THE
CARTER CENTER

Summary of the Nineteenth Meeting of the International Task Force for Disease Eradication (II) April 12, 2012

The Nineteenth Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 4:00pm on April 12, 2012 to discuss the potential eradicability of schistosomiasis. The Task Force members are Sir George Alleyne, Johns Hopkins University; Dr. Stephen Blount, Centers for Disease Control and Prevention (CDC); Dr. Mickey Chopra, UNICEF; Dr. Donald Hopkins, The Carter Center (Chair); Dr. Adetokunbo Lucas, Harvard University; Dr. Montserrat Meiro-Lorenzo, The World Bank; Professor David Molyneux, Liverpool School of Tropical Medicine (retired); Dr. Mark Rosenberg, Task Force for Global Health; Dr. Lorenzo Savioli, World Health Organization (WHO); Dr. Harrison Spencer, Association of Schools of Public Health; Dr. Dyann Wirth, Harvard School of Public Health; and Dr. Yoichi Yamagata, Japan International Cooperation Agency (JICA) (retired). Eight of the Task Force members (Alleyne, Blount, Hopkins, Lucas, Meiro-Lorenzo, Molyneux, Rosenberg, and Savioli) attended this meeting.

Presenters at this meeting were Dr. Dan Colley, University of Georgia; Dr. Dirk Engels, WHO; Dr. Charles King, Case Western Reserve University; Dr. Lorenzo Savioli, WHO; and Dr. Jürg Utzinger, Swiss Tropical and Public Health Institute.

Schistosomiasis Control, Elimination and Eradication

The ITFDE reviewed schistosomiasis previously in 2001, when it concluded that the disease was "not now eradicable" using available tools, mainly because of animal reservoirs of infection, increasing breeding sites for snail intermediate hosts, and cost of the drug for treatment. The Task Force noted then, however, that it was "possible to achieve much better control of the vast morbidity from schistosomiasis now", and emphasized topics needing additional research. The current review was undertaken at the request of the World Health Organization (WHO).

Schistosomiasis may result from infection with one or more of three major species of *Schistosoma* parasites (*S. mansoni, S. japonicum, S. haematobium), and three minor species (S. mekongi, S. guineensis, S. intercalatum,*) that occur in specific areas of Africa, Asia, the Caribbean and/or South America. The WHO estimates that at least 230 million people, mostly in

52 countries, require treatment annually, about 80-90% of whom live in Africa.[1] Nearly 800 million persons are at risk of the infection.[2]

Larval forms of the parasite that emerge from certain species of fresh water snails penetrate the skin of humans and migrate to blood vessels of the intestines and/or bladder, where they mature. The adult worms produce thousands of eggs which, once released in the victim's urine or feces, may contaminate fresh water, where immature forms can emerge and enter intermediate host snails that allow the parasites to transform and multiply before emerging from the snails in the stage that can infect humans. Epidemiologically, these species cause different infections requiring different disease control tactics, depending on the habitat of the intermediate host snail, and whether parasite eggs are excreted only by humans, or there are animal reservoirs such as water buffalo and cattle (*S. japonicum*), or rodents and non-human primates (*S. mansoni*). *S. haematobium* is not known to involve an animal reservoir. Schistosomiasis is strongly associated with poverty and the lack of sanitation and safe sources of water. Man-made lakes, dams, open irrigation systems and other agro-engineering projects have sometimes increased breeding sites of the snail intermediate host and spread of the diseases.

Infections with *Schistosoma* parasites may cause the disease schistosomiasis (Bilharziasis) due to local and systemic damage and scarring as a result of immune responses to thousands of eggs that lodge in tissues of urinary organs, intestines, liver, lung and other organs. Disease may manifest as hepato-splenomegaly, hydronephrosis, anemia, stunting, genital disease, infertility, cognitive impairment and other signs or symptoms. School age children 5-14 years old usually suffer the highest rates of infection, and intensity of infection, but pre-school children and adults may have significant disease also. Adults in endemic areas suffer the consequences of repeated and chronic infections over many years. People in certain occupations such as fishermen and rice farmers may be at high risk.

Clinical damage can be prevented or often reversed by annual or more frequent chemotherapy with the drug praziquantel, which is administered orally at a dose of 40mg/kg. In areas of low prevalence, treatment every two years may suffice for morbidity control. Other interventions to prevent infection, and reduce the intensity of infection, include effective health education to convince people in at risk areas to avoid exposure to contaminated water and to not contaminate water with their urine or feces; control of intermediate host snails by chemical, biological or environmental modification of habitat; sanitary disposal of human waste in latrines or toilets; and provision of safe water sources for household use and recreation. Modified agricultural practices may also be indicated.

Over the years, beginning as early as the 1940s in some cases, several countries have used different combinations of interventions to reduce morbidity from intense schistosomiasis, and in some instances (e.g., Japan, some Caribbean islands; parts of China, Morocco, Egypt) to control or eliminate transmission of the infection altogether. Japan eliminated *S. japonicum* by 1977, using several interventions, including lining of irrigation channels. Fencing of water buffalo was

[1] World Health Organization. Schistosomiasis: population requiring preventive chemotherapy and number of people treated in 2010: Estimates of the population requiring preventive chemotherapy for schistosomiasis annually. *Wkly Epidemiol Rec* 2012; 87:37—44.

[2] Steinmann P et al., 2006. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. *Lancet Infect Dis* 2006; 6:411–25.

part of the strategy used in China. In sub-Saharan Africa, only 10 countries account for 72% of the regional burden of schistosomiasis, but only seven of those countries currently have large scale treatment programs and in those seven countries only 6.1% of the 110.5 million people requiring large scale treatment were treated in 2010. The Schistosomiasis Control Initiative (SCI) helped Burkina Faso achieve national coverage of >90% of the school age population with praziquantel treatment in 2005, a level of coverage that was also attained by Sierra Leone in 2010. Globally, about 14.5% (33.5/230 million) of persons requiring treatment for schistosomiasis received it in 2010,[1] more than were treated in any previous year.

As schistosomiasis is a highly focal disease, mapping to determine which areas require attention, including mass treatment or more targeted chemotherapy, is a challenge. Although the urinary form of disease (*S. haematobium*) can be assessed fairly accurately by screening for blood in urine of school-age children, detection of eggs in the feces of people infected with other forms of the parasite is much more difficult, slow, and expensive, for example using the traditional Kato-Katz technique, which requires microscopic examination of stool specimens. Researchers supported by the Bill & Melinda Gates Foundation and coordinated by the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) have concluded that a point-of-contact circulating cathodic antigen (POC/CCA) assay of urine specimens can detect *S. mansoni* infections at a cost of about US$1.75 per test. However, neither of these tests appears to be sufficiently sensitive for an elimination program. SCORE is also coordinating studies of different options for praziquantel treatment and other interventions for achieving and maintaining control of schistosomiasis, as well as elimination of *S. haematobium* from parts of Zanzibar.

The Task Force discussed the WHO report on schistosomiasis that was presented to WHO's Executive Board earlier in 2012, especially the proposed "steps towards elimination of schistosomiasis": 1) "control of morbidity" (prevalence of heavy-intensity[3] infection <5% across sentinel sites), 2) "elimination as a public health problem" (prevalence of heavy-intensity infection <1% in all sentinel sites), and 3) "interruption of transmission" (reduction of incidence of infection to zero). The ITFDE suggested that both of the first two steps are stages of disease control, and that use of the phrase "elimination as a public health problem" is confusing, misleading, and should be avoided. The value of defining two different levels of disease control so that countries may advance from one level of control to the next is clear, but the two levels of control might more accurately be described as "control" and "enhanced control", for example, leaving "elimination" to describe the third level, when transmission appears to have been interrupted completely. It was also noted that understanding the epidemiological relevance of suspected and confirmed animal reservoirs of schistosomal infections will become increasingly important as more countries approach interruption of transmission among humans.

An estimated peak of 700 million tablets of praziquantel would be needed annually to eventually cover the population requiring treatment up to 2017 after which that number would decline. This scenario is based on the assumption that 5-6 years of large scale annual treatment will reduce schistosomiasis transmissionto a level where a more focal approach with less need for praziquantel would be sufficient, provided the mass drug administration is combined with other interventions such as snail control and waste management. Capacity for implementing

[3] *≥ 50 eggs/10 ml urine or ≥ 400 eggs per gram of feces.*

chemotherapy in endemic countries in 2011 was about 100 million tablets. E-Merck's decision to expand its donation of praziquantel from 50 million to 250 million tablets annually within the next few years will require scaling up countries' capacities for mapping the infection and for delivering mass drug administration effectively.

Conclusions and Recommendations

1. Great progress has been made in combating schistosomiasis since the ITFDE reviewed this topic in 2001. More persons were treated for the disease in 2010 than ever before. Several countries appear to have interrupted transmission (eliminated) of schistosomiasis already and some other countries appear close to doing so soon.

2. The ITFDE does not believe it is possible to eradicate all species of schistosomes that affect humans, using currently available tools, given the challenges of environmental changes that are conducive to transmission of these parasites (e.g. large dams), the existence of animal reservoirs, agricultural practices (e.g. expanded irrigation), and other factors.

3. It is, however, now possible to greatly improve control of schistosomiasis by expanding available interventions judiciously, including use of as many of the five interventions (health education, access to safe water, sanitation, snail control, mass chemotherapy) as possible , not just chemotherapy, and by extending large scale chemotherapy to all necessary age groups, not only school-age children.

4. The ITFDE urges WHO to define its goals in quantifiable terms, and to reserve the term "elimination" for indicating complete interruption of transmission.

5. Schistosomiasis programs are encouraged to co-administer praziquantel with other drugs wherever possible and indicated, including albendazole or mebendazole in areas where soil-transmitted helminthiases are co-endemic, or triple drug administration of praziquantel, albendazole, and ivermectin in areas where schistosomiasis, onchocerciasis and lymphatic filariasis are co-endemic in Africa.

6. The Task Force commends E-Merck for increasing the donation of praziquantel, and urges advocacy for increased manufacturing capacity. The Task Force also recognizes that countries need greater capacity for effective use of the existing donation, which is an important prerequisite for obtaining enhanced drug supplies for the needed global scale up of schistosomiasis programs.

7. Endemic countries that have not yet done so need to complete mapping to determine the extent and distribution of different schistosome species, and consider local epidemiology and available resources in deciding on optimal strategies for treating school-age children and other age groups, and use of other interventions to complement and reinforce chemotherapy.

8. National health authorities should coordinate the assistance for combating schistosomiasis provided by various inter-sectorial groups and international partners.

9. The global effort against schistosomiasis might benefit from a broad Global Alliance representing interested countries, donors, industry and other interested parties for advocacy purposes and to enhance communications on this topic among policy makers, researchers, and implementers at international levels.

10. Researchers and program staff should document systematically the impact and cost/benefit ratio of each of the five interventions for schistosomiasis, as well as the economic benefits of controlling the disease. Particular attention is needed for research to enhance the effectiveness of behavioral change communications (health education) in combating these parasites.