DIAGNOSTIC TARGET PRODUCT PROFILES

for monitoring, evaluation and surveillance of schistosomiasis control programmes

World Health Organization

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1. Introduction

Schistosomiasis is a parasitic disease of 240 million people globally (*1*). Infection occurs when people come into contact with contaminated water populated with the appropriate intermediate host snail. Larval parasites penetrate the skin and enter the body where they mature into adult male and female worms, mate and produce eggs. Some eggs released by adult females exit the body to continue the parasite's life cycle; other eggs become trapped in host tissues where they stimulate immunological responses that cause the morbidity associated with schistosomiasis.

2. Epidemiology

Human schistosomiasis, also known as bilharzia or "snail fever", is caused by five main species of trematodes of the genus *Schistosoma*. Approximately 90% of infections and the vast majority of morbidity occur in sub-Saharan Africa, where the two primary species responsible for human disease are *S. mansoni* and *S. haematobium*. Adult *S. mansoni* worms live in the mesenteric veins surrounding the intestines. To complete the life cycle, eggs must make their way to the lumen of the gut where they are excreted in host faeces. However, many eggs are washed by the portal circulation to the liver where they become trapped and stimulate granulomatous responses. Over time, untreated schistosomiasis can stimulate fibrosis of the liver and increased portal pressure, resulting in liver and spleen enlargement. In the most severe cases, ascites and oesophageal varices develop and can lead to haematemesis and death. Asian schistosomiasis caused by *S. japonicum* and *S. mekongi* has clinical manifestations like those of *S. mansoni* infections (*2*).

S. haematobium adult worms live in the blood vessels surrounding the bladder; eggs are excreted in the urine, resulting in haematuria which can be microscopic or visual. Chronic infection can result in bladder fibrosis with obstructive uropathy and is associated with increased risk of squamous cell carcinoma of the bladder. Worms in the venous plexus can also result in egg deposition in genital tissues, causing female and male genital schistosomiasis, which is associated with greater risk of HIV transmission (*3*). These severe morbidities tend to affect older individuals who have been infected for several years. However, the bulk of the more than 1.6 million disability-adjusted life years (*4*) caused by schistosomiasis worldwide affect children, who have the highest prevalence and intensity of infections. Morbidities in children include anaemia, delays in physical and cognitive development, and reduced tolerance to exercise (*2*).

3. Public health response

Because the prevalence and intensity of infection peaks at 7–15 years of age, the main strategy for control of schistosomiasis focuses on mass drug administration (MDA) of praziquantel, in priority to primary school-aged children. Praziquantel is safe for people who do not have infections, and it is more cost-effective to treat all school-aged children in a community above a certain prevalence threshold than to test and treat each individual. MDA is typically administered by control programmes in areas endemic for schistosomiasis once each year. However, MDA is not enough to interrupt transmission without additional measures such as increased access to clean water and sanitation, control of intermediate host snails, or education and behavioural change. As a result, WHO guidelines for most countries target control and then elimination of morbidity.

In general, higher intensities of infection are associated with higher levels of morbidity, but these relationships are poorly defined, and most control programmes monitor only prevalence of infection and not intensity (*5*). Research is under way to better define the relationship between prevalence, intensity of infection and various manifestations of morbidity; for the time being, the working guidance for control programmes is to administer MDA annually in communities with ≥ 10% prevalence among primary school-aged children (*6*). Because distribution of schistosomiasis is highly focal, implementation decisions are applied at the subdistrict level. Operational research is required to determine the frequency and design of epidemiological assessments to measure the impact of schistosomiasis programmes and support decision-making aligned to the focality of infection as well as determining persistent hotspots of transmission where community levels of infection are not responding to current MDA intervention.

4. Available diagnostic tools

Traditionally, schistosomiasis has been diagnosed by detecting parasite eggs in host stool (*S. mansoni S. mekongi, S. japonicum*) or urine (*S. haematobium*) (*7*). These methods have the advantage of providing information on both prevalence and intensity of infection and, theoretically, they can distinguish active infection from successful cure and/or subsequent reinfection. However, it is sometimes difficult to obtain samples for egg detection methods, their sensitivity for low intensity infections is poor, and they require access to microscopes and trained personnel. Usually, samples are processed in a laboratory distant from the site.

Circulating cathodic antigen (CCA) is regurgitated from the blind gut of schistosomes, cleared by the patient's kidneys and excreted in the urine. Like eggs, urinary CCA disappears after successful cure and resumes after reinfection. It also provides a relative intensity of infection and is considered much more sensitive than egg detection. A point-of-care CCA test is commercially available. Unfortunately, current formulations of the test are reliable only in high-prevalence areas and the false-positivity rate is too high to accurately determine prevalence < 10% (*8*). Furthermore, recent manufacturing issues have yielded product lots of variable performance and very high false-positive rates (*9, 10*). Even when working well, the point-of-care CCA test is much more effective at detecting *S. mansoni* infections than other schistosomiasis species infections (*11, 12*).

Like CCA, circulating anodic antigen is also detectable in an infected host's blood or urine, is a marker for active infection, provides information on relative intensity of infection and has the added advantage of being produced in detectable amounts by both *S. mansoni* and *S. haematobium* (*13*). However, it is not available as a commercial test, and current developmental tests require laboratory equipment for sample concentration and final test readout. Polymerase chain reaction to detect parasite DNA in stool