Schistosomiasis

By Ravi Chavali

Etiologic Agent

Schistosomiasis is a disease caused by parasitic worm of genus Schistosoma [1]. It belongs to phylum Platyhelminthes, class Trematoda and genus Schistosoma [2]. Most human infections are caused by the three species: S. mansoni, S. haematobium, and S. japonicum [3]. There are two more species S. intercalatum and S. mekongi known to cause Schistosomiasis [3]. The most infections caused by a particular species appears to be more a matter of geographic distribution of the species rather than contagiousness of the species. New species has been reported in Malaysia [4]. Humans are the definitive hosts for S. mansoni, S. haematobium, and S. japonicum [4]. All of these species are blood flukes.

Transmission

When the skin of a human comes in contact with fresh water containing the larval form of Schistosoma called cercariae they bore into the skin. Typically, the water is pooled (such as lakes or rice fields) or slow moving and has been contaminated by fecal or urine matter containing eggs of Schistosoma from people infected with Schistosomiasis [3]. Also, the contaminated water needs to contain certain genus of snails, depending upon the species of Schistosoma, which serve as intermediate host [4]. The cercariae are the larval forms that have bored their way out of snail intermediate host. The cercariae bore through intact human skin and transform into Schistosomulum, a larval form of the definitive host. Through blood vessels Schistosomulum migrate to lungs and from there to liver where they mature and eventually migrate to mesenteric branches of the hepatic portal vein in the intestinal region [4].

Reservoirs

Host reservoirs do not seem to be considered as important to all species of Schistosoma [4]. For S. mansoni, and S. haematobium a reservoir is not considered to be important in the perpetuation of the transmission of Schistosomiasis [2, 4]. However, recent research indicates that wild rodents and wild and domesticated animals might be important reservoirs in the spread of S. mansoni [5, 6]. S. haematobium has no known animal reservoir [7]. S. japonica has several known domesticated animal species such as dogs, water buffaloes, horses, cats, pigs as well as wild animals [7]. S. intercalatum has rats as reservoir and has been experimentally determined to cause zoonotic infections in primates, sheep, goats and other animals [4]. Dogs are the reservoirs for S. mekongi [8].

General Characteristics

The five Schistosoma species are all flatworms – flukes. They are dioecious and are found in the blood vessels [4, 7]. They have two suckers – a ventral sucker and an oral sucker – with which they maintain their position in the blood vessels. They all have a complex life cycle with snails as an intermediate host and humans as definitive host. Without intermediate host they cannot perpetuate. The mature adults in definitive human host produce eggs most of which leave the human body through the digestive tract along with fecal matter or through the urinary tract along with urine depending on the species. The eggs that are trapped in host body and so cannot leave are the cause of pathogenicity of the disease [4]. The egg that leaves the body and finds
its way to fresh water hatches to become a larva, called miracidium. The eggs can survive on dry land for about a week [8]. The miracidia carry their food and can survive 4 to 6 hours after hatching. They need to find a snail as intermediate host to continue their lifecycle in this time frame. Using their ability to detect light and gravity they swim to water surface where the snails typically are. Once in the vicinity of a snail intermediate host they use chemotaxis to swim to it. They attach to the snail and bore into it. They form a primary sporocyst in the snail intermediate host [4, 7]. Each species of Schistosoma uses a specific genus of snails as an intermediate host: Bulinus (S. haematobium), Biomphalaria (S. mansoni) and Oncomelania (S. japonicum) [7]. Each primary or mother sporocyst produces many daughter sporocysts. Each daughter sporocyst produces many cercariae in the digestive and reproductive system of the snail. These are the infective larval form of the Schistosoma. They bore their way out of the snail into water. It takes 25 to 30 days from the time a snail is infected to the time cercariae bore their way out of it [4]. Once in water they have 5 to 8 hours to find and attach to a human host. After contact with human skin they bore into the intact skin and transform into Schistosomulum, the human larval form. Schistosomulum bores through epidermis and dermis till it finds a blood vessel (about a day or two) [4]. It bores into the blood vessel. The blood carries it into the lungs through pulmonary artery. In the lung it transforms by becoming longer and slender without increase in body weight to facilitate its migration through the blood vessels. It then travels to liver via blood vessels passing through left side of heart and the hepatic portal vein. In the liver the Schistosomules grow into sexually mature adult male and female and pair up. The male has a groove along the length of its body, gynacophoric canal, in which the female is held. The combined pair migrates out of the liver back into the hepatic portal vein against the flow of blood and into the mesenteric branches around intestines [4]. The location in the mesenteric branches seems specific to species but is not always the case: S. mansoni – superior mesenteric veins draining the large intestines, S. japonica – superior mesenteric veins draining small intestines and S. haematobium – venous plexus of the bladder but also can be found in the rectal venules [9]. The male Schistosoma fertilizes the female in the gynacophoric canal and eggs are released. The eggs move gradually through gut walls into the lumen of intestinal tract (S. mansoni and S. japonica) to exit the body along with feces or they gradually move into the lumen of bladder and ureters (S. haematobium) to exit along with urine. Some of these eggs released in the mesenteric veins get lodged in the liver due to flow of blood causing granulomas.

The eggs of S. mansoni and S. haematobium are about 140 μm x 60 μm in size, oval in shape. The eggs of S. mansoni have a lateral spine while that of S. haematobium have a terminal spine. The eggs of S. japonica are smaller in size, about 80 μm x 63 μm, with a reduced spine and are rounder rather than oval. The S. mansoni female lays eggs one at a time while the S. haematobium and S. japonica lay in batches. The miracidium is 150 - 180 μm in length and 70 - 80 μm in width. Adult males of S. mansoni and S. haematobium are about 1 cm long and about 1 mm wide while adult males of S. japonica are about 1.2 cm by 0.5 mm. Females are longer than males [4].

**Key tests for identification**

The main and most practical method of identification for all five species of Schistosoma is laboratory based morphological identification of eggs. Fecal samples are used for all species except S. haematobium for which urine samples are used. Due to intermittent nature of egg laying by flukes multiple stool and urine samples are collected over different days and times and these samples are concentrated to enhance the ability to detect eggs. Rectal biopsy may be used
to detect all species except *S. haematobium* in case stool samples are negative and bladder biopsy can be used in case urine samples are negative [9].

Antigen based antibody detection can be used when tests to detect presence of eggs have failed. Serum samples can be tested using FAST-ELISA based on *S. mansoni* adult worm antigen. This test though very sensitive is not very specific except for *S. mansoni* and therefore immunoblots based on travel history of a patient can be performed to identify specific species [9].

The above tests are used in developed countries. However, in the developing countries these are not economically viable. World Health Organization recommends using Kato-Katz technique for stool samples and urine filtration kits for urine samples to detect eggs or dipsticks for urine samples of children to detect microscopic blood particles in urine caused by bladder Schistosomiasis [10, 11].

**Signs and Symptoms of Disease**

The pathogenicity of *Schistosoma* is due to body response to eggs that get trapped in the body rather than the adult *Schistosoma* [9]. The symptoms of the disease depend upon species to which the fluke belongs and the phase of infection [7]. In early stages of infection the skin could be itchy or rashes may develop. A month or two later fevers, chills, cough and muscle ache might develop. Most people are asymptomatic at this stage of infection [9]. If untreated, in the long run, the infection may damage liver, intestine, lungs, and bladder. In rare cases when the eggs get trapped in the spinal cord or brain they cause seizures, paralysis and spinal cord inflammation [9].

If the infection is caused by *S. haematobium* it results in Urogenital Schistosomiasis. Blood in urine (haematuria) is a sign of this disease. If untreated it may lead to fibrosis of bladder, ureters and kidneys and possible bladder cancer. Some of the signs in women suffering from Urogenital Schistosomiasis are genital lesions, vaginal bleeding, pain during sexual intercourse and nodules in vulva. In men this disease can induce pathology of prostate, seminal vesicle and other organs as well as infertility [10].

If the disease is caused by *S. mansoni* or *S. japonica* it results in Intestinal Schistosomiasis. The acute phase of this disease is associated with laying eggs by the parasite which if symptomatic can result in fever, nausea, headache, cough and possibly diarrhea with blood in stool. This stage may be asymptomatic. If the symptoms do appear they last weeks to several months especially for *S. japonica* and are also known as Katayama Fever [4, 10]. The chronic phase of this disease can lead to cellular granulomatous inflammation around trapped eggs leading to fibrosis of the intestines and liver. Liver and spleen enlargement are seen as well as lesions in the intestines and in some cases polyps in the colon [4, 10].

**Historical Information**

The descriptions of the symptoms of Schistosomiasis – bloody urine (caused by *S. haematobium*) – are found in the hieroglyphics of “Papyrus Ebers” as well as in ancient Assyrian records. Theodor Bilharz in 1851, working at the Kasr-el-Aini hospital in Cairo, discovered the organism in the portal vein while performing post-mortem examination. Yoshiano Fuji, a Japanese physician described the symptoms of Schistosomiasis caused by *S. japonica* in 1847 and also noted the zoonotic aspect of the diseases mentioning that the cattle and horses exposed to the water also suffered from the same disease as man. It was known as Katayama Disease in Japan at that time. In 1904 the causative agent of Katayama Disease was identified by Fijiro
Katsurada as a helminth which was similar to *S. haematobium*. However, the morphology of this helminth’s egg was different from that of *S. haematobium*. He named it *Schistosoma japonica*. He described the pathology of the disease and noted that unlike *S. haematobium* it did not cause bladder problems. It was assumed that *S. haematobium* was responsible for both bladder and intestinal infections. In 1906 Sir Patrick Manson discovered that eggs (laterally spined) in fecal samples of Intestinal Schistosomiasis patients were different from the eggs (terminally spined) in urine samples of Urogenital Schistosomiasis patients. He speculated that these two were different species. It was proved in 1907 to be true and the new species was called *Schistosoma mansoni* in his honor. In 1909 Kan Fujinami and Hachitaro Nakamura determined the mode of transmission as skin contact by performing experiments with cattle. In 1913 Keinosuka Miyairi and Masatsuga Suzuki established the lifecycle of *Schistosoma japonica* by taking cow dung containing the eggs of *S. japonica* as well as human feces containing the eggs of *S. japonica* and adding them to water. They saw that the eggs when added to water hatched forming the larva.

**Virulence Factors**

Peptidases are considered as the main virulence factors in the pathogenesis of Schistosoma by some among the scientific community [12]. Some consider surface protein identified as SnMPP-5 as a virulence factor because suppression of a gene that produces this protein has rendered the parasite ineffective in causing infection [13]. Another point of view is that since an adult fluke does not cause infection by itself but it is egg that causes pathogenesis, egg should be considered as the virulence factor, specifically the spine of an egg which cuts through tissue. The advent of proteomics has spurred new research in identifying virulence factors associated with this disease.

**Control / Treatment**

The treatment for Schistosomiasis is same irrespective of species causing it. The chemotherapy drug of choice is praziquantel. The treatment is effective in individuals whose body has developed mature antibody response to the adult worms. A dosage of 40 mg/kg of body weight per day orally administered in two divided doses for one day is required for *S. mansoni*, *S. haematobium* and *S. intercalatum*. A higher dosage of 60 mg/kg of body weight per day orally administered in three divided doses for one day is required for *S. japonica* and *S. mekongi* [9].

There are various mechanisms proposed and implemented for control of this disease. Proper sanitation so that the fecal matter and urine do not contaminate the fresh water that people get in skin contact with. Control of snail intermediate host to disrupt the life cycle of the parasite is another mechanism. Avoiding exposure to water bodies known to be contaminated to prevent reinfecion especially of children which is a major issue.

**Prevention/ Vaccine**

There is overlap of prevention and control mechanisms. A lot of methods have been tried and implemented. Once again, all methods of prevention aim at one or more of the following: 1. Avoidance of exposure to known contaminated water bodies; 2. Preventing contamination of water bodies with feces and urine of infected people by proper sanitation methods; 3. Control of the intermediate snail host – elimination to reduction in their population levels by various means.
Vaccine for animals have been developed especially *S. japonica* but per WHO there is no human vaccine that has achieved 40% or more in the worm load reduction. There are quite a few candidates for vaccine in Proof of Concept stage - mostly in preclinical stage and Phase I trials [14].

**Local Cases or Outbreaks**

There are no local outbreaks of Schistosomiasis as the intermediate host snail is not found in the water bodies of US. However, there are quite a few cases of Schistosomiasis in US due to immigrants and travel of US residents through endemic parts of the world. It has been found in quite a few immigrant communities that have moved to US from endemic parts of the world.

**Global Cases or Outbreaks**

Per WHO there are over 249 million cases that needed preventive treatment in 2012. About 42.1 million have been treated for Schistosomiasis in 2012. Most of these infections are due to exposure to infested water during routine agricultural, domestic, occupational and recreational activities [10]. The current estimate is that 252 million people are infected with Schistosomiasis – about 66% by *S. haematobium*, 33% by *S. mansoni* and about 1% by *S. japonica* and *S. mekongi*. About 90% of the infected population is from African continent and the remainder is from Brazil, Latin America and Middle East [14].

**References:**


   http://web.stanford.edu/group/parasites/ParaSites2006/Schistosomiasis/2.html
   http://www.cdc.gov/dpdx/schistosomiasis/dx.html
    http://www.who.int/mediacentre/factsheets/fs115/en/
    http://www.who.int/neglected_diseases/preventive_chemotherapy/pctnewsletter11.pdf
    http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3187234/
    http://who.int/immunization/research/meetings_workshops/Schistosomiasis_VaccineRD_Sept2014.pdf?ua=1