Schistosomiasis (bilharzia) is caused by a worm of the trematode family. All of these flukes (flatworms) require a freshwater snail as an intermediate host and do not replicate in their definitive hosts, humans. Schistosomiasis is widespread in the tropics and subtropics (Figure 1). The prevalence of infection and its clinical consequences depend on interactions between the distribution of the intermediate hosts, and the social and cultural behaviour of humans.

Life cycle
Free-living cercariae are released from the snail intermediate host into the surrounding water. Cercariae have small, forked tails and are motile. They can penetrate intact human skin and, once inside the definitive host, become larvae (schistosomulae). The schistosomulae migrate via the bloodstream, eventually maturing to adult worms, and reach the mesenteric veins (Schistosoma mansoni) or the venous plexus around the bladder (S. haematobium). Oral and ventral suckers allow the worms to maintain their position in the vein lumen.

Adult female schistosomes live in the gynaecophoric canal of the male and produce hundreds, or sometimes thousands, of eggs per day. Many eggs are excreted in the urine and faeces. Eggs that are excreted into fresh water hatch after about 10 days, releasing miracidia that are attracted to and infect the snail intermediate host. Within the snail, the miracidia progress through two sporocyst stages, to form cercariae that are then released to complete the cycle.

Epidemiology
There are five recognized species of schistosome that affect humans.
- *S. haematobium* is the most widely distributed, being found in Africa, Asia, South America, the Caribbean and the Middle East.
- *S. mansoni* is found in Africa, Asia and the Middle East.
- *S. japonicum* is restricted to Asia.
- Two more recently described species, *S. mekongi* and *S. intercalatum*, are restricted to South East Asia and Africa respectively.

Worldwide, about 200 million individuals are affected by schistosomiasis and at least 600 million are at risk. It is estimated that schistosomiasis causes about 200,000 deaths per year, mainly

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from renal failure and haematemesis. There is evidence of a world-wide increase in the prevalence of infection, possibly related to expansion of irrigation projects and the increasing movement of populations. In the last few years, many travellers from the UK have become infected following swimming in Lake Malawi.¹

Most infections occur in childhood, from the age of about 4 years, with a peak at age 15–20 years. The age of peak prevalence coincides with the age of greatest intensity of infection (maximum egg excretion). After the age of 20 years, excretion of eggs begins to decline, possibly as a result of increasing immunity, or perhaps because of behavioural changes leading to reduced exposure to fresh water. Only about 5–15% of a given population becomes heavily infected; the limiting factors are unknown. A recent study suggested that CD4 lymphocytes may have a role in controlling susceptibility to re-infection and that HIV infection may increase the risk of re-infection.²

The prevalence of symptoms varies considerably. Clinical symptoms occur in about 80% of individuals with *S. haematobium* infection, but in only about 20% of those with *S. mansoni*.

**Pathogenesis**

When the cercariae penetrate human skin, they cause acute symptoms sometimes called ‘swimmer’s itch’. This occurs a few hours to days after infection and is probably related to the development of humoral and cellular immunity to the cercariae. A few weeks later, some patients experience a syndrome termed ‘Katayama fever’, in which cough, fever, urticaria and other symptoms occur. Katayama fever is thought to represent an immune complex disease, similar to serum sickness, as the immune response to schistosomal eggs begins.

The chronic features of schistosomiasis are organ-specific and relate to the host response to deposited eggs. Egg deposition starts about 6–9 weeks after infection. Although the eggs are released into the venous blood, many reach the lumen of the gut or the bladder. It is unclear whether this occurs by active enzyme secretion by the eggs or by the natural motion of fluid in the bladder and bowel. Eggs reaching the lumen are excreted and subsequently hatch to form miracidia, which may then complete the life cycle by infecting a snail. Eggs that are not excreted lodge in the mucosa of the bladder and bowel, and some reach the liver via the portal circulation. In the tissues, a cell-mediated response to the egg leads to granuloma formation. When the miracidium in the egg dies after about 6–8 weeks, the antigen load decreases and the granuloma tends to shrink. Healing leads to fibrosis.

**Clinical features**

**Acute**

Swimmer’s itch occurs 1–2 days after exposure to fresh water containing cercariae. Affected individuals develop a macular, papular, itchy rash that lasts for a few days before remitting spontaneously. It is more common in newly exposed individuals. Swimmer’s itch is mainly seen in association with *S. haematobium* and occasionally with *S. japonicum*. More severe forms of swimmer’s itch are sometimes encountered when humans are infected with cercariae from avian hosts.

Katayama fever (acute schistosomiasis) is most commonly seen with *S. japonicum* (up to 50% of infected individuals). Symptoms include fever, malaise, cough, wheeze and urticaria. There may be lymphadenopathy and sometimes hepatomegaly. Patients usually exhibit peripheral blood eosinophilia. Cases involving transient
pulmonary infiltrates have recently been described. Schistosomal serology may be positive and eggs may be found in urine or stool, but both tests may be negative in the early stages. Rare cases of fatal Katayama fever have been reported.

Chronic

**Urinary tract** – *S. haematobium* and, to a lesser extent, *S. intercalatum* primarily cause symptoms and signs in the urogenital tract. Up to 80% of those infected with *S. haematobium* have symptoms including dysuria, frequency and terminal haematuria. (In some African cultures, haematuria may be considered a ‘rite of passage’ for boys.) Haematospermia is a relatively common symptom in expatriate males. Renal ultrasonography may show bladder wall thickening, hydronephrosis (if granulomata lead to ureteric obstruction) and calcification in the bladder and ureters. Cystoscopy may reveal ‘sandy patches’ on the bladder mucosa, mucosal hyperaemia or, occasionally, polyps. Untreated individuals may be prone to frequent urinary tract infections and occasionally develop bladder outflow obstruction, ureteric stones or even chronic renal failure.

There is an association between chronic schistosomiasis and *Salmonella* infection. Patients may become bacteraemic or may develop *Salmonella* urinary tract infections. Rarely (1–2 per million), those with heavy, chronic *S. haematobium* infection prematurely develop bladder cancer, typically squamous cell carcinoma.

**Intestinal and liver disease** – infection with the non-haematobium species (particularly *S. mansoni*) leads to egg deposition in the intestinal mucosa and liver. For reasons that are poorly understood, less than 20% of individuals infected by these species develop symptoms. The most common symptoms are vague abdominal discomfort and/or diarrhoea. Egg deposition in the liver may lead to hepatic enlargement. Over time, granuloma formation leads to fibrosis, and this may lead to portal hypertension as the biliary and portal tracts are distorted by the fibrotic reaction. In these circumstances, splenomegaly, oesophageal varices and ascites can occur. Liver function is relatively well preserved in schistosomiasis with portal fibrosis, but variceal bleeding is not uncommon. If this is not dealt with by sclerotherapy and/or appropriate transfusion, death from haematemesis ensues. This is a common cause of death from schistosomiasis.

**Other sites of disease**

- Eggs may be deposited in the lungs, usually in patients with severe hepatic fibrosis when blood is shunted from the gut to the lungs, bypassing the liver. Multiple granulomata then form in the lung, leading to pulmonary hypertension and, eventually, cor pulmonale.
- Schistosomal eggs occasionally migrate to the brain. The mechanism by which this occurs is not clear. It is sometimes reported in *S. mansoni* infection, but most commonly occurs with *S. japonicum*. The usual clinical presentation is with generalized or focal seizures. CNS disease is said to complicate 2–4% of *S. japonicum* infections.
- Rarely, eggs from *S. haematobium* migrate to the venous plexus around the spine. It is presumed that they flow retrogradely from the bladder venous plexus, through the valveless connections, to the spinal venous plexus. Patients present with transverse myelitis or cauda equina syndrome caused by the inflammatory response to the eggs.
- Some patients with *S. mansoni* infection develop chronic glomerulonephritis. This appears to be more common in South America than elsewhere. Patients may present with nephrotic syndrome or with chronic renal failure.
- Rarely, eggs migrate to the skin, producing a nodular rash. This is most common in the genital area and may be mistaken for genital warts.

**Diagnosis**

Diagnosis is aided by a history of exposure, but depends on the finding of eggs (Figure 2) or a positive serological result.

**Eggs of *S. haematobium*** are often excreted in the urine; maximal excretion occurs around midday, so a midday sample is ideal for egg detection. Urine filtration and centrifugation increase the yield. Eggs of other schistosomal species may be detected in stool samples, and detection rates may be increased by various concentration techniques (e.g. the Kato method). Biopsy of affected tissues can also demonstrate eggs. This is easiest on rectal biopsy, but eggs may also be seen when bladder biopsy is performed in suspicious cases, and in liver and skin biopsy samples.

**Serological tests** are based on the detection of circulating antibodies using egg antigens in an enzyme-linked immunosorbent assay (ELISA). These tests are sensitive, but remain positive for a long time after infection. They are not useful for diagnosis of active infection in endemic areas, where many individuals have been infected in the past, but are useful for detecting infection in returning travellers. Newer serological tests to detect adult worms may distinguish active from past infection, but are still under development.

**Other tests** – many infected returning travellers have peripheral blood eosinophilia (a nonspecific marker) and some have dipstick-positive haematuria. Plain abdominal radiographs show-
ing ‘egg-shell’ calcification of the bladder are highly suggestive of schistosomiasis.

Management

Praziquantel – in the last 20 years, treatment of schistosomiasis has improved with the introduction of praziquantel, a broad-spectrum antihelminthic drug. The standard oral dose is 40 mg/kg in a single dose. *S. japonicum* and *S. mekongi* may require a higher dose; 50 mg/kg single dose or 20 mg/kg given three times in 24 hours is recommended. Praziquantel cures schistosomiasis in 80–90% of patients and achieves a 90% reduction in egg excretion in those who are not cured. The drug is extremely well tolerated; the main side-effects are abdominal pain, and sometimes nausea and vomiting. In patients with CNS involvement, corticosteroids are often used in conjunction with praziquantel to minimize the inflammation around granulomata.

There are now concerns about praziquantel resistance. This can be demonstrated in animal models, and there have been a few case reports in humans.

Other drugs have been used in schistosomiasis. Metrifonate has activity against *S. haematobium*, but not other species. Niridazole can be used against *S. japonicum* and oxamniquine against *S. mansoni*. In practice, these drugs are now seldom used. Artemether has been shown to have activity against *S. mansoni* and may kill immature schistosomes. However, this drug is valuable in the treatment of malaria and should probably be reserved for the latter disease.

Follow-up – it may take up to 6 months for praziquantel treatment to eradicate infection, so patients should be seen at 6 months to ensure that urine or stool is egg-free. It may be longer before schistosomal ELISA becomes negative, and this method is therefore not useful for monitoring response to therapy.

Complications – once fibrosis has developed, drugs have little impact; treatment is then focused on managing the complications (e.g. portal hypertension). Anticonvulsants may be needed in patients with CNS involvement with *S. japonicum*.

Katayama fever can be treated symptomatically. Katayama fever is treated symptomatically. There is controversy about the role of praziquantel in the acute stage; some authorities suggest that praziquantel exacerbates the symptoms of Katayama fever. However, most clinicians use praziquantel in this setting, with non-steroidal anti-inflammatory drugs and, in severe cases, corticosteroids.

Prevention

In travellers to tropical areas, schistosomiasis can be prevented by avoiding exposure to fresh water. Travel clinics can provide advice on reducing the risk of exposure.

In endemic areas, prevention is more difficult. Provision of clean water and proper sewage control are probably the most important means of reducing the burden of schistosomiasis, in addition to improvements in the general socioeconomic status of the population. Molluscicides can be used to reduce snail populations in fresh water and thereby remove the intermediate host from the parasite’s life cycle.

Mass chemotherapy applied to villages has been shown to be effective. This involves treating every member of the community with praziquantel at the same time; it reduces the disease burden, makes individuals less infective and reduces transmission rates. There is currently no available vaccine.

REFERENCES


FURTHER READING


King C H, Mahmoud A A F. Drugs five years later: praziquantel. *Ann Intern Med* 1989; 110: 290–6. (A good review of this broad-spectrum antihelminthic drug, which is widely used to treat schistosomiasis.)


Practice points

- Schistosomiasis in returning travellers is associated with exposure to fresh water
- Katayama fever occurs 2–6 weeks after exposure; it presents as an acute illness with fever, myalgia, cough, wheeze, rash and marked eosinophilia
- Chronic schistosomiasis in endemic areas may lead to portal hypertension in *S. mansoni* infection, or to chronic bladder problems with *S. haematobium*
- CNS involvement can occur, particularly with *S. japonicum*
- Praziquantel is the drug of choice for the treatment of schistosomiasis