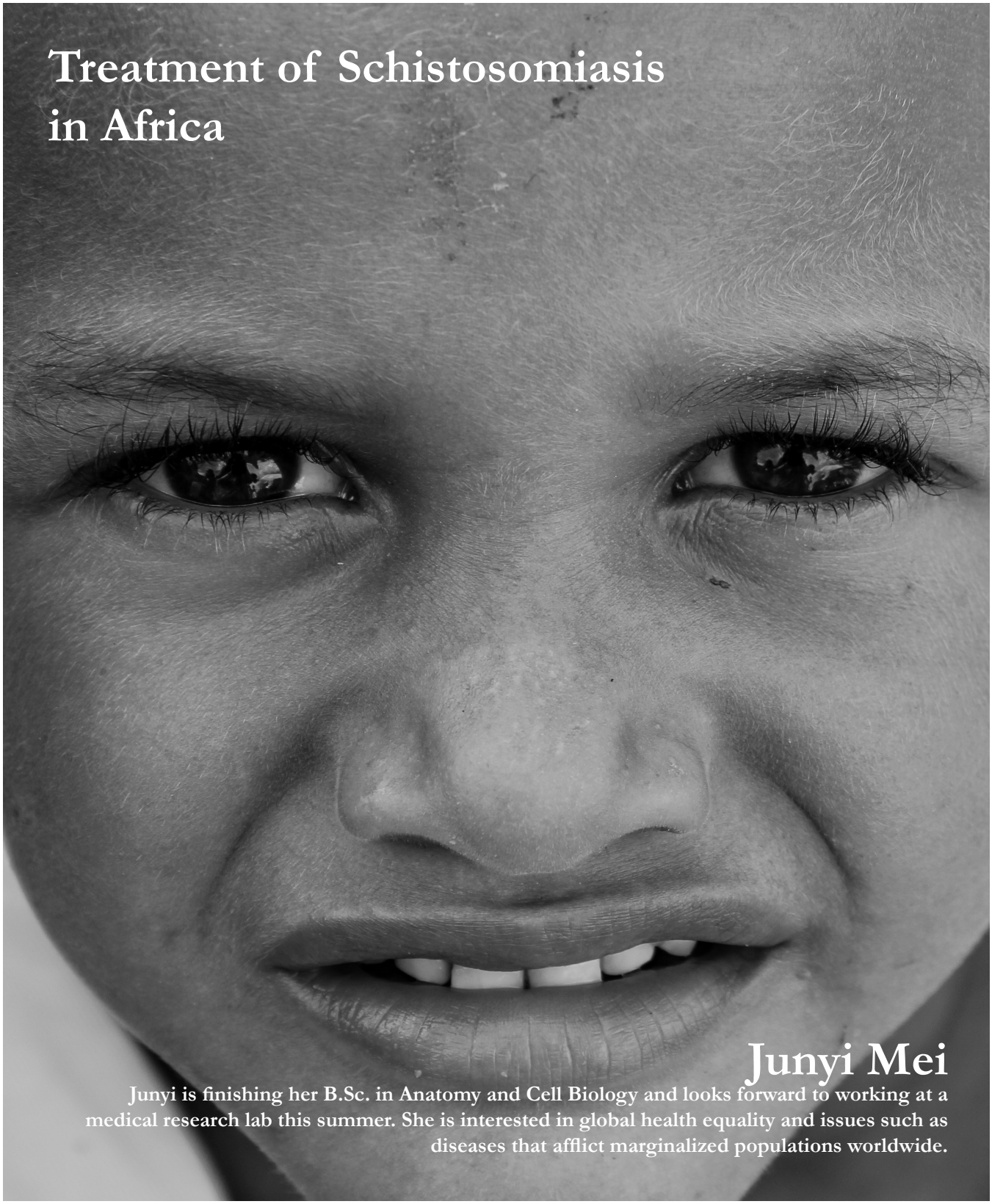
Treatment of Schistosomiasis in Africa



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Schistosomiasis is part of a group of diseases that generally afflict the poorer regions of the world. These diseases are collectively called neglected tropical diseases because historically, little funding has been put into researching cures or treating the afflicted population; instead, efforts have been focused on more fatal diseases, such as AIDS, tuberculosis, and malaria (WHO, 2013). Schistosomiasis is caused by tropical flatworms whose larvae enter the body directly through the skin and develop into reproducing adult worms (Thétiot-Laurent et al., 2013). The body's reaction to the worms' eggs results in chronic "abdominal pain, diarrhea, and blood in the stool," which, over time, causes permanent damage to the vital organs of the body (WHO, 2013). Although schistosomiasis has a low mortality rate, severe economic and health consequences arise from this debilitating disease; it impairs growth and cognitive development in children and decreases productivity and quality of life in adults (WHO, 2013). Over 90% of cases are found in Africa, affecting over 200 million people (Steinmann et al., 2006; Utzinger et al., 2009) and causing more than 200,000 deaths each year (WHO, 2013). This number is likely to be an underestimation since lighter infections may not be detected by current diagnostic methods (King, 2010). These factors make schistosomiasis a significant global health issue.

In recent years, more and more people have become aware of neglected tropical diseases, and both donors and governments have started to invest money and research efforts to treat schistosomiasis on a global scale. International organizations, such as the World Health Organization (WHO), have also coordinated efforts to implement treatment in various African countries. In 2002, the WHO passed Resolution WHA 54.19, aimed at decreasing the number of children infected by schistosomiasis by 75%. Although this target has not been achieved, some progress has been made. A decade later, the WHO passed Resolution WHA 65.21 to encourage governments to intensify the control of schistosomiasis by calling countries with lower transmission rates into action (WHO, 2013). The development of praziquantel, a safe and effective drug for treating schistosomiasis, has accelerated these efforts (Stothard et al., 2009). It has been included in a rapid impact package of several drugs, used in mass drug implementation campaigns that have been met with considerable success (Rollinson et al., 2013). However, issues arise as to what future course of action should be taken to build on this success and strive towards elimination of the disease altogether. For sustainable control of schistosomiasis, morbidity control programs should continue to be used in the short-term, but they should be complemented and eventually replaced by environmental measures in the long-term.

Morbidity-Control Programs

Morbidity control programs have been widely successful. After the introduction of praziquantel in Germany in the 1970s, it has become the sole commercially available drug used for the treatment of schistosomiasis (Hotez et al., 2010). Praziquantel is cheap, at just 20 cents per dose, safe for children and pregnant women alike, and extremely effective against adult worms (Doenhoff et al., 2009). Cure rates of 80 to 90 percent have been observed (Doenhoff et al., 2009). The latter half of the twentieth century saw praziquantel become increasingly affordable on the international market (Stothard et al., 2009). In 2008, Merck KGaA, a biochem-

ical company, partnered with WHO to further make available the drug through the Merck Praziquantel Donation Program which donates 200 million tablets over the next decade to treatment efforts. Morbidity control programs are based on preventative chemotherapy, which involves the mass administration of drugs to a population once or twice a year without the need for individual diagnosis (USAID, 2009). Since many of those afflicted have neither the knowledge nor resources to seek treatment, these programs are comparatively effective in treating those in need without too high a cost (Hotez and Fenwick, 2009).

In addition, mass drug administration of several drugs together, which are safe to take even if one is not infected is viable due to the "considerable geographical overlap and co-infection" of many neglected tropical diseases (Brooker et al., 2009) and eliminates the need of individual screening. A rapid impact package of five drugs has been developed to treat five of the most harmful neglected tropical diseases all at once (Giving What We Can, 2012). Due to the "strong safety profile" of the drugs, not only can nurses and doctors administer them but, with some basic training, volunteers and teachers as well (Stothard et al., 2009). To target school-aged children who are most at risk, the drugs are administered through schools, taking advantage of the existing "educational infrastructure and resources" (Miguel and Kremer, 2004). The drugs keep for four years without refrigeration, reducing distribution costs (Giving What We Can, 2012). These factors all help to alleviate the strain on already overwhelmed local health systems, as well as reduce the costs of undertaking such an enormous task. Morbidity control programs have been overall successful. In 2009, 21 out of the 76 (27.6%) afflicted countries reported to the WHO a total of 19.6 million people who had been treated (Rollinson et al., 2013). In addition to the development of a suitable drug, administration aspects have been streamlined to reduce costs while making a significant impact.

Although morbidity control based on mass drug administration has been fairly successful in the short-term, it is not sustainable due to certain limitations of the drug and the inability of administration programs to accommodate them. Praziquantel is not as effective against worms in the larval stage and does not prevent reinfection (Rollinson et al., 2013); hence, treatments must be repeated annually in highly afflicted populations and every two years in other areas (Hotez and Fenwick, 2009). Problems also exist in the administration of treatment through these campaigns. Although school-aged children, who have the highest risk of being infected, are targeted, an estimated 40% of children in sub-Saharan Africa are not enrolled in schools (Rollinson et al., 2013). Infants and preschool children are also not treated (Stothard et al., 2013). Efforts have been made to widen the target population to include other high-risk group such as pregnant women and those who work in infected waters (Savioli et al., 2009). A move towards community-based intervention has been made to close this "significant treatment gap" (Stothard et al., 2013). Still, less than 50% of the high-risk population receives treatment, while many healthy people in the areas of administration are treated unnecessarily. An improvement could be in "initial disease surveillance," to focus drug delivery on the areas that truly need it (Stothard, 2009). The geographical distribution of schistosomiasis is being mapped with Bayesian geo-statistical modelling, using data collected primarily

through school-based questionnaires, microscopy, and reagent strips (Chammartin et al., 2013). These methods require a minimum of tools and staff, but are not, unfortunately, the most accurate (Rollinson et al., 2013). New diagnostic tests are still in development; for example, a new test called POC-CCA is currently being tested, whose "accuracy, performance time, and cost all surpass the universally used Kato-Katz test" (Speich et al., 2010; Colley et al., 2013).

Even if preventative chemotherapy programs have been met with considerable success, there is the need to improve "identification of the most vulnerable groups and promote equitable access" (Gray et al., 2010) while maintaining the low levels of morbidity that have been achieved. Campaigns would have to be repeated yearly because, once interrupted, morbidity could return to pre-treatment levels within 18 months to 2 years (Gray et al., 2010). As a result, morbidity-based control programs need continuous input of money over many years and rely on ceaseless funding by external donors and governments. Solely using morbidity control programs cannot be considered effective because they are not sustainable with the current resources available.

Funding

The lack of funding prevents sustainable treatment of schistosomiasis. There are severe shortages of praziquantel; Merck KGaA's donation of 200 million tablets a year is just a small fraction of what is required (Hotez et al., 2010). Even though each praziquantel tablet costs just 20 cents, the scale of the goal is enormous: approximately $100 million a year is required to purchase the 1200 million praziquantel tablets needed to treat a target of 400 million people (Hotez and Fenwick, 2009). Furthermore, Hotez and Fenwick estimate ancillary costs (including delivery, advocacy, training, monitoring, and evaluation) of an additional $100 million. These efforts must then be sustained over several years. Evidently, treating such a large population is extremely costly. In recent years, the Bill and Melinda Gates Foundation and other private donors, the U.S. and British governments, and major pharmaceutical companies have donated large sums of money to treat neglected tropical diseases, with over $350 million committed until 2013 (Gray et al., 2010). However, Hotez and Fenwick estimate that funds of two to three billion over the next five to seven years are required to sustain treatment efforts. Although funding in this area has greatly increased with growing international interest in these diseases, it remains vastly short.

Secondly, efforts made by various groups—charities, governments, the WHO—must be coordinated. In recent years, there has been significant progress in integrating different programs into larger, more effective initiatives. These donor agencies have collaborated with several afflicted African countries and WHO and its regional offices to implement treatment for neglected tropical diseases (Stothard et al., 2009). In addition, a variety of different collaborative approaches to treating schistosomiasis have been initiated, such as the Schistosomiasis Control Initiative (SCI), CONTRAST, and SCORE (Stothard et al., 2009). Nevertheless, even with better coordination efforts, the lack of funding limits what can be done to sustain the treatment of schistosomiasis.

Environmental Measures

Preventing infection by improving environmental factors is another approach to treat-

ing the schistosomiasis epidemic. In particular, transmission-based control programs should be explored in addition to morbidity- based ones (Rollinson et al., 2013). Snail control through biological and chemical means, sanitation, and health education are some of the environmental means that can be used to limit the transmission of schistosomiasis (Gray et al., 2010). Past successes in eliminating schistosomiasis in countries such as Egypt, Brazil, and China have demonstrated the effectiveness of complex, sustained national integrated programs based on these means (Utzinger et al., 2005) when complemented by morbidity control. In Africa, waning rates of compliance in preventative chemotherapy campaigns have been observed because people in the treatment areas may not be sufficiently aware of the significance of the health problem at risk due to the low mortality rates of the disease (Rollinson et al., 2013). Health education in schools and communities to increase knowledge and understanding of schistosomiasis transmission is important for increasing treatment participation. Snail control, on the other hand, has not been sufficiently developed and has been found to be costly and environmentally damaging (Fenwick et al., 2011).

Afflicted countries must take ownership of schistosomiasis control through political commitment and active community involvement (Aagaard-Hansen et al., 2009). Doing so would empower the local people, for they would be in control of their own health. Local research networks and integration of vertical programs into existing health care systems should also be pursued, in addition to national control programs (Aagaard-Hansen et al., 2009). Such an approach would be beneficial for both donors and recipients: as recipient countries take matters into their own hands, donors no longer need to give as much support as before and can focus funds on research and other long-term solutions. Although the quickest and cheapest way to obtain results is no doubt through morbidity control, it is only a temporary fix that cannot be sustained. Permanent long-term results can only be achieved through environmental health measures aimed at creating a lasting improvement in sanitation and living conditions (Rollinson et al., 2013).

However, such measures are comparatively difficult to implement at this point. The WHO targets for safe water, sanitation, and hygiene are far from being met (WHO, 2010). An effective national control program would require significant political commitment to organize the complex inter-sectorial collaboration and community involvement needed for "the design, implementation, and long-term monitoring of the impact and cost-effectiveness of hygiene, water, and sanitation interventions" (Rollinson et al., 2013), something that afflicted countries do not yet have. The health and social institutions in many of the afflicted African countries are not yet sufficiently developed to take control of such a large task; some have neither enough desire nor resources to do so (Rollinson et al., 2013). Even if a national control program were to be implemented, past examples in other countries have demonstrated that success in schistosomiasis control comes gradually (Utzinger et al., 2005). Thus, continuous support from donors and governments are necessary for such a program to take place and be sustained over many years. At present, it is not feasible; instead, morbidity-based programs should be continued in the short-term while more permanent fixes are being developed.

Researching a Cure

The need for research is omnipresent in both the short-term and long-term. There is always the risk of the flatworms developing drug resistance against praziquantel; consequently, signs of resistance should be carefully monitored and research and development of an alternative drug must stay ahead. Since the development of a vaccine would be an immense step in eliminating schistosomiasis, vaccine research should also be a priority (Gray et al., 2010). With growing interest in neglected tropical diseases in recent years, more research is being done. Incentives offered by governments and public-private partnerships encourage companies to invest in new drugs and vaccines for neglected tropical diseases. For example, the U.S. Food and Drug Administration priority review voucher is awarded to a company that has obtained approval for their treatment and can later be used "to accelerate review of an unrelated drug" (USAID, 2009). The multidisciplinary CONTRAST project established an African research network for local schistosomiasis research and an open-access global neglected tropical diseases database for data sharing to promote "effective research partnership" (Bergquist, 2013). In addition to drug and vaccine development, research could focus on diagnostic tools as well as on the acceptability of diagnostic and screening procedures and determinants for treatment seeking practices and adherence, among other social science factors (Aagaard-Hansen et al., 2009). Although there are many research efforts in progress, insufficient funding restricts these efforts (Keiser and Utzinger, 2012); furthermore, the drug development pipeline is long and takes many years for applicable results (Stothard, 2009). Thus, treatment of schistosomiasis continues to rely on morbidity control programs.

Conclusion

Although large-scale preventative chemotherapy has proved to be an "affordable, feasible and effective strategy" for schistosomiasis control in African countries (Rollinson et al., 2013), limitations of praziquantel necessitate continuous donor support over many years. Control programs based solely on morbidity control will be neither completely effective nor sustainable, but transmission control through environmental measures is not yet practical. Afflicted African countries currently do not have enough desire or resources to implement a national control program focused on improving sanitation, health systems, and health education (Rollinson et al., 2013). Therefore, morbidity control programs should be continued in the short-term. Perhaps, reducing the disease in the short-term would help give the afflicted population tools to break free of the so-called poverty cycle, where being sick with disease impairs one's ability to work or achieve one's full potential and thus, perpetuates one's poverty. The afflicted countries can then develop the resources needed for long-term management of schistosomiasis and move towards the ultimate goal of elimination. In the long-term, there should be a shift to national integrated control programs centered on improving sanitation, health systems, and health education in afflicted countries, as demonstrated by past successes in China, Brazil, and Egypt (Stothard et al., 2009). Such an approach gives permanent benefits while empowering local governments. All in all, widespread treatment and elimination of schistosomiasis is possible, but considerable time and effort, with the cooperation of many

parties, are needed to achieve such a goal.

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