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Three years after leaving his native Somalia, a 32-year-old man stepped into the Marshfield Clinic in Rice Lake, Wisconsin complaining of ongoing abdominal pain and discomfort on going to the bathroom. He had been referred there by his healthcare practitioner who had been unable to help him, and referred him to the clinic’s Dr Peter Neal.

When I spoke with Dr Neal, he told me he remembers the day well because at that time it was unusual to have a patient from Africa. He also remembers how the patient had been increasingly frustrated at questions asked by his regular healthcare practitioner about his lifestyle, sexual history and family history that had thrown no light on the problem, a course of the antibiotic ceftriaxone had been ineffective, and tests for ophthalmic and rheumatologic illnesses had all come back negative.

Intrigued and concerned, Dr Neal found a clue in the form of traces of blood in the urine (hematuria). Then, as detailed in his November 2004 article in *Clinical Medicine & Research*, Dr Neal scheduled an intravenous urogram that revealed mild dilation in the ureter. A subsequent cytoscopic examination showed the bladder urothelium was peppered with punctate white lesions. Ureteroscopy revealed a build-up of tissue in the distal ureter. By themselves, these results illustrated the root of the pain, but not the root of the problem. However an additional biopsy of both tissue areas showed the cause right away. The tissue was laden with the eggs of *Schistosoma haematobium*: a parasite largely unknown in the United States, but which is responsible for widespread debilitation in countries across Africa.

Dr Neal had gained some knowledge of schistosomiasis through his work that resulted in an article published in the *Nebraska Medical Journal* in August 1995. He was also fortunate to be working alongside several doctors with firsthand experience of
practicing medicine in Africa. So he was immediately aware of the medicine that was needed, and put the patient on praziquantel 20 mg/kg every 6 hours for 24 hours. The treatment was successful, and after several months of post-treatment monitoring, the patient was declared fit and free from any lasting damage.

For this patient in Rice Lake, Wisconsin, the treatment of schistosomiasis was simple and cost effective. Additionally, it was final as long as the patient continued to live in an affluent country with easy access to clean, filtered water and reliable sewage systems. However, in many African countries without access to clean water and biomedicine, schistosomiasis can take a much stronger hold with frightening consequences. In fact, it is considered by World Health Organization (WHO) to be the most devastating parasitic disease in terms of public health impact and socioeconomic loss. Indeed, WHO estimates in their "Scientific Working Group's Report on Schistosomiasis (2005)" that more than 600 million humans are at risk of schistosomiasis worldwide, while a further 200 million are already infected. Furthermore, approximately 85% of these cases are found in sub-Saharan Africa, where it compounds existing problems of poverty and disease, and hampers hopes for future prosperity through its impact, particularly on the young. But since 2002, more action is being taken and more progress is being made through the work of the Schistosomiasis Control Initiative (SCI), an organization based at Imperial College, London that began operations in 2002 thanks to an award of GBP20 million from the Bill and Melinda Gates Foundation.

Mapping the problem

According to the article Epidemiology and geography of Schistosoma mansoni in Uganda: implications for planning control, which appeared in Tropical Medicine and International Health in 2004, approximately 16.7 million humans in the Uganda were at risk of schistosomiasis infection and a further 4 million humans in Uganda were already infected when the SCI first targeted the country. So the biggest question for the SCI was one of where to start. Of course, the obvious answer to this question was to begin with the worst-affected populations. But where were they exactly?

The SCI took a technologically advanced approach to this question, as described in an article by Kabatereine et al that was published in WHO's Scientific Working Group, Report on Schistosomiasis, 2005. The SCI began by mapping the parasitological data of 23,627 humans in a total of 271 schools or...
communities from 1997 to 2002 throughout the country using Geographical Information Systems (GIS). Then, by overlaying the map of parasitological data over another map illustrating environmental data, the SCI was able to see the ecologic limits of transmission, and to reveal that no transmission was occurring in areas with total rainfall of less than 900mm or with altitude of more than 1400m. Not only did this help them in their immediate mission, but it also made for more efficient future methodology by allowing all such areas to be discounted from further surveys. The SCI then took its next step against schistosomiasis from space, using high-resolution Landsat satellite data to integrate the whereabouts of lakes and rivers into their existing knowledge. Through this, they discovered that the prevalence of schistosomiasis was highly likely to exceed 50% in areas within 5km of lakes Victoria, Kyoga, and Albert, and the Albert Nile. Armed with this wealth of information, the SCI was then ready to take the fight against schistosomiasis to the ground.

An expanding wave of action

To make the best use of funds, the SCI began rolling out control activities in an expanding manner. This method allowed the organization to gain valuable experience during smaller scale operations, and then apply everything learned when the time came for full-scale action. This is described in detail in Working Paper 3. Implementation Strategies For Schistosomiasis Control In Uganda, And Research Needs Under The Programme that appeared in the WHO Scientific Working Group Report on Schistosomiasis, 2005, which states that the SCI began with a pilot wave of control activities limited to 450,000 humans in a single sub-county of each of the 18 worst affected districts of Uganda. The SCI then progressed to a second wave of treatment in 2004 that expanded activities in each of these 18 districts to include 2 or 3 more sub-counties and to treat approximately 1.5 million humans. Then, in April 2005, they launched their major attack on schistosomiasis, scaling up efforts to cover all endemic areas in the country and to give treatment to approximately 3.5 million humans. Following this, the Uganda programme moved into its maintenance phase, where it will continue to treat the worst affected areas until they are at a level where schistosomiasis is no longer a public health problem.

Methods for successful control

In each of these areas of treatment, the same tried and trusted methods were applied. Sixty boys and 60 girls of school-age were selected at random from each community. These children were then photographed for identification purposes and for treatment records before being taken through a health questionnaire by staff from Uganda's Vector Control Division, from the SCI, or specially trained school teachers. Height, weight, and other anthropomor-
Physic measurements were taken for each child as an early means to identify organomegaly. Then a trained nurse performed palpation of the liver and spleen or the Vector Control Division used mobile ultrasound equipment to perform an examination to investigate liver fibrosis as well as liver and spleen morbidity. Following these checks, each child was asked to bring in a urine sample and a stool sample wrapped in a small piece of plastic film - the former was subjected to a rapid Hemastix urine test for the presence of blood, while the latter was subjected to microscope examination for the presence of schistosome eggs. In line with WHO guidelines, 100 to 400 eggs /g were taken to indicate a moderate infection and more than 400 eggs per gram were taken to indicate a severe infection. The results of the sample populations were then calculated in percentage terms and de-worming chemotherapy were also administered in accordance with WHO guidelines - with a rate of infection of 20% or more necessitating medication of the entire school and an infection rate of 50% necessitating medication of the whole community.

As the only effective medicine against schistosome infection, all patients were administered praziquantel with a dosage calculated through use of a validated dose pole that allows teachers and community health workers to dispense within an acceptable range of accuracy. This pole effectively does away with the need for weighing scales and calculations, both of which are prone to error, and more information on it can be found in the Uganda National Bilharzia And Worm Control Programme District Officials and Training of Trainers Manual 2004 that can be downloaded from the SCI website. All patients were also given albendazole (400mg) to combat other helminth-associated diseases. Finally, at the end of the same extremely busy day, the location data for each school was logged using satellite technology to enable accurate progress.

Highly affordable, highly viable

In addition to being highly effective, Praziquantel is also highly cost-efficient. Indeed, since its development in the mid 1970s by Bayer and E. Merck, various factors have continued to push the price of the drug downwards. A 1998 article entitled “International strategies for tropical disease treatments. Experiences with praziquantel” by MR Reich describes how price competition for praziquantel began in 1983 with the development of a new process patent for the product by the Korean company Shin Poong Pharmaceutical. Prices were then cut further through Shin Poong licensing production of praziquantel to EIPICO in Egypt, a move that helped Shin Poong to become the world’s largest producer of the drug by 1993 with a 55% share. Then, when the patents held by Bayer and Merck expired in various countries between 1989 and 1994, market competitiveness for the drug exploded with a large number of generics producers and formulators from Europe rushing into the market. And while all of these factors were occurring on the corporate side, organizations such as SCI were using their power as bulk buyers to exert further downward pressure on price. In fact, according to Dr Alan Fenwick of the SCI: “the price for praziquantel has fallen by an approximate 93%, bringing the cost of a single tablet down to a mere USD0.07.”

When affordability is considered along with efficacy, it is even easier to see why the Bill and Melinda Gates Foundation considers the actions of SCI’s wor-
thy of funding.

Emphasising education

Though the aforementioned efforts provided millions of Ugandans with relief from their schistosome infections, the efficacy of praziquantel does not, unfortunately, extend to the fight against reinfection. So in communities where the main body of water is the place to fish, to draw drinking water, to wash clothes, as well as the source of schistosome infection, the SCI recognized a strong need for education that could enable communities to better protect themselves. By providing school teachers with health education materials, they promoted unified, accurate dissemination of information to their pupils. And by encouraging children to take part in activities such as writing and acting out small plays in which a naughty child ignores advice and becomes sick from playing in dirty water, the SCI made it fun to learn how best to avoid reinfection. The SCI also introduced education programs to the wider community, alerting humans to such dangers as leaving human excreta near water sources and grazing potential host animals at the water’s edge. When one considers that the patient is unaware of the moment of schistosome infection and that many humans remain asymptomatic long after initial infection - as demonstrated by the Somali patient in Wisconsin - such educational efforts are an excellent complement to de-worming medication in terms of helping to break the life cycle of the schistosomes.

Highly encouraging results

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Expanded efforts, refined methods

Following upon the success in Uganda, the SCI has
moved on to lend its efforts and expertise to the launch of schistosomiasis control campaigns in the 5 other African countries mentioned earlier - having already dispensed 43 million treatments to some 20 million humans in these 6 countries according to Dr Alan Fenwick of the SCI. Now, having reached the end of the initial 5-year award from the Bill and Melinda Gates Foundation, the SCI has received a further award of USD10 million from the same foundation to continue the fight against schistosomiasis. Furthermore, the SCI is employing new methods to realize higher efficacy in the field at lower cost and to raise awareness in general.

One recent development has been the use of Lot Quality Assurance Sampling (LQAS) as a means to identify high-risk communities requiring mass treatment with praziquantel. Unlike previous sampling methods used by the SCI that made use of a fixed sample size (WHO recommends sampling of 50 children per school because this is the approximate largest size of sample believed to be possible to be taken by 1 survey team in 1 day), LQAS allows data to be analyzed cumulatively after each observation, effectively merging data collection and data analysis into a single, smooth process. Not only does this method reduce overall sample size and save time and money, but it also appears to be accurate for the field of schistosomiasis. In fact, in an article that appeared in the July 2005 edition of Tropical Medicine and International Health, field testing in Uganda using LQAS was shown to have resulted in 100% sensitivity, 96.4% specificity, a positive predictive value of 85.7% and a negative predictive value of 92.3% from a sample of just 15 humans.

The SCI is also recognizing the need for more accurate and accessible methods of training and advocacy both to teach program managers, district health officers, and those operating in the field in general, and to draw the attention of decision-makers and donors to the nature and scale of the problem of schistosomiasis. One way in which this issue is being addressed is through the use of Information and Communication Technologies (ICTs) recommended by the G8 Digital Opportunity Task Force of 2002 and explained in a September 2006 article in Memórias do Instituto Oswaldo Cruz, Rio de Janeiro. In line with the Task Force recommendations, multimedia materials have been developed at the Wellcome Trust in collaboration with the SCI in the form of a CD-ROM in both English- and French-language versions. So far, the discs appear to have been well received, with significant numbers of users feeling that the CD-ROMs had helped improve quality of training and raised the profile of the schistosomiasis problem.

Supporting control of the “Big 3”

As the SCI extends its efforts further into sub-Saharan Africa, the importance of controlling schistosomiasis is becoming more evident. Despite its high prevalence rates, the condition is often seen to be a neglected disease, with major efforts and funds dedicated to the big 3 diseases comprising HIV/AIDS, malaria, and tuberculosis. But with studies such as that of Kallestrup et al that appeared in the Journal of Infectious Diseases in June 2006, perspectives may be beginning to change. This study demonstrated how successful treatment of schistosomiasis can positively affect the human immune system to reduce the rate of viral replication and increase CD4+ cell count in patients with HIV/AIDS. Such reduced viral replication may also significantly decrease the likelihood of passing HIV/AIDS from mother to baby, and there is reason to believe that a strengthened immune system as a result of successful anti-schistosome treatment may have a positive and cost-effective impact on patients with malaria and tuberculosis, too.

By D Reilly