

Water and health

Dangers in our water – Fighting the scourge of bilharzia

The waterborne parasitic disease schistosomiasis is not being taken seriously as a public health issue in South Africa, despite a growing body of evidence that it increases susceptibility to HIV infection and raises the risk of cancer.

Sue Matthews reports.



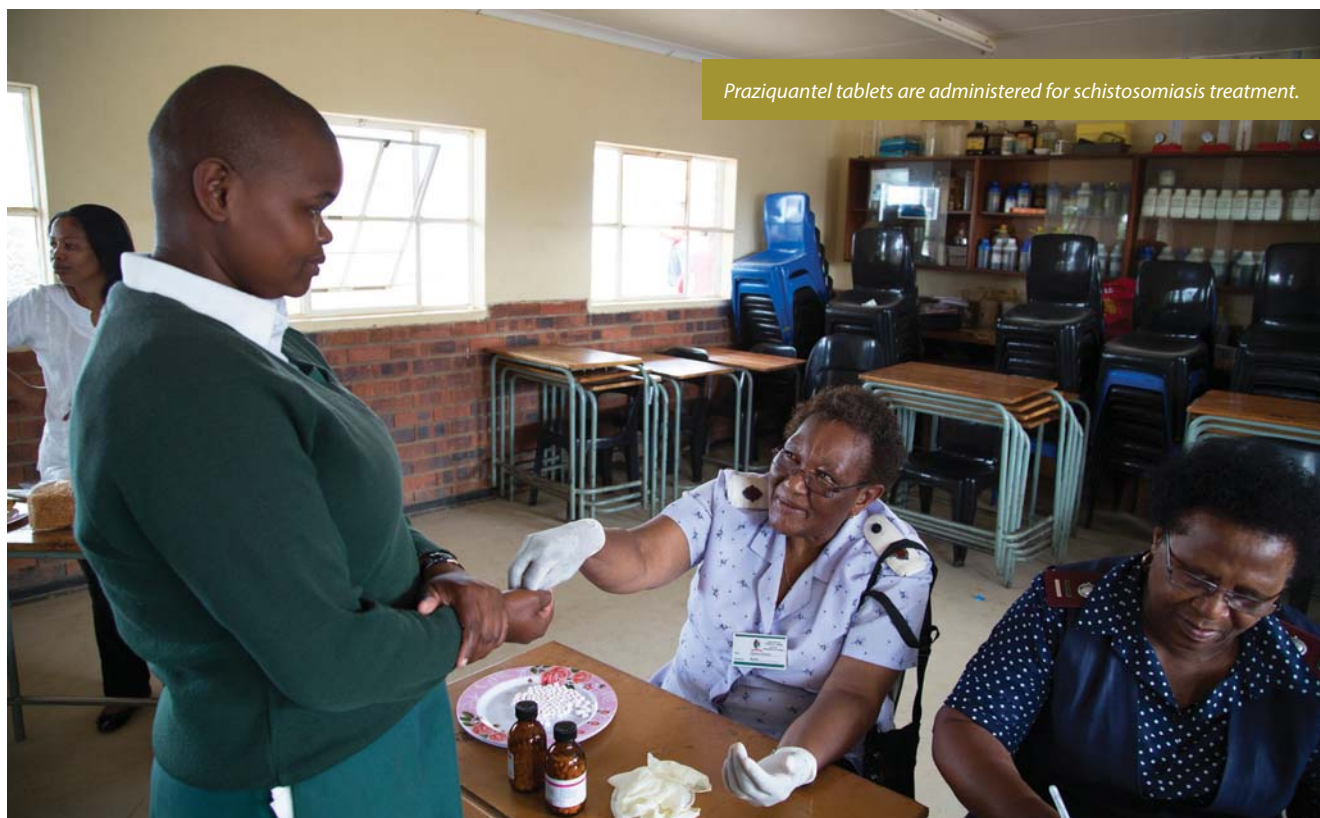
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When schistosomiasis – commonly known as bilharzia after its discoverer, Dr Theodor Bilharz – first came to the attention of South Africa’s medical professionals, it was thought to affect mainly boys. After initially being recorded in 1863 in Port Elizabeth, numerous case reports until the turn of the century (when the disease disappeared from the south-eastern Cape) indicated that it was primarily boys between the ages of 3 and 16 who were infected with the parasitic blood fluke *Schistosoma haematobium* – a species of trematode flatworm – after swimming in local waterbodies.

The most common symptom was haematuria, the medical term

for blood in the urine, but colloquially referred to as ‘redwater’ at the time. This often stopped by the age of 20 because men rarely swam, reducing the chance of further infection, although it was recognised even then that the parasite probably persisted in the body. Girls and women were thought to be seldom affected because their contact with waterbodies was more limited.

In 1899, however, 48 years after Bilharz had discovered the worm in the veins of an Egyptian man during an autopsy, *The Lancet* published a paper entitled ‘A case of bilharzia of the vagina’, describing a prominent warty mass. This was the first report of schistosomiasis in the genitals of a woman – perhaps not so



Praziquantel tablets are administered for schistosomiasis treatment.

coincidentally an Egyptian woman, given that evidence of the disease has since been detected in Egyptian mummies dating back 5 000 years!

Today, female genital schistosomiasis is known to affect all parts of the internal and external female genitalia. Adult worms in the surrounding veins and venules lay copious quantities of eggs, many of which become lodged in tissues of the bladder, ovaries, fallopian tubes, uterine cervix, vagina and vulva. There they cause lesions, bleeding and painful inflammation, as well as a variety of secondary effects. For example, alteration of tissues in the fallopian tubes has been linked to infertility and life-threatening ectopic pregnancies, while lesions in the vagina and cervix increase susceptibility to HIV infection. The disease is also associated with an elevated risk of bladder cancer, and possibly cervical cancer too.

With the growing understanding that *Schistosoma haematobium* infection affects both the urinary and genital tracts (in men, eggs are commonly found in the seminal vesicles and prostate), the name of the disease has been changed in recent years from urinary schistosomiasis to urogenital schistosomiasis. The parasite occurs primarily in Africa and the Middle East, although since 2013 there has been an outbreak in Corsica, which infected visiting tourists from other nationalities. By contrast, five other species of *Schistosoma* cause intestinal schistosomiasis in various parts of the world, but only one of these, *Schistosoma mansoni*, occurs in South Africa and is more limited in distribution.

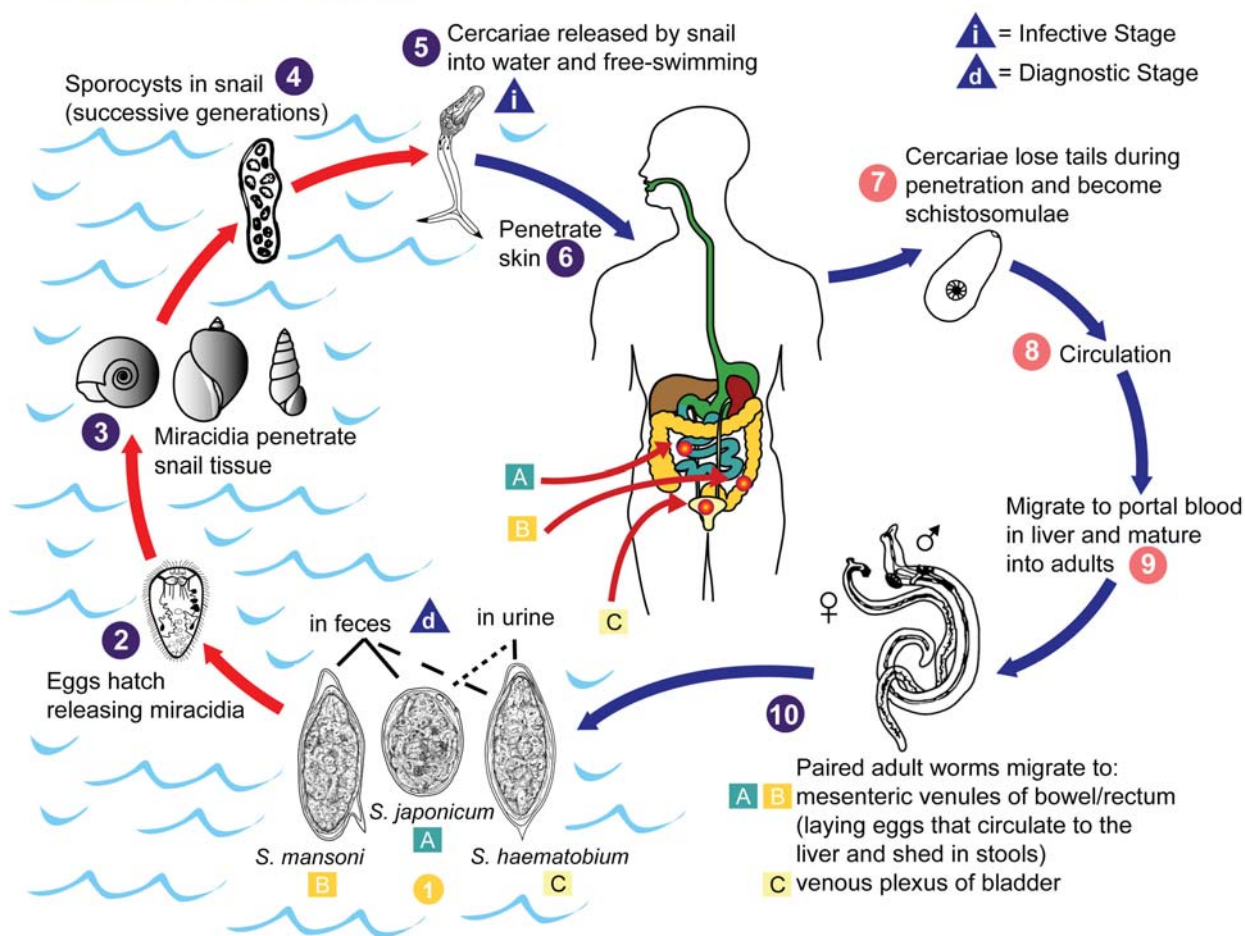
Schistosoma eggs may travel beyond the target organs to other parts of the body and become trapped in the brain, spinal

cord, pancreas, kidneys, liver or lungs, leading to neurological symptoms, high blood pressure, kidney failure, liver damage and other serious complications. The mortality rate due to schistosomiasis is unknown because the cause of death is often linked to these complications, but has been estimated at more than 200 000 deaths per year.

Many people are not even aware they have been infected by the parasite, however, because they either have no symptoms or develop a fever, cough, swollen glands, aches and pains, or a general feeling of malaise and fatigue that they put down to the flu, their living conditions or some other illness. It may take years before a sudden deterioration in health prompts them to seek medical attention. One young woman in the United States had seemed perfectly healthy until she had a seizure due to *Schistosoma* eggs in her brain, four years after spending a semester in Ghana, where she had swum in a river on just one occasion!

In the case of female genital schistosomiasis, patients presenting at clinics with pelvic pain, abnormal discharge or genital itching are often given antibiotics for sexually transmitted chlamydia, gonorrhoea or trichomoniasis before the possibility of cervical lesions due to schistosomiasis is considered, while lesions on the vulva may be confused with genital warts caused by the Human Papilloma Virus. Many girls and women might be too embarrassed to seek treatment, but others are simply misdiagnosed. Even those that are given a gynaecological exam are at risk of unnecessary referral for cervical cancer treatment.

Schistosomiasis



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People may contract schistosomiasis after wading, swimming, bathing or washing in contaminated water. Parasite larvae that have been shed from the intermediate host snails penetrate the skin and then develop into adult flatworms inside the body, where they form mating pairs. Some of the eggs produced are excreted in urine and faeces, and hatch if deposited in freshwater. These larvae enter the intermediate host snails to continue the cycle.

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In 2014, in an effort to increase knowledge of female genital schistosomiasis and improve its diagnosis, an expert group of medical researchers and clinicians published a comprehensive ‘atlas’ of the disease’s manifestations in the lower genital tract in the open-access, online journal *PLoS Neglected Tropical Diseases*. More recently, the World Health Organisation (WHO) has published a more user-friendly ‘pocket atlas’ for distribution to clinical health-care professionals. This is essentially an illustrated guide to schistosomiasis lesions on the cervix and vaginal wall, using photocolposcopic images captured during gynaecological exams of consenting patients in Malawi, Madagascar and South Africa. The lesions are divided into four types – grainy sandy patches, homogenous yellow sandy patches, abnormal blood vessels or rubbery papules – all of which can be identified during visual inspection with the naked eye or a colposcope.

The pocket atlas was launched in May at the South African Congress for Gynaecologists and Obstetricians, and is being widely distributed as both a hard copy and PDF. The booklet was compiled with the assistance of a number of clinicians and researchers working in southern Africa, with staff from the University of KwaZulu-Natal’s medical faculty playing a leading role. The university has long been the main academic centre for schistosomiasis research in South Africa, focussing on the freshwater snails that serve as the intermediate hosts of the parasites, as well as the disease itself. Two members of its Discipline of Public Health Medicine – Dr Eyrun Kjetland and Prof Myra Taylor – founded and currently co-lead the international research group BRIGHT, an acronym for ‘Bilharzia Research Improving Global Health Today’.

BRIGHT is a collaboration of eight partner institutions in South Africa and Europe, and was specifically set up to study female genital schistosomiasis. Work began in the Ugu District in southern KwaZulu-Natal in 2009. Urine sample collection from approximately a thousand girls of 10-12 years of age from 18 rural primary schools revealed that 32% had *Schistosoma haematobium* eggs in their urine. During interviews, many of these girls reported symptoms such as stinking, bloody

discharge, ulcers, tumours and a burning sensation in their genitals.

Subsequently, BRIGHT researchers have extended their reach to more than 40 schools in three districts, collecting urine, stool and blood samples, conducting confidential interviews and physical examinations, offering counselling and group discussions, and taking part in information sessions and parents' meetings. Working with nurses from the three district health departments, more than 175 000 learners were treated between 2011 and 2014.

The recommended treatment for all forms of schistosomiasis is a single dose of 40 mg/kg of praziquantel. This kills the adult worms, but is probably not sufficient to eliminate all eggs. Furthermore, while it may resolve or provide some relief from urogenital lesions, especially in children, advanced cases in adult women are resistant to treatment.

The WHO therefore recommends regular treatment from an early age to prevent schistosomiasis from progressing to genital damage and other complications. In high-transmission areas, praziquantel should be administered every year to entire communities or routinely in health facilities.

At the 2001 World Health Assembly, a resolution urging countries to start tackling worms – specifically *Schistosoma* species and soil-transmitted helminths – was endorsed by all WHO Member States, including South Africa. The 'Global Target', against which each country's progress would be measured, was for at least 75%

of all school-aged children at risk of illness from schistosomiasis or soil-transmitted helminths to be regularly treated by the year 2010. In order to reach that goal, a 'sub-goal' was set, stating that all health services in endemic areas should be stocked with the drugs to treat these infections.

By the time 2010 came around, however, it was clear that the Global Target had not been met, and in May 2012 a new resolution was adopted at the 65th World Health Assembly. This calls on countries endemic for schistosomiasis to intensify control interventions and ensure the provision of essential medicines, amongst other matters.

But in a paper published recently in the *South African Journal of Science*, entitled 'A review of the control of schistosomiasis in South Africa', Taylor, Kjetland and co-authors from the University of KwaZulu-Natal lament the lack of progress in this regard, given that more than 4 million people are estimated to be infected with the disease in this country.

"In South Africa, only Bayer's Biltricide® (praziquantel) is available for the treatment of schistosomiasis. The Department of Health purchases praziquantel for schistosomiasis at a cost of US\$4.49 per tablet, making mass treatment programmes unaffordable and almost impossible to run in South Africa. Praziquantel is not even fully stocked in local clinics at the moment as it is too expensive."

"Contrary to the current practice in South Africa, other countries accept WHO-accredited generic praziquantel. These simple,

Dr Eyrun Kjetland hands out consent forms during a BRIGHT school visit





Urine samples are collected to check for blood cells and *Schistosoma haematobium* eggs.

Håvard Holme

effective, cheap and commercially available generics are of excellent quality, have been on the market for more than 20 years and have been used widely in schistosomiasis control programmes.”

The authors note that, as a Schedule 4 drug, praziquantel must currently be dispensed by a professional nurse. They encourage the relevant authorities to consider rescheduling this drug, which does not have serious side effects, and also to take urgent action towards registering the generic forms of praziquantel. They conclude by pointing out that a well-structured schistosomiasis control programme has the potential to contribute to a reduction in the prevalence of HIV amongst young women.

Since the publication of the paper, the government has launched the National School Deworming Programme, which will be rolled out annually to Grade R to 7 learners in quintile 1 to 3 schools – the poorest schools in the country. However, this will target only soil-transmitted helminths, namely roundworm, whipworm and hookworm, which can be treated with mebendazole. This is registered as a Schedule 1 drug, which anybody can access over the counter. The WHO has donated seven million mebendazole tablets for the South African programme.

Fast-tracking the registration of praziquantel generics that are already widely used in schistosomiasis control programmes elsewhere in the world would pave the way for further assistance. Since 2007, Merck has donated 340 million of its generic tablet to the WHO, with over 74 million patients, mainly school children, treated to date. In 2015 alone, more than 100 million tablets were distributed across 23 African countries. The intention is to increase this donation to 250 million tablets per year, corresponding to the number of people believed to be infected with schistosomiasis worldwide. The pharmaceutical giant hopes to advance the WHO’s goal of eliminating the

disease, and to this end it launched the Global Schistosomiasis Alliance with other partners in December 2014.

“Many people are not even aware they have been infected by the parasite.”



The WHO Female Genital Schistosomiasis Pocket Atlas is an illustrated guide to the lesions that would be visible during a gynaecological exam.

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Of course, mass treatment campaigns are only one means of addressing schistosomiasis. In the past, before safe drug therapy was available, control of the intermediate snail hosts via molluscicides and/or habitat modification was an important part of the WHO-recommended strategy. Although these methods had negative environmental impacts and were labour-intensive, the World Health Assembly’s 2012 resolution stimulated debate as to whether snail control should again be promoted.

There is general agreement, though, that multi-faceted, integrated control programmes are needed, incorporating education and awareness-raising to encourage avoidance of infested waters, and – of course – safe water supply and sanitation for all.