Our Success was no Fluke:
The Life and Times of *Schistosoma mansoni*

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Parasitic organisms create discomfort and fear in humans. In popular culture, for example, this fear has been used by science fiction writers. In the *Alien* movie series, the alien requires a human host in order to grow and hatch out of a human chest in order to complete its lifecycle. A personal favourite, however, is Flukeman from an episode of *The X-Files* called “The Host” (see figure 1). The Flukeman inhabits the sewage system and transmits small flatworms into human hosts via bites. While these examples are not based directly on one particular parasitic organism, they do make for an interesting illustration of our relationship with parasites. Here, however, I will provide a depiction of the life of a real parasite, *Schistosoma mansoni,* discussing its lifecycle and research into treating those who are infected. I will also show how humans have allowed the parasite to spread, and why, perhaps it is even more frightening than any fictional parasite.

Figure 1. Flukeman of the *X-Files*

Schistosoma mansoni is an acoelomate parasitic worm that belongs to the Phylum Platyhelminthes and to the Class Digenea or Trematoda (Biological Sciences, 2016). Due to their lack of coelom, digeneans are dorso-ventrally flattened in order to allow the diffusion of nutrients across the body wall. They are triploblastic organisms, meaning they have three distinct germ layers, and they also have a degree of cephalization, meaning that all sense organs are located at one end of the body (Biological Sciences, 2016). While most parasitic worms are monoecious, or hermaphroditic, *S. mansoni* are dioecious, having two separate sexes. Male and female adults pair in the host body to mate, with the much smaller female fitting into the male’s copulatory groove (Biological Sciences, 2016; see figure 2).

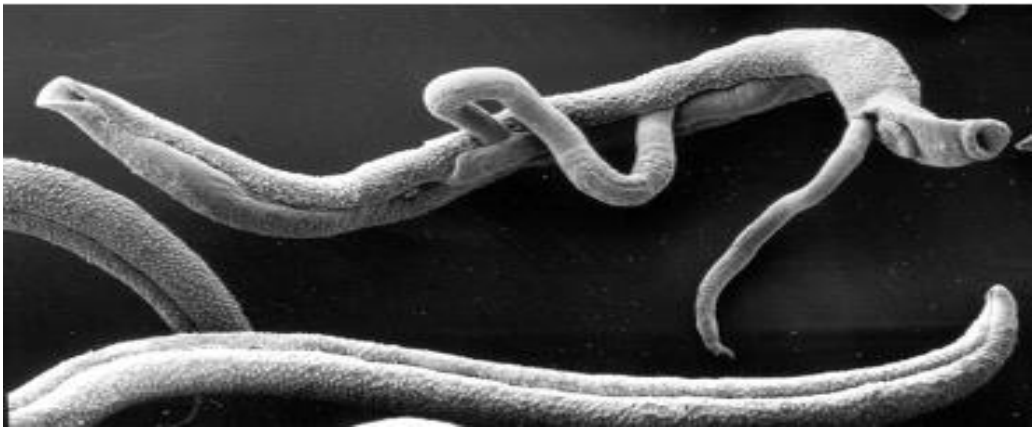

Figure 2. Electron micrograph of *Schistosoma mansoni*, male and female.

S. mansoni are endemic to Africa, parts of the Middle East, the Caribbean, Brazil, Venezuela, and Suriname – mainly destitute and impoverished regions that are typically lacking in funding for medical resources and quality sanitation systems (WHO, 2016; Mafudb *et al*., 2016). *S. mansoni* are the cause of schistosomiasis, a neglected tropical

disease also known as Bilharziasis, Snail Fever, and Katayama Fever. While this disease currently infects 200-million people worldwide, the World Health Organization reports that only 40-million people were treated for the infection in 2013 (Marilliaa *et al*., 2016; WHO, 2016). Sadly, *S. mansoni* are thought to possess elaborate mechanisms for avoiding a protective immune response from humans. (El Azzouni *et al*., 2016).

Like many parasitic organisms, *S. mansoni* has a complex life cycle, requiring both an intermediate and primary host in order to mature and reproduce. Their class name Digenea means “two lives,” in reference to this lifestyle (Biological Sciences, 2016). The lifecycle begins with the oval, operculated eggs of the parasite being deposited in freshwater environments with human fecal matter. These eggs hatch to release a miracidium, a ciliated larva, which swim through water using these cilia to find their intermediate host (CDC, 2012). *S. mansoni* have a high degree of specificity regarding their intermediate host, with the host of choice being *Biomphalaria glabrata* – a type of freshwater snail.

The snail host is located by chemotaxis and phototaxy. *S. mansoni* miracidia then burrow through the foot tissues of the organism and eventually undergo asexual reproduction, producing sporocysts, found throughout the snail’s internal organs (http://parasite.org.au/para-site/text/schistosoma-text.html). These sporocysts asexually produce cercariae, fork-tailed and free- swimming parasitic larvae, which are released into water, roughly four weeks after initial infection of the snail host. They make their way to the primary host, *Homo sapiens* (http://parasite.org.au/para-site/ext/schistosoma-text.html). Cercariae penetrate human skin and lose their tails, at which point they are referred to as schistomula. These are carried to the liver via blood vessels where they mature to adult worms for a period of roughly three weeks (http://parasite.org.au/para-site/text/schistosoma-text.html).

Adult schistosomes pair up and make their way up the blood stream to the superior mesenteric veins, which drain from the large intestine (http://parasite.org.au/para-site/text/schistosoma-text.html). Females then lay their eggs in the venules, as near as possible to the intestine. The spined eggs cross into the lumen of the intestine, and are eliminated with waste material into aquatic environments, to start the lifecycle again (CDC, 2012; see figure 3).

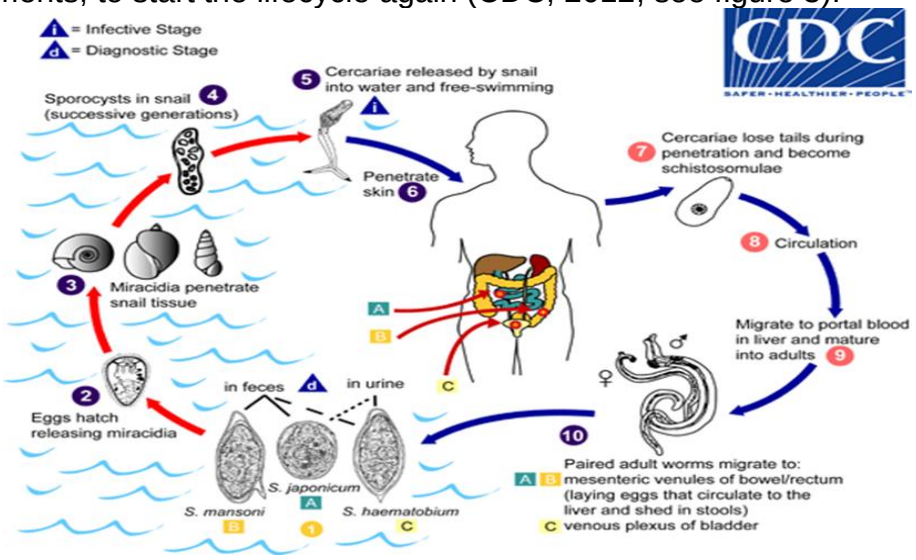

Figure 3. *Schistosoma mansoni* life cycle.

Symptoms of schistosomiasis induced by *S. mansoni* can vary in severity depending on the parasitic load being carried by the host. The infection presents both acute and chronic symptoms, but it is more likely to disable a person for a period that can last many years than to be fatal (WHO, 2016). Symptoms tend to focus around the gastrointestinal tract, because the eggs laid in the venules near the intestine cause a significant amount of tearing damage to the intestinal walls as they cross into the lumen due to the hooks on their surface (see figure 4). This causes abdominal pain, blood in the stool, and diarrhea. There can also be hepatomegaly, enlargement of the liver, from the toxic products released from the adults; splenomegaly, enlargement of the spleen, due to chronic blood loss; tumour development due to inflammatory tissue replacement around the eggs caught in the intestinal lumen; and ascites, fluid accumulation in the peritoneal cavity, due to portal hypertension and pressure imbalances (WHO, 2016; Biological Sciences, 2016). These symptoms often ultimately result in organ failure or the development of cancers in the affected organs (WHO, 2016).

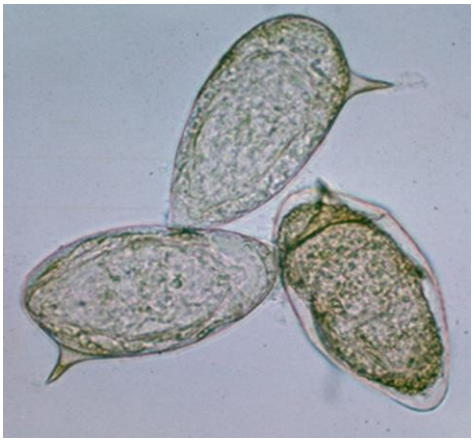

Figure 4. *S. mansoni* eggs.

The current accepted treatment method being advised by the World Health Organization (WHO) involves preventative chemotherapy with single dose administration of the anthelminthic drug Praziquantel (PZQ) (WHO, 2016). A 2013 review of medications being used compared the effectiveness of varying dosages of PZQ only, PZQ combined with Artesunate, Oxamniquine, as well as a placebo. PZQ was found to be the most effective, at a dosage of 40mg/kg of body weight (Danso-Appiah *et al*., 2013). Some degree of resistance has been observed, however. In a study published in 2015, researchers looked at strains of *S. mansoni* exhibiting resistance to PZQ and determined that it was likely due to efflux pumps of the ATP-binding cassette (ABC) transport proteins (Pinto-Almeida *et al*., 2015). These ABC transport proteins include a large variety of membrane proteins that have been implicated in multi-drug resistance by pumping select drugs outside of the cells that the drugs are targeting. (Pinto-Almeida *et al.*, 2015). Tests on mice infected with a resistant parasite strain, determined that administering the efflux inhibitor drug Verapamil in conjunction with PZQ provided an effective method of reversing resistance (Pinto-Almeida *et al*., 2015).

There is currently a great deal of research being done to try to establish a cost effective way of improving both prevention and treatment of schistosomiasis. One example is a 2016 report on the first human clinical trials of a vaccine. In the late 1980s, WHO promoted the study of six vaccine antigens which were extensively tested on animals but never reached human clinical trials. The 2016 report details the results of this Phase 1 safety testing trial of the Sm14 vaccine antigen, derived from adult schistosomes, and found that there was very little in terms of adverse side effects from a course of three vaccinations; and that based upon the previous body of knowledge

and the bloodwork results from the participants, a Phase 2 efficacy study should proceed (Mariliaa *et al*., 2016).

A second example comes from another 2016 study which tested the effectiveness of crude cercarial antigens obtained from the cercariae of *S. mansoni* on mice. Results demonstrated damage to the ventral suckers and tegument of the schistosomes, so this shows potential for the development of a vaccine using these antigens (El Azzouni, 2016). A third example, from another 2016 study, tested the effectiveness of various terpene compounds at killing adult *S. mansoni*. Terpenes are a large group of natural compounds often found in plants and usually possessing a strong odour, and it was found that dihydrocitronellol – a compound isolated from roses and lemongrass – was effective in varying concentrations at causing tegumental damage and death in adult schistosomes (Mafudb *et al*., 2016). This compound has low toxicity levels in humans and can be inexpensively isolated, and as such could lead to future studies of its effectiveness and potential as a main compound involved in the development of medical treatments (Mafudb *et al*., 2016).

In addition to trying to fight Schistosomiasis, humans have also inadvertently influenced its spread. The Aswan Dam is an example of this. This dam was built across the Nile River in Egypt in 1967 as a part of a negotiation between Egypt and the USSR that granted the USSR access to the Suez Canal and Egypt aid in the construction of the dam (Barakat, 2012). While there had always been schistosomiasis in the region, building the dam drastically changed the ecology of the region by halting the yearly flooding of the Nile – which also damaged the fertility of the soil and the livelihood of farmers in the region (Barakat, 2012). Because of this, the Egyptian government built irrigation canals running from the Nile further inland, which created an ideal environment for the snail hosts of two species of Schistosoma where it had previously not been present, increasing infection rates (Barakat, 2012).

Clearly, *S. mansoni* has played a large role in human lives throughout history and, given the current level of infection, it will continue to do so until some major control mechanisms are implemented in countries where infection is prevalent. Given the state of ongoing research and interest in the field, there appears to be hope for finding a more efficient and cost effective mechanism for controlling *S. mansoni* populations.

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