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Global Health and Societal Impacts of Schistosomiasis

By

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Introduction

Schistosomiasis, a parasitic infection, is classified as a Neglected Tropical Disease (NTD). While there are many NTDs that impact poor people across the world, schistosomiasis is one of the most prevalent. Currently 200 million people worldwide are infected with schistosomiasis and 800 million more are at risk for infection. Like other NTDs, this infection is preventable and treatable. Without treatment, the infection can cause serious harm to the host.¹

The parasite that causes schistosomiasis comes from the genus Schistosoma. Schistosoma is a helminth and more specifically a trematode (blood fluke). Three main species of trematode cause infection, *S. mansoni*, *S. japonicum*, and *S. haematobium*. Knowledge of all three species is important as the infecting species occur in different parts of the world and infect different organ systems. *S. mansoni* infects in Africa, the Middle East, and South America, *S. japonicum* in China and Southeast Asia, and *S. haematobium* in Africa and Middle East. *S. japonicum* and *S. mansoni* cause intestinal and hepatosplenic schistosomiasis, and *S. haematobium* causes urinary schistosomiasis.¹

Analysis of the Schistosoma life cycle will help to understand how it infects the host and how to treat the infection. Infected hosts defecate or urinate into a lake or stream releasing eggs into the water, which stimulates them to hatch miracidium within minutes.³ Eggs survive 1-2 weeks inside or outside the host.⁴ Miracidium have up to 16 hours to infect snails (intermediate hosts). They develop over 1-2 months, and then are released as cercaria which have 1-3 days to infect the host. Cercaria are motile and able to penetrate human skin at which point they are swept into blood circulation. They mature into adults in the portal venous system in the liver and then crawl into the mesenteric venous plexus (*S. japonicum* and *S. mansoni*) or the veins that drain the bladder (*S. japonicum*). Male and female adults become intimately attached and engage in sexual intercourse for the remainder of their lives, which on average is 3-10 years. They continuously produce thousands and thousands of eggs. The purpose of this is to get the eggs out of the host to repeat the cycle. However, many eggs don’t make it and will become
trapped in the bladder or intestinal wall. The immune system reacts with eosinophils and form granulomas. Much of the disease of schistosomiasis is due to the host’s immune response to the eggs.\(^2\)

Initial penetration of the cercaria can cause cercarial dermatitis, a local pruritic maculopapular rash, which can appear within minutes. This reaction is commonly known in the U.S. as swimmer’s itch. However, in the U.S. this is a result of bird Schistosoma which is unable to get into the bloodstream and cause a generalized infection. Acute schistosomiasis (Katayama syndrome) occurs 1-4 weeks after infection and is thought to be an allergic reaction to egg antigens. The host will experience fever, shakes, chills, myalgias, and arthralgias, which resolves in days to weeks. Chronic schistosomiasis occurs due to the immune response to the eggs. It lasts years and presents differently depending on the type of schistosomiasis. Urinary schistosomiasis presents with hematuria. Intestinal and hepatosplenic schistosomiasis present with abdominal pain, loss of appetite, and diarrhea (leading to reduced weight to height from undernutrition). Eggs may end up in the brain or spinal cord causing neuroschistosomiasis.\(^1\)

Definitive diagnosis of schistosomiasis is determined by schistosome eggs on microscopic evaluation (Kato-Katz smear) of feces or urine. For acute disease (exposure within the last 2 months) serology can be performed. The acute infection CBC will show eosinophilia, and in chronic disease, anemia. The anti-parasitic agent praziquantel (40mg/kg) is used for the treatment and prevention of schistosomiasis, however praziquantel only kills the adult worms and does not kill the eggs.\(^1\)

To better manage or eliminate schistosomiasis, it first must be understood who gets schistosomiasis, what factors lead to becoming infected, the negative health and economic burden of the disease, and what is being done to fight this prevalent infection. This paper answers these questions and further explores schistosomiasis. It also contemplates the question of future vaccinations, accurate epidemiological surveying, and new management strategies. Schistosomiasis is a NTD that can be eliminated with proper funding and management.
Background

The data from research articles on the prevalence of infection, socioeconomics, quality of life of people infected with schistosomiasis, and mass drug administration (MDA) must be understood when working towards the elimination of schistosomiasis.

Prevalence of infection

To properly manage schistosomiasis countries and their health organizations must collect data on the prevalence of infection. In 2012 the World Health Assembly (WHA) committed to the elimination of global schistosomiasis. In response to that decision, Zoni et al. was written to make epidemiologic data more accessible for Latin America and Caribbean countries. A main finding of the study is the lack of data that is available in many of the endemic countries. For example, some countries have not updated their data since the 1970s. Brazil was the only country with epidemiological data after 2001 of the ten endemic countries (Brazil, Venezuela, Suriname, Saint Lucia, Antigua and Barbuda, Guadeloupe, Martinique, Montserrat, Puerto Rico, Dominican Republic). The lack of data may be due to a low level of resources available to conduct epidemiological surveys and/or the issue of schistosomiasis not given priority. The study emphasizes that this data is needed to best optimize health interventions meant to disrupt transmission.5

Koroma et al. looks at the geographical distribution and preventative chemotherapy strategies of schistosomiasis in Sierra Leone. The study demonstrates the focal nature of schistosomiasis infections. The north and east regions of the country had prevalence rates as high as 70%, while the coast and west regions had prevalence rates less than 10% (Figure 1). The infection was positively associated with population and elevations greater than 250 meters. Efficient MDA depends on surveys and with 800 million people in need of MDA, it must be cost effective if schistosomiasis is to be eliminated.6
Prevalence studies are important in managing schistosomiasis, as effective MDA cannot occur without knowing the population that needs the drug.

**Socioeconomics and access to clean water**

In low income countries, neglected tropical diseases are highly prevalent. Schistosomiasis is one of the conditions with the strongest evidence for substantial socioeconomic inequalities in the distribution of the disease. A systematic review found that not only is there an economic link but also a geographic link with schistosomiasis infection rates. In a Chinese study of *S. japonicum* higher infection rates were found near lake areas and among fisherman. The study found a prevalence rate in poorer villages of 4.7% compared to 2.5% in richer villages. A study from the Cote d’Ivoire found the prevalence of *S. mansoni* to be 39%, 48%, and 57% among those with secondary education, primary education, and no schooling, respectively. A Ugandan study showed the poorest were 54.5 times more likely to become infected than the richest. A Nigerian study found 40% of the participants with household incomes of less than $50.00 had a moderate to severe infection, compared to 0% for households with more than $140.00 monthly income.\(^7\)

Inadequate water, sanitation and hygiene (WASH) are estimated to be responsible for 4.0% of deaths and 5.7% of disease burden primarily from helminths and diarrheal disease. A systematic review and Meta-analysis looked at the relationship between water and sanitation and schistosomiasis. The results of the study showed that access to safe water was associated with an odds ratio of 0.53 (95% CI: 0.47-0.61). Adequate sanitation had an odds ratio of 0.59 (95% CI: 0.47-0.73) for *S. mansoni* infection and an odds ratio of 0.69 (95% CI: 0.57-0.84) for *S. haematobium*. Access to clean water and sanitation for all people would eliminate schistosomiasis.\(^8\)

**Quality of Life and Economics**

The sequelae of schistosomiasis have serious health and economic impacts on more than just the infected individual. Some patients have objective findings that lead to impairment, others may
report subjective findings. A Chinese study looked at how advanced *S. japonica* affects quality of life (QOL) and disability in patients. The study used a EQ-5D questionnaire to self-report QOL in six dimensions (mobility, self-care, participation in usual activities, the presence of anxiety or depression, the presence of pain or discomfort, and altered cognition), ran laboratory tests and performed ultrasonography on subjects with advanced *S. japonica*. The mean hemoglobin was 9.49 g/dl, the main portal vein was 3.9 mm larger than normal values, 96.5% had hepatic fibrosis, and 32.8% had the hepatitis B surface antigen. This objective data means the patients suffer from anemia, portal hypertension, splenomegaly, esophageal varices, ascites, and a comorbid infection of hepatitis B causing the associated symptoms of fatigue, abdominal pain, bloody stools, hematemesis, and loss of appetite. Almost all patients complained of some impairment, moderate impairment in 54.4% and extreme impairment in 41.9%. 90.7% of patients experience pain or discomfort. Disability weight (DW) is a measure of disease severity on a scale of 0 (no disability) to 1 (death). The DW from all the subjects in the study was 0.447.9

Due to fatigue and other symptoms schistosomiasis leads to negative economic impacts from decreased work production. Redekop et al. looks at the productivity loss related to the five most prevalent NTDs (one of them being schistosomiasis). Using the formula (Figure 2) the study projected a loss in U.S. dollars of $102 billion for all five NTD combined for the period 2011-2020, and $127 billion for 2021-2030. Schistosomiasis accounts for $5.5 billion and $11.9 billion respectively for the above time frames, with most of this cost due to the anemia symptom. Soil transmitted helminths are the largest economic contributor of the NTDs. Only individuals older than 15 were included in the productivity loss even though many children work in developing countries. Out of pocket payments including direct costs were also calculated but were significantly less than productivity loss. This can be attributed to the medications being cheap and most people get them for free due to international donations. The study estimates that every dollar invested in NTDs will return $42.80 in the period 1990-2030.10
To further demonstrate the economic impact of schistosomiasis, Lenk et al. quantifies the productivity loss from schistosomiasis. Lenk et al. presents a table of studies and their results. A study in 1998 in Mali of 412 households found that schistosomiasis cost 69 man-days per family worker, which was a 23% annual productivity loss. A Tanzania study from 2008 found that those with acute schistosomiasis missed an average of 7.8 workdays. A 2002 study in China showed that 4.11 workdays were lost for those with advanced *S. japonicum* compared to 0.86 days for the control group.¹¹

**Management**

Schistosomiasis is a focal infection that depends on intensive epidemiological surveying for effective mass drug administration (MDA). MDA is being supplemented with livestock control in China. Surveying showed that Brazil had the highest prevalence of *S. mansoni* infections in Latin America with distinct hot spots in Minas Gerais, Bahia, and Pernambuco. In 2012 only 1.8% of the population that needed praziquantel receive the drug in Brazil and Venezuela, the lowest of any endemic schistosomiasis region in the world. This may be due to health professionals not supporting or not reporting interventions and/or countries not implementing preventative chemotherapy (PC). The study also looks at the intensity of infection because with PC the first indication of its efficacy is the decrease in intensity of infections. With lower intensity infections, it takes less time to reduce prevalence within a population. Therefore, epidemiologic studies should include both frequency and intensity of infection.⁵

Effective MDA starts with accurate information on the geographic distribution of the infection. Knowles et al. performed schistosomiasis mapping in three countries Malawi, Côte d’Ivoire, and Liberia. The study’s goal was to determine the most cost-effective method for gathering epidemiologic data on schistosomiasis without underestimating prevalence. They tested 2, 5, 10, 15, or 20 schools per district and 10, 20, 30, 40, and 50 students per school. Current WHO guidelines suggest 5 schools per district, and 50 children per school. This study presents data that suggest that 15-20 schools per district and 20-
30 children per school would be the most cost effective. The cost efficiency was more effected by schools per district than by students sampled in a school.\textsuperscript{12}

A Ugandan study demonstrates a few ways to increase praziquantel uptake. In 2001, the WHA set a target of 75\% of school-age children to receive praziquantel by 2010, this goal was not achieved. School age children are addressed because the highest prevalence and intensity of infection is among children 10-14 y/o. Currently this is the main technique of controlling schistosomiasis. Muhumuza et al. discusses the strategy of the endemic country of Uganda’s praziquantel program. The study performed a survey in September of 2011, then a follow-up survey in July 2012 after certain strategies were put in place such as training the teachers in drug distribution, printing relevant T-shirts, and supervision from district health staff. This strategy was partially successful with an increase from 28.2\% at baseline to 48.9\% at follow-up. However, among schools that had >50\% participation at baseline, none of these schools had an increase at follow-up.\textsuperscript{13}

The following prevalence study demonstrates that a focused effort against schistosomiasis can have a positive impact on prevalence. Li et al. is a Chinese study that presents recent data on the prevalence of infection and the strategies used by the People’s Republic of China to combat acute schistosomiasis. \textit{S. japonicum} infection control has been given top priority with HIV/AIDS and tuberculosis in China. Strategy has shifted from morbidity control to the control of infection sources (cattle). The following are the new strategies: use of tractors for agricultural activities, keeping livestock in pens and away from marshlands where snails live, requiring fisherman to defecate in containers, gathering stool from humans and domestic animals to produce methane, improving the environment in high risk areas, snail survey and elimination, regular surveys and treatments, and health education. These strategies were implemented in 2004, data collection occurred from 2005 until 2012 (Figure 3). Lake and marshland areas were identified as endemic areas. Most infections occurred in school-age children (42\%), farmers (32\%), and fisherman (9\%). Acute Schistosomiasis cases steadily declined during
the collection time-period. In 2005, there were 564 cases, that number was 207 the next year and in 2012 it was 13. In 2003, 843,011 people were infected with *S. japonicum* (not acute schistosomiasis). In 2011, 286,864 people were infected by *S. japonicum*. The rates of schistosomiasis have reach historically low levels in China.¹⁴

The above data shows the prevalence, the negative effects, the current management, and factors leading to schistosomiasis. It demonstrates why the WHA has called for its elimination by 2020.

**Methods**

I started in-depth research through PubMed. I did an advanced search selecting only systematic review articles. I searched “schistosomiasis”, “schistosomiasis and praziquantel”, “schistosomiasis and effects”, and “schistosomiasis and water.” I saved and printed six relevant research articles. I travelled to Nicaragua where I personally interviewed Gabriel Serrano, the head of nursing of La Mascota Hospital and Dr. Leonel Arguello, an epidemiologist and president of the Nicaraguan Association of General Practitioners. Upon return I searched the Public Library of Science (PLOS) with “schistosomiasis and economics” and “schistosomiasis epidemiology”, and I found 5 more relevant research articles.

**Discussion**

The above research suggests that schistosomiasis is a prevalent disease with significant negative health effects but it is preventable and treatable. With this research, the disease is gaining attention, as the World Health Organization (WHO) has developed standards for preventative chemotherapy and set a goal to eliminate transmission by 2020. The Chinese government is also taking note, as it now lists advanced schistosomiasis as a leading healthcare priority due to its health and economic effects.⁹

Jia et al. demonstrates the negative impact that schistosomiasis can have on the host. The immune system’s response to the eggs leads to portal hypertension, splenomegaly, esophageal varices, ascites, anemia, and a comorbid infection of hepatitis B. These conditions lead to the negative QOL and disability. Many patients in China get a therapeutic splenectomy when they have portal hypertension
due to *S. japonicum* to prevent ascites, upper GI hemorrhage, and helps prevent hypersplenism which causes anemia. Ascites is the strongest predictor of elevated disability level and upper GI hemorrhages leads to mortality in these patients. Those with HBV infection and *S. japonicum* have higher morbidity and mortality than compared with either infection alone.\(^9\)

The impacts on the host extend beyond the health of the host. Schistosomiasis affects an individual’s ability to be a productive member of society. Lenk et al. and Redekop et al. are studies discussed above that focus on this aspect of schistosomiasis. Workers with schistosomiasis are more likely to be at work and less productive (presenteeism) than missing work (absenteeism). This means that these workers are not being replaced with healthier workers because they are still showing up for work. Schistosomiasis is seen in poor populations in developing countries. Most of the work that this population performs is manual labor. One of the main sequelae of schistosomiasis is anemia, which the main symptom is fatigue. Therefore, workers with schistosomiasis will not be able to perform the same amount of work as a healthy worker. Following this thought process, it is not surprising that Redekop et al. found that anemia was the largest economic burden of schistosomiasis.\(^{10,11}\)

Schistosomiasis is managed with mass drug administration (MDA) with praziquantel, snail control, host control, and improving access to safe water and sanitation. MDA is currently the main way of controlling schistosomiasis because it is more achievable and realistic than providing the world population with clean water. Obviously, clean water would be the best solution, not only for Schistosomiasis but many other NTDs. China has started to focus on controlling not just snails but also livestock that are able to transmit the infection to humans. Li et al. is an important study as it demonstrates a different and effective way of reducing schistosomiasis. It also demonstrates that this infection, which impacts the entire world either directly or indirectly, can be significantly reduced given the attention it requires. It is important to note that most parts of the world with schistosomiasis do not have infected livestock. The focus remains on MDA with praziquantel.\(^{14}\)
The MDA study in Uganda was not able to reach the goal of 75% set forth by the WHO despite making significant improvements. The strategies they had did not include education of the teachers or the children, in fact the study states that “no change in proportion of children who had correct knowledge of schistosomiasis transmission and control at follow-up.” I believe education is a strategy that could achieve the goal of 75%. Education should give the children the motivation to take the medication and the teachers the ability to encourage the children to take it. The side effects of praziquantel can cause discomfort and are worse without food. Providing food before a dose of the medication may increase uptake.13

Knowles et al. and Koroma et al. discuss the need for epidemiological surveying in schistosomiasis prior to praziquantel distribution. As Zoni et al. demonstrated that many countries with schistosomiasis have outdated epidemiologic surveys. These surveys are important for several reasons. First, schistosomiasis is a very focal infection where a high prevalence of infection in one village is a poor indicator for the level of infection in a neighboring village. Second, the WHO treatment guidelines are based on local prevalence, and the treatment differs based on prevalence (Table 1). Third, praziquantel causes unpleasant side effects that should be avoided if the drug is not indicated for use. Finally, proper surveying can save money as unnecessary doses are avoided. The recommendation from Knowles et al. is that 15-20 schools per district and 20-30 children per school is the optimal survey template for schistosomiasis. Following these guidelines, countries can minimize their cost per district treated, develop accurate epidemiologic data, while minimizing the risk of failing to detect a treatable level of infection.6,12

Global companies should be concerned with schistosomiasis. With modern travel and communication, many global companies export their factory or field jobs to developing countries where the work is cheap and workers are bountiful. If workers in these developing countries have schistosomiasis, Redekop et al. demonstrates that productivity will be lost. Lost productivity equals
money lost for these large companies. This may be the best way to get developed countries fully
invested in the elimination of a developing countries’ disease. Based on the cost to funders compared to
the cost of productivity loss an investment of one dollar in eliminating schistosomiasis could return
$42.00. This statistic alone could pique the interest of those in business who seek to optimize their
return on investment. However, certain businesses have taken an interest in schistosomiasis, as the Bill
and Melinda Gates Foundation have spent close to $50 million for MDA in six African countries.\textsuperscript{10,15}

Most of the money that is spent on schistosomiasis is on praziquantel. Praziquantel is
affordable, effective, and available. However, it does not address the clean water issue that causes other
diseases and demands indefinite drug distribution. Praziquantel can cure schistosomiasis but reinfection
rates are high, as it does nothing to prevent transmission. This makes it an incomplete solution as the
long-term outlook is limited by reinfection. Bergquist et al. discusses the need for a vaccine which could
work to prevent transmission. Vaccines would not act alone but with MDA. For instance, the vaccine
may be given after a dose of praziquantel. This article calls for more research and development into the
creation of a vaccine, and another drug if schistosomiasis were to start developing resistance to
praziquantel (Figure 4). The article is from 2008 and discusses the low disability-adjusted life year (DALY)
score from the WHO. Suggesting that it should be in the top category with malaria and tuberculosis. Li et
al. and Jia et al. from China both support this argument, as does the Chinese government in more recent
articles. A vaccine has not been developed, but there is the potential for one, and it is being worked
on.\textsuperscript{15}

Schistosomiasis is not prevalent in Nicaragua. However, mass drug administration is used for
other parasitic infections. We met with the head nurse of La Mascota Hospital, a public children’s
hospital in Managua. He stated that schistosomiasis was present in the country, they give nationwide
praziquantel twice a year to every kid until the age of 12, and that the drug was cheap and available to
all children. Shortly after, our guide informed me that his children have never received that drug. The
next day we visited an epidemiologist at a private health clinic. He told a different story. Nicaragua does not have schistosomiasis and they give albendazole to children to prevent other parasitic infections such as ascariasis, whipworm, and hookworm. It appears they use albendazole to eliminate other parasitic infections in a similar strategy as other countries use praziquantel to eliminate schistosomiasis.\textsuperscript{16,17}

**Conclusion**

The neglected tropical disease schistosomiasis is a parasitic infection that has a complex life cycle including a snail as an intermediate host. The snail enables the growth of cercaria that penetrate the skin of a host, enter the bloodstream and mature into adults. Adults continuously reproduce, producing eggs which leave the host through stool or urine, or they implant in tissues and cause disease. 200 million people worldwide have schistosomiasis and 800 million are at risk. Three species of the genus schistosoma account for most schistosomiasis cases. The species vary in location, organs they infect, snail hosts, and severity of illness. Schistosomiasis can be a life-long illness that significantly impacts the host’s quality of life. Workers with the infection are less productive, costing billions of dollars. Schistosomiasis disproportionately infects poor people in developing countries, and therefore struggles to gain the attention that it requires. Mass drug administration of the anti-parasitic drug praziquantel (the only drug available to treat schistosomiasis) is currently the main method of control. Although, China has recently demonstrated success by employing strategies that involve controlling the infection in the livestock population. Epidemiological surveys should be performed to maximize cost efficiency and proper distribution of praziquantel. Praziquantel cures schistosomiasis but it does not help to prevent reinfection. Therefore, it must be continuously supplied and is a temporary fix. A vaccination would be key to the elimination of schistosomiasis since clean water and proper sewage disposal for everyone in the world is a task that is far from completion and may never occur.
References


Appendices

Figure 1. Geographical distribution of intestinal schistosomiasis and soil transmitted helminthiasis in Sierra Leone. (A) Intestinal schistosomiasis (B) Hookworm (C) Ascaris lumbricoides (D) Trichuris trichiura

\[ TPC_{cNTD} = \sum_{y} \left( PS_{1c,y} * PLs_{1c,y} * I_{c,y} \right) + \left( PS_{2c,y} * PLs_{2c,y} * I_{c,y} \right) + \ldots \]

\[ \frac{1}{(1 + D)^t} \]

Fig 2. General formula for calculating productivity loss.
TPC = Total productivity costs (in US$ 2005)
NTD = Neglected Tropical Disease
c = Country
y = Year
PS1 = Number of prevalent cases aged 15+ years with sequela 1
PS2 = Number of prevalent cases aged 15+ years with sequela 2
PLs1 = % productivity loss related to sequela 1 of NTD
PLs2 = % productivity loss related to sequela 2 of NTD
I = GDP per capita in the lowest quintile
D = Annual discount rate (%)
t = Time (years beyond 2010).
Figure 3. Annual and weekly trends of acute schistosomiasis cases from 2005-2012.

Table 1. WHO treatment guidelines for schistosomiasis, according to estimated prevalence.13

<table>
<thead>
<tr>
<th>Endemicity level</th>
<th>Schistosomiasis prevalence (pooled species) based on parasitological methods</th>
<th>WHO recommended treatment strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-endemic</td>
<td>&lt;1%</td>
<td>No treatment</td>
</tr>
<tr>
<td>Low</td>
<td>≥ 1% and &lt;10%</td>
<td>Treat school-age children twice during primary school years</td>
</tr>
<tr>
<td>Moderate</td>
<td>≥ 10 and &lt;50%</td>
<td>Biennial treatment of all school-age children; as well as special risk groups in adults</td>
</tr>
<tr>
<td>High</td>
<td>≥ 50%</td>
<td>Annual treatment of all school-age children; as well as special risk groups in adults</td>
</tr>
</tbody>
</table>
Figure 4. Yardstick for Financial Resource Allocation Based on the Global Burden Awarded to Each Disease in TDR’s Portfolio in the 2001–2002 Biennium (Top) and the 2007–2008 Biennium (Bottom). The figures show that the diseases fall into two relatively distinct groups, (i) well-funded (i.e., malaria and tuberculosis), and (ii) less well-funded, including leprosy, which is now targeted for elimination as a threat in public health. Note the particularly low amounts currently allocated to schistosomiasis and lymphatic filariasis in relation to the estimated global burden of these diseases.15
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