Schistosoma mansoni* • *Schistosoma haematobium*
• *Schistosoma japonicum* • Praziquantel • Neglected tropical diseases • Helminths

KEY POINTS

- Schistosomiasis is a tropical parasitic disease, caused by blood-dwelling, macroscopic worms of the genus *Schistosoma*, a trematode characterized by separate sexes.
- *Schistosoma mansoni* and *S japonicum* live in the mesenteric venules, *S haematobium* in the perivesical venules; the male worms holds the female in a permanent embrace.
- The worms excrete eggs that are excreted with the feces of urine, and release larvae (miracidiae) that can infect the intermediate hosts i.e. specific aquatic of amphibious snail species.
- Infection occurs through the skin during contact with surface water by secondary larvae (cercariae) that are released by the snails.
- *S mansoni* occurs in Africa and South America, S haematobium in Africa, *S japonicum* in South and East Asia; in endemic areas, prevalences can be very high especially among children.
- Eggs that are trapped in the tissues provoke immunogenic inflammatory, granulomatous and fibrotic reactions that cause intestinal, hepatosplenic or urinary disease which develops over many years.
- Most infected people show no, limited or non-specific symptoms. Severe disease develops in people with heavy, long-standing infections and probably unbalanced immune responses.
- Intestinal disease includes bloody or intermittent diarrhea, abdominal pain, colics, dysenteric syndromes, fatigue and anorexia.
- Hepatosplenic disease results in inflammatory and later fibrotic hepatomegaly and/or splenomegaly, portal hypertension, esophageal bleeding, ascites and cachexis.
- Urinary schistosomiasis presents with hematuria, dysuria, secondary infections, ureteral fibrosis and hydronephrosis.
- Schistosomiasis can be complicated by ectopic lesions especially in the central nervous system, the pulmonary system or in the genital area.
- Swimmers' itch can occur shortly after cercarial infection.
- Acute schistosomiasis is an allergic reaction occurring in the weeks after primary infection and presents as a flulike syndrome; it is a regular finding in travel clinics.
- The diagnosis of schistosomiasis relies on microscopic examination of stools or urine, serologic tests, PCR and imaging.
- Praziquantel is the drug of choice, active against all species in a single or oral dose. In some cases adjunct therapies may be useful.
- Current control strategies consist mainly of preventive therapy in communities or groups at risk. There is as yet no vaccine against schistosomiasis.
- On the long-term, only sanitation, water supply, education and socio-economic development can reduce and eliminate the transmission of schistosomiasis.

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Infect Dis Clin N Am 26 (2012) 383–397
doi:10.1016/j.idc.2012.03.004 **id.theclinics.com**
0891-5520/12/$ – see front matter

THE PARASITES

Adult schistosomes are macroscopically visible worms, with a white-grayish, cylindrical body approximately 1 to 1.5 cm in length.[1–3] Taxonomically, they belong to the class of Trematoda (flukes) and the phylum of Platyhelminthes (flatworms). The worms live in the bloodstream of the human host, where they can survive for up to 30 years with an average of 3 to 5 years. This is a remarkable evolutionary achievement, which requires intricate evasion mechanisms to all forms of innate and acquired immunity.

Schistosomes are also special by having separate genders, with the male holding the female in a continuous, monogamous embrace. The worms further feature two suckers, a complex tegument, a blind digestive tract, and reproductive organs (**Fig. 1**). They feed on blood cells and globulines, which they digest in a blind intestinal tract and the debris of which are regurgitated in the human bloodstream. The anaerobic metabolism serves mainly for the movements of the male schistosomes, and the egg production of the females.

TRANSMISSION

The transmission cycle of schistosomes is shown in **Fig. 2**. The female worms produce hundreds (*Schistosoma mansoni* and *S haematobium*) to thousands (*S japonicum*) of eggs per day, which are 100 to 180 μm in size and have a typical shape and spine that varies per species. Each egg contains one ciliated larva, the miracidium, which secretes enzymes that help the eggs to migrate from the blood vessels through the tissues into the lumen of the bladder (*S haematobium*) or the intestine (*S mansoni* and *S japonicum*). Most of the eggs are carried away with the bloodstream or trapped in tissues during this journey, but up to one-third are eventually excreted with urine or

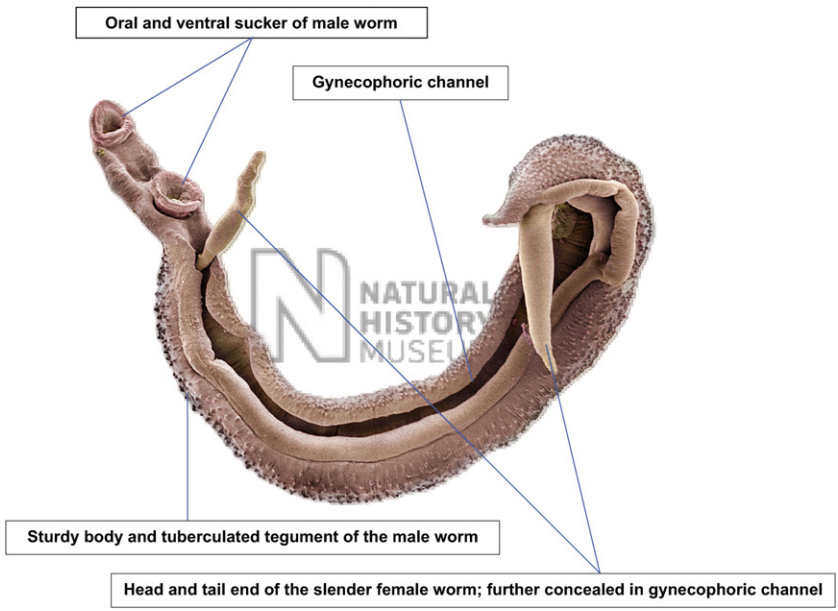

Fig. 1. The morphology of adult schistosomes. (Reproduced with permission of the Natural History Museum, London.)

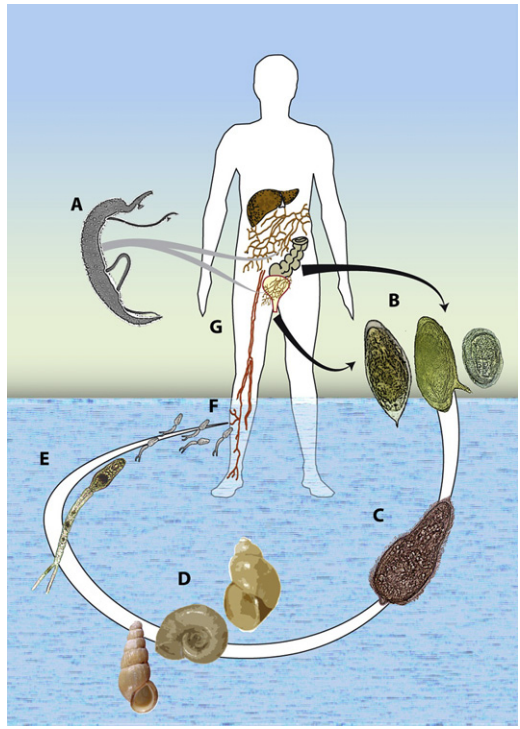

Fig. 2. Transmission cycle of schistosomes. (A) Adult schistosomes in small blood vessels around the intestines or bladder. (B) Schistosome eggs leave the body with excreta. Left-to-right: *S haematobium*, *S mansoni*, and *S japonicum*. (C) Miracidium hatches and swims freely in water. (D) Snail intermediate hosts are infected by miracidium. Left-to-right: *Oncomelania*, *Biomphalaria*, and *Biomphalaria*. (E) Cercariae hatch from snails 4 to 6 weeks later. (F) Cercariae infect humans through the skin. (G) Cercariae develop into schistosomula, which migrate with the bloodstream to the portal vein and mature into adult schistosomes, which mate and migrate to the destination. (*From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission.)

feces. If an egg comes in contact with water, the miracidium escapes and uses its cilia to swim around in search for a suitable intermediate host.

The miracidium penetrates the snail and develops over a period of 4 to 6 weeks into multicellular sporocysts, which split into a multitude of secondary larvae. These "cercaria" consist of a large head with embryonic features of the adult schistosomes and a bifurcated tail. They leave the snail by the hundreds, under the stimulation of light. Cercarial shedding therefore occurs mainly between 10 AM and 4 PM, when the sun is high and human water contact most frequent.

The cercariae whirl around in the water for up to 72 hours. When they come in touch with human skin, they penetrate the dermis, shed their tail and migrate as "schistosomula" with the bloodstream to the heart, through the lungs, and into the liver and the portal veins. Here they mature in 4 to 6 weeks, mate, and migrate upstream to their final destination in the mesenteric veins, where the cycle starts again.

Each schistosome species can be transmitted only by a few specific snail species, belonging to the genus *Biomphalaria* (*S mansoni*), *Bulinus* (*S haematobium*), or *Oncomelania* (*S japonicum*).[4,5] *Biomphalaria* and *Bulinus* are purely aquatic snails; *Oncomelania* are amphibian and spend part of their lives in the mud where they can

survive low temperatures.[6] Therefore, *S japonicum* is found also in areas with cold winters but long, hot summers. *S japonicum* is furthermore a truly zoonotic infection, with a huge animal reservoir in cattle, pigs, dogs, rodents, and some 20 other mammals. *S mansoni* is found also in primates and rodents, but humans are the main reservoir. *S haematobium* can be bred in some rodents, but has no known animal host in nature.

DISTRIBUTION AND EPIDEMIOLOGY

Humans are host to six *Schistosoma* species, which are morphologically very similar. Their distribution is primarily determined by the presence of the intermediate hosts. The different location of the species in the human body leads not only to a different excretion path, but also to different pathology. Three species are of global or regional importance (**Fig. 3**): *S japonicum* (China and Southeast Asia) and *S mansoni* (Africa, Arabia, and South America) dwell in peri-intestinal venula, and cause intestinal and hepatosplenic schistosomiasis. *S haematobium* (Africa and Arabia) live in the perivesical plexus and causes urinary schistosomiasis of the bladder, ureters, and kidneys. *S intercalatum* (West and Central Africa), *S mekongi* (Mekong Delta), and *S malayensis* (Malaysia) are limited to a few local foci and of minor importance.[1–4,7,8] The World Health Organization estimates the number of infected people worldwide for decades at 200 million, and the number of deaths caused by schistosomiasis at 41,000 annually.[9] More than 90% of current cases occur in sub-Saharan Africa. Indeed, the number of cases in large historical foci as Brazil, Egypt, and China has been reduced to a few million. It is possible that global figures need to be reviewed downward. Transmission usually occurs in streams, ponds, lakes, and irrigation and drainage canals. Hydraulic development, human migration, and sanitary neglect have contributed greatly to the spread of schistosomiasis in rural areas, but increasingly also in urban slums.[1–3,10,11] Depending on local determinants, the epidemiology can vary strongly from one locality to another. Typically, prevalences and intensities of infection increase in young children to a peak around age 8 to 15 years, and then decrease to

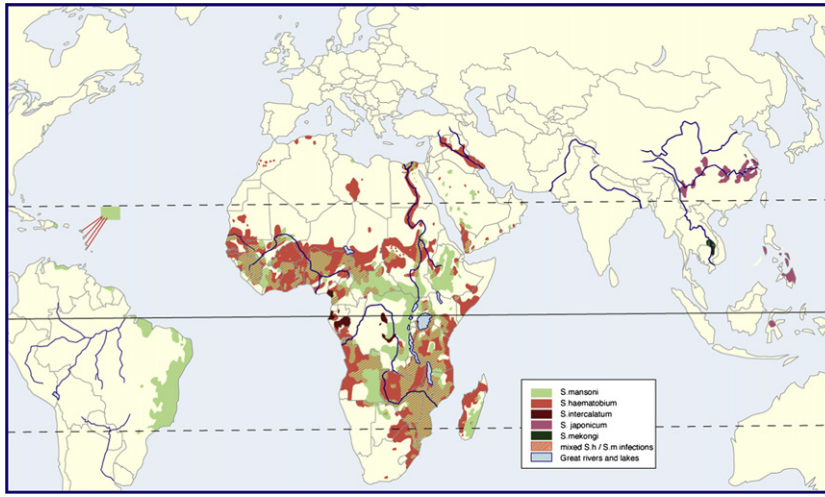

Fig. 3. World distribution map of schistosomiasis. (*From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission.)

a plateau in adults.[1,3] Also within age groups, the distribution of parasites is strongly skewed so that a small part of the community is responsible for the largest part of egg output and most at risk for severe pathology. This predilection is thought to be determined by water contact patterns and immunogenetic factors.

ACUTE PATHOLOGY

Minutes after the cercarial infection, local urticaria may appear that usually last for a few hours but sometimes persist for days as more papulous lesions (**Fig. 4**). This "swimmers itch" is mainly seen after primary infections, especially in tourists and migrants. A similar syndrome can also be caused by animal trematodes in temperate climate zones, including North America and Europe.

One to four weeks after infection, the migrating and maturing schistosomula can cause a systemic hypersensitivity reaction. This acute form of schistosomiasis, also known as Katayama fever (after the marshy district in Japan where it was first described), starts as a flulike syndrome with protracted fever, fatigue, myalgia, headache, and dry cough.[1–3,12–14] Stool or urine examinations are still negative, but eosinophilia, positive serologic tests, and a history of tropical water contact usually indicate the diagnosis. The liver or spleen may be swollen and tender, and thorax radiography may reveal patchy infiltrates. Later, the migration and positioning of the mature worms to the mesenteric veins can lead to more pronounced abdominal symptoms, including intestinal cramps and diarrhea. Acute schistosomiasis can also be complicated by ectopic pathologies (discussed later).

Cercarial dermatitis and acute schistosomiasis caused by *S mansoni* or *S haematobium* are rarely seen in local people, probably because they have been desensitized at an early age but probably also because of underdiagnosis. Katayama fever is a frequent finding, however, among people being infected for the first time and thus also in western travel clinics. Most cases are tourists and travelers who have toured in sub-Saharan Africa. Typical sources of infection include the lakes Malawi, Victoria, and Volta; the Zambesi and Niger deltas; and some lake resorts in South Africa.[3,10] Many cases present in clusters of family members or tour groups.

Katayama fever caused by *S japonicum* is also common among local people, including adults who have been exposed for years, some even with a previous history of acute schistosomiasis.[6] The syndrome can be more severe and protracted than in

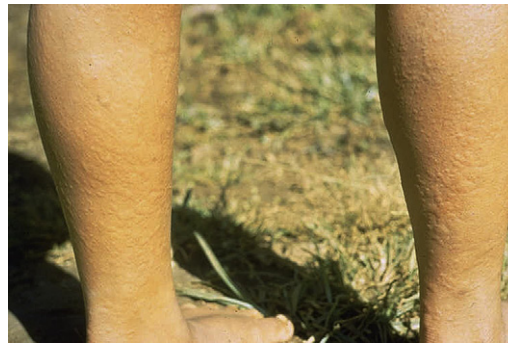

Fig. 4. Swimmers' itch. (*From* Topics in International Health Series: Schistosomiasis. Multimedia CD-ROM. New York: CABI Publishing, 1998. Copyright © The Trustee of The Wellcome Trust; with permission.)

other schistosome infections, and include also serious intestinal disease, outspoken splenomegaly and cachexia, or progress directly to advanced fibrotic pathology.

CHRONIC PATHOLOGY

Particularly in local populations, the main morbidity is caused by years of chronic infection in which not the worms but the eggs are the culprit.[1–3,15] As described, during their migration most eggs are trapped in tissues surrounding the intestinal or urinary systems, or in the liver and spleen after being evacuated by the bloodstream. The enzymes excreted to assist their penetration cause subsequently inflammatory and granulomatous immune reactions, characterized by eosinophilic infiltrations around the egg (**Fig. 5**). These reactions protect the human host against the foreign bodies and molecules, but if numerous and uncontrolled lead themselves to severe pathology. The nature of the symptoms is determined by the location of the worms and their eggs, and the severity by the intensity of infection and individual immune responses.

Urinary Schistosomiasis

Most *S haematobium* eggs are trapped in the vesical and ureteral walls, often in clusters (**Fig. 6**). Inflammatory and granulomatous reactions lead to ulcerations, micropolyps, and macropolyps and eventually fibrosis and calcification. The most typical symptom is hematuria, which in endemic areas is very common among children.

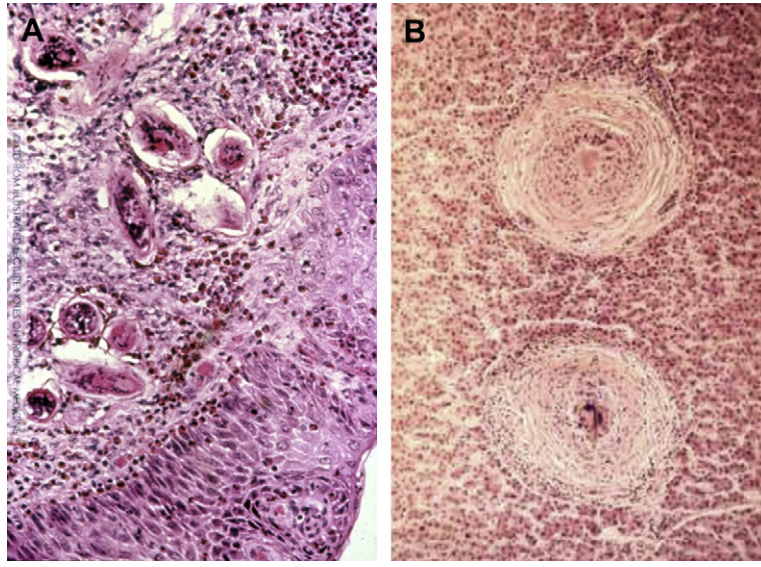

Fig. 5. Histopathology in schistosomiasis. (*A*) *S haematobium* eggs in a bladder biopsy, surrounded by granulomatous eosinophilic inflammation. (*B*) Eosinophilic granuloma around decaying egg of *S mansoni* in a portal sinusoid (hematoxylin-eosin stain, original magnification x100). ([*A*] *Courtesy of* Erwin Vandenenden, Institute of Tropical Medicine, Antwerpen, Belgium; and [*B*] *From* Topics in International Health Series: Schistosomiasis. Multimedia CD-ROM. New York: CABI Publishing, 1998. Copyright © The Trustee of The Wellcome Trust; with permission.)

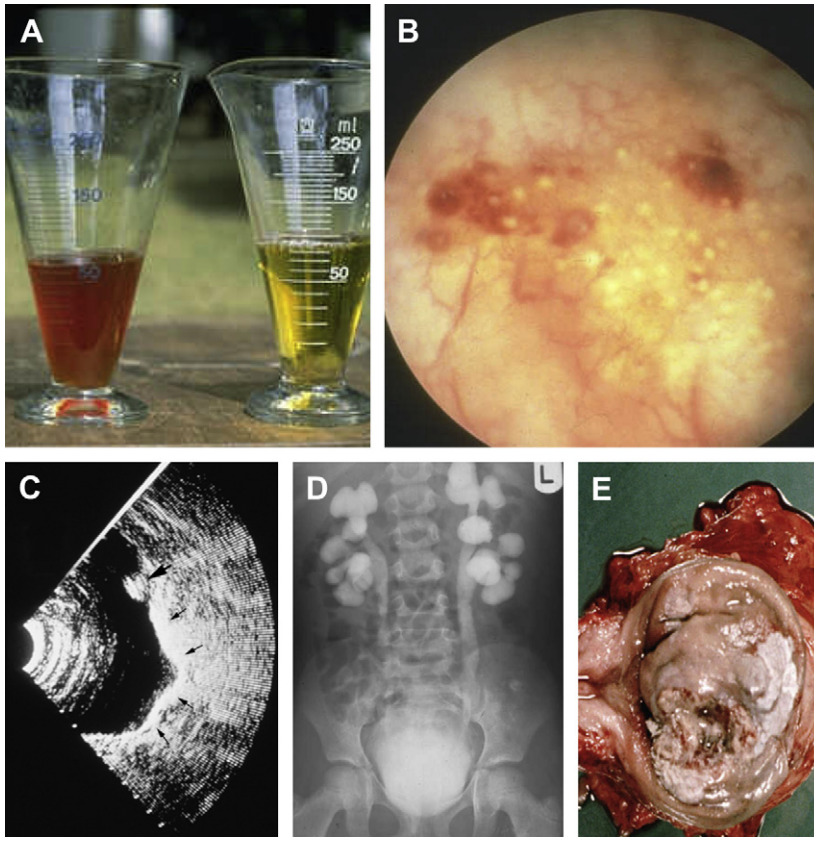

Fig. 6. Urinary schistosomiasis. (*A*) Hematuria. (*B*) Cystoscopy showing "sandy patches" lesions in bladder wall. (*C*) Irregular bladder wall (*small arrows*) and polyp (*large arrow*) on ultrasound. (*D*) Bilateral hydroureter and hydronephrosis on pyelography. (*E*) Squamous cell bladder carcinoma associated with chronic urinary schistosomiasis. ([*A*] *From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission; and [*B–E*] *From* Topics in International Health Series: Schistosomiasis. Multimedia CD-ROM. New York: CABI Publishing, 1998. Copyright © The Trustee of The Wellcome Trust; with permission.)

In light forms the blood may only be microscopically detectable, or just visible in terminal urine. In more severe cases the entire urine can be dark-colored, and micturition painful and frequent.[1–3] Secondary bacterial infections and bladder stones may develop and exacerbate the symptoms. Although difficult to demonstrate or discern from the consequences of other poverty-related infections and conditions, schistosomiasis is believed to affect also the general well-being and productivity, translating into reduced work and school performance.[16]

The hematuria usually disappears after the age of 12 to 15 years, but the lesions may evolve to fibrosis or calcification of the bladder and lower ureters, unilateral or bilateral hydroureters, and hydronephrosis. Radiology or sonography may reveal frequent and impressive extensions in adults, but clinical morbidity often remains surprisingly limited. Hydronephrosis is mostly caused by compression rather than destruction of the parenchyma, although kidney failure may eventually develop. Direct mortality

caused by urinary schistosomiasis has been rarely demonstrated.[3] Epidemiologic studies in Egypt and other foci point, however, to an association of chronic urinary schistosomiasis with squamous bladder cancer.[1–3,17] Although several carcinogenic pathways have been hypothesized, the causal relation is not yet and possibly never will be proved. Indeed, both diseases have dwindled simultaneously over the past decades, possibly as a combined result of successful schistosomiasis control programs. The schistosomiasis lesions may also have indirectly facilitated the impact of other mutagenic substrates, such as tobacco or industrial chemicals.[3]

Intestinal and Hepatosplenic Schistosomiasis

The eggs of *S mansoni* or *S japonicum* are trapped mainly in the wall and mesenterium of the large bowel and the rectum, much less in the small bowel. The surrounding granulomatous inflammation provokes microulcerations, pseudopolyps, muscular irritation, and microscopic bleeding. Abdominal pain, loss of appetite, and diarrhea with or without blood are common but atypical symptoms (**Fig. 7**). The frequency and severity of the symptoms is related to intensity of infection, and thus generally higher in children. Many people remain asymptomatic or have only intermittent complaints, but the same "subtle morbidity" as described previously is thought to have substantial impact on community health, especially in school-aged children.[16]

Hepatic schistosomiasis is initially caused by granulomatous inflammation around the eggs trapped in the liver, and in later stages by the resulting fibrosis that may aggregate to long fibrotic streaks, occluding the portal veins.[3] In children and adolescents the pathology is usually inflammatory and reversible, even if some mild fibrosis may be present. Typically, the left liver lobe is enlarged, extending a few to sometimes

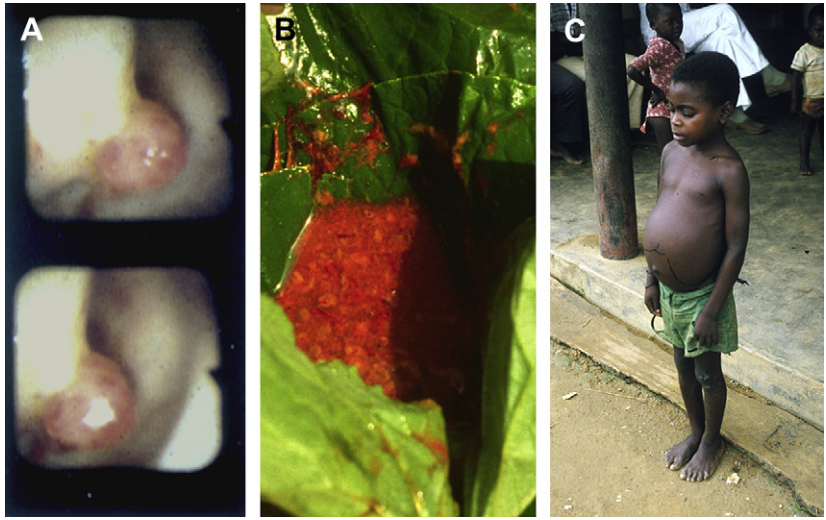

Fig. 7. Intestinal and early hepatic schistosomiasis (*S mansoni*). (*A*) Sigmoidal polyposis on endoscopy. (*B*) Severe bloody diarrhea caused by heavy infection. (*C*) Gross inflammatory hepatosplenomegaly in a young boy (see marks). ([*A*] *From* Topics in International Health Series: Schistosomiasis. Multimedia CD-ROM. New York: CABI Publishing, 1998. Copyright © The Trustee of The Wellcome Trust; with permission; and [*B*, *C*] *From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission.)

15 cm below the costal arch (see **Fig. 7**). The spleen may be normal to grossly enlarged, because of increased portal blood pressure, hypersplenic reactions, or inflammation around locally deposited eggs. The organomegaly in children is strongly correlated with intensity of infection. In most cases, there is no apparent sign of hepatic dysfunction. Mild anemia may be associated with intestinal blood loss or hypersplenism, and may reinforce the general lack of well-being.

In older adolescents and young adults who have carried heavy infections over 5 to 10 years or more, the lesions become ever more fibrotic, larger, and irreversible (**Fig. 8**). Because only some heavily infected people develop such pathology, it is thought that some form of immunogenetic predisposition also needs to be present. The progression may also be more rapid in *S japonicum* infection, sometimes with little or no interval between acute and chronic disease.[1,6]

The fibrotic streaks, which take the pathognomonic form of "clay stem fibrosis," progressively occlude the portal veins, leading to portal hypertension, splenomegaly, portocaval shunting, and external or gastrointestinal varices. Liver enlargement is now typically discrete, hard, and nodular on palpation. Hepatocellular function remains usually preserved. However, ascites may occur but then usually has multiple causes.[3,18] The most dangerous, potentially fatal complication is gastroesophageal bleeding from the internal varices. Repeated or occult bleeding can lead to severe anemia and hypoalbuminemia. Advanced hepatosplenic schistosomiasis was a frequent cause of morbidity and mortality in Egypt, Sudan, Brazil, China, and the Philippines until the advent of modern schistosomicides.[1,3,10] Remarkably, advanced liver fibrosis caused by schistosomiasis has always been less frequent in all but a few areas in sub-Saharan Africa, which is attributed to ethnic and genetic factors.[3] Although cases have been described in long-term expatriates, it is not seen in accidentally infected tourists.

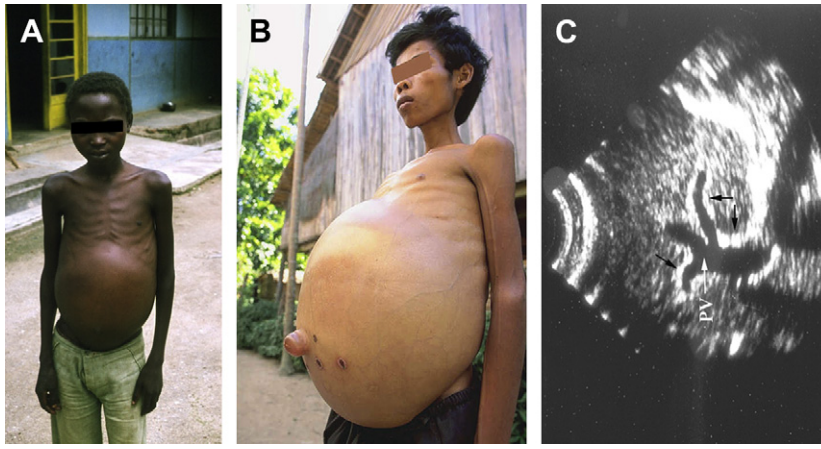

Fig. 8. Advanced hepatic schistosomiasis. (*A*) Chronic hepatic *S mansoni* with splenomegaly, moderate ascites, and growth retardation. (*B*) Advanced *S japonicum* in a young adult with splenomegaly, external varices, and severe ascites. (*C*) Ultrasound image of advanced periportal fibrosis (*black arrows*) and portal venodilatation (*white arrow*). ([*A*] *From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission; and [*B*, *C*] *From* Topics in International Health Series: Schistosomiasis. Multimedia CD-ROM. New York: CABI Publishing, 1998. Copyright © The Trustee of The Wellcome Trust; with permission.)

Ectopic Schistosomiasis

In advanced hepatic schistosomiasis complicated by portal-caval shunting, pulmonary pathology can occur because of the deposition of eggs and subsequent granuloma formation in the lungs.[1,19] Initially, these give rise to bronchial symptoms. Eventually, fibrosis can develop followed by pulmonary hypertension and right heart disease. Glomerulonephritis caused by the deposition of immune complexes in the kidney has been described in long-standing *S mansoni* infections.[1,20] These complications have become rare in endemic areas where treatment is available, and are not common among travelers.

Eggs of *S haematobium* and *S mansoni* are easily transported to the genital and reproductive tract, where they give rise to hypertrophic or ulcerative lesions that may cause female infertility or facilitate the transmission of sexual infections, including HIV.[21] In men, inflammation of the epididymis, testicles, and prostate can be observed, also in travelers with light and recent infections. Sporadically, ectopic schistosomiasis lesions are also found in the skin, the peritoneum, or other organs.

Eggs or worms that are transported to the spinal cord or the brain can cause serious neurologic damage.[1,3,22,23] Neuroschistosomiasis caused by infection with *S mansoni* or *S haematobium* mainly leads to transverse myelitis, a syndrome that is sometimes also seen as a complication of acute schistosomiasis in travelers. Ectopic *S japonicum* infections have a tendency for the brain, leading to focal cerebral symptoms of an epileptic or paralytic nature.

DIAGNOSIS

The gold standard for the diagnosis of *Schistosoma* infection is the microscopic detection of eggs in stools or urine.[1–3,24] The typical size and shape allow an easy distinction from other helminth eggs, and among schistosome species (**Fig. 9**). Concentration methods and examination of several specimens may be needed to detect light infections.[25] For epidemiologic purposes, the eggs can be counted in a fixed amount of urine or feces, allowing an estimation of intensity of infection.[1–3] Quantitative measures are important to assess the intensity of transmission, the risk of morbidity, the need for control measures, and the evaluation of their impact.[26]

Antibody-based serologic assays are sensitive but may cross-react with other helminth infections and remain positive long after the active infection has disappeared.[1,26] Their main medical application is in travel clinics, where they are most useful in the diagnosis of acute schistosomiasis when microscopic examination is still negative.[14] An alternative is the detection of circulating antigens in serum or urine with labeled monoclonal antibodies, which, however, is not very sensitive for light

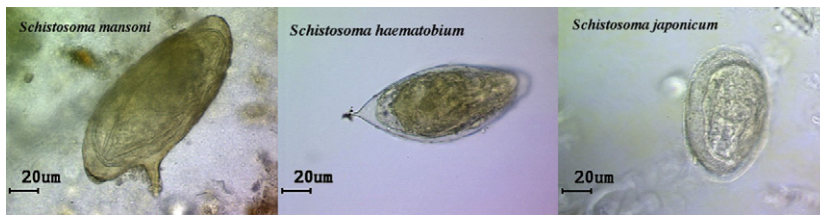

Fig. 9. Schistosome eggs under the microscope. Typical size, shape, and spine of *S mansoni*, *S haematobium*, and *S japonicum*. (*From* Gryseels B, Polman K, Clerinx J, et al. Human schistosomiasis. Lancet 2006;368:1106–18; with permission.)

infections, such as in tourists.[27] Recently, the detection by PCR of schistosome DNA in the sera of recently infected patients was shown to outperform parasitological and serological methods.[28]

In endemic areas, rapid assessment, indirect diagnosis, and population screening of urinary schistosomiasis can be done easily and cheaply with hematuria dipsticks or simple questionnaires.[29,30] Such tools are less readily available for *S mansoni* and *S japonicum*. The confirmation or assessment of organ complications requires radiologic, sonographic, or endoscopic methods by experienced specialists.[31] Calcifications of the urinary tract can easily be detected on direct radiographs. Contrast radiography is suitable to visualize other renal, urinary, and bladder pathology, and can also be applied for the diagnosis and measurement of portal vein distention or esophageal varices. For the latter, endoscopy is also suitable but must be handled carefully to avoid iatrogenic ruptures. In difficult cases, the assessment and differential diagnosis of hepatic fibrosis may require laparoscopy and wedge biopsy. Myelography and MRI can be useful for detailed imaging, especially for neuroschistosomiasis.

Ultrasonography has become a major tool for the diagnosis, assessment, and study of schistosomiasis pathology in hospital settings and in the field.[32] Urinary tract pathology and liver fibrosis or portal vein extension can be diagnosed and measured. Standardized protocols are available for epidemiologic studies and clinical applications.

TREATMENT

Until the 1970s, the treatment of schistosomiasis was almost as difficult and toxic as it still is today for trypanosomiasis and leishmaniasis.[10,33] Because pathology was limited in many cases, the decision to treat or not could be a real dilemma and wide-scale application for control purposes was a hazardous undertaking. In the early 1980s, praziquantel, an acylated quinoline–pyrazine active against all schistosome species in a single oral dose, came on the market.[33] It paralyzes and kills the worms within a few hours and adverse effects are usually few and limited to transient nausea or malaise. In heavy infections, transient colicky and bloody diarrhea can occur shortly after treatment, probably provoked by massive worm shifts. No long-term toxicity is known and praziquantel is safe for infants and pregnant women.[34]

The recommended doses range from 40 to 60 mg/kg according to the circumstances, species, and intensity. The lower dose is widely used in endemic areas and in control programs, where reduction of intensity of infection and risk of morbidity is the main objective, rather than absolute cure. In individual patients who are not exposed to reinfection, the dose may be increased to 60 mg/kg, in one or two takes with a 4-hour interval, and possibly repeated for 2 or 3 days.

Praziquantel does not kill eggs or schistosomula. Therefore, the etiologic treatment of acute schistosomiasis may have to be repeated or deferred until 2 to 3 months after the likely date of infection. In the meantime, symptomatic treatment can be given with standard analgesics and corticoids.[12–14]

Because eggs that are migrating through the tissues are not affected by praziquantel and may be excreted for weeks after the worms are killed, microscopic follow-up of treatment must be given sufficient time (ie, up to 4–6 weeks). In endemic areas, new infections may be contracted in that period, which may make it difficult to distinguish rapid reinfection from treatment failure.[35]

The organ pathology usually dissolves or decreases substantially in the weeks and months after treatment, as can be shown by radiographic or sonographic examination.[36] However, advanced liver fibrosis or severe nephropathy may be

irreversible. The acute treatment of esophageal bleeding may require β-blockers, sclerotherapy, splenectomy, or portocaval shunting.[33] In the treatment of neuroschistosomiasis, praziquantel should be associated with corticosteroids and possibly anticonvulsants, to avoid acute exacerbations after the death of ectopic worms.[23]

It has been shown that artemisinin and derivatives are active against schistosomula and, to a lesser extent, adult schistosomes.[37] Although they could be used as prophylaxis, this is not appropriate in malaria-endemic areas where artemisinin resistance in malaria must be avoided at all cost. Its curative use in acute schistosomiasis, in combination with praziquantel, is still being investigated.

Whereas some worrying results have been reported, and praziquantel tolerance can easily be induced in animal models, there is no clinical or epidemiologic evidence for the emergence of praziquantel resistance in the field.[35] Caution is needed, however, because there are no other multivalent schistosomicides available or in the development pipeline.

CONTROL

The control and prevention of schistosomiasis used to be largely based on the chemical destruction or environmental management of snail populations, a difficult, costly, and mostly inefficient method (**Fig. 10**).[1,3,10] Some countries, most notably Japan in the 1950s, have nevertheless been able to eliminate schistosomiasis by combining this approach with water supply, sanitation, and environmental interventions.[38] Nowadays, the emphasis has entirely shifted to preventive chemotherapy of communities and groups at risk.[39,40] Depending on the local epidemiology and resources, communities in endemic areas are either screened and treated if positive, or the entire population is treated regardless of individual infection status. This strategy especially targets school-aged children, who are most at risk and are easily accessible in schools. The drugs are distributed by special teams, local healthcare staff, community healthcare workers, or school teachers.

Although the primary objective of preventive chemotherapy is to control and prevent morbidity, it is also hoped that eventually transmission will be affected and even halted by sustained "mass drug administration." The dynamics of transmission are not linear, however, and eliminating schistosomiasis with drugs alone without additional measures in terms of sanitation, water supply, and education is unlikely to succeed.[3] In countries that are moving up the income and development ladder, such as Brazil, China, Egypt, and the Philippines, mass screening and treatment has resulted in quick advances that seem to be sustainable because of concurrent socioeconomic progress. In other areas, most notably sub-Saharan Africa, preventive chemotherapy has to be repeated at regular intervals for an as yet undetermined period to remain effective. Because logistical conditions are difficult and healthcare systems weak, this requires considerable resources and tenacity; the cost of the drug, actually at less than $ 0.15 per treatment, is no longer a limiting factor.

Recently, development agencies, global philanthropists, and pharmaceutical companies have teamed up in a massive effort to assist endemic countries with the introduction of preventive chemotherapy and mass drug administration for helminthic diseases, including schistosomiasis.[41] The stated objective is to eliminate these health problems and ensuing poverty by the year 2020. Critical issues are a balanced and sustainable integration in health service activities, appropriate adaptations of the global strategy to local priorities, circumstances and resources, and the avoidance of drug resistance.[3,42,43] The commitment and discipline must remain strong when

Fig. 10. Schistosomiasis control in the field. (*A*) Mass treatment with praziquantel in the community. (*B*) Safe water supply. (*C*) Snail control with molluscicides.

prevalences wane after a few treatment rounds. Most of all, the expected quick wins must be consolidated by the rapid improvement of living conditions, which can only be achieved by political and socioeconomic progress. Schistosomiasis remains a disease of poverty, and the one cannot be eradicated without the other.

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