

SUMMARY OF THE THIRD MEETING OF THE ITFDE(II) October 18, 2002

This meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 9:00am to 4:00pm on October 18, 2002. The Task Force reviewed the status of global efforts to eliminate lymphatic filariasis, as well as the control of African trypanosomiasis. The names of members of the Task Force or their representatives who participated in the meeting, the presenters, and the other invited guests are included below. During a special recess, participants joined staff of The Carter Center in congratulating President Jimmy Carter on being awarded the 2002 Nobel Peace Prize.

The Task Force members are: Sir George Alleyne, Pan American Health Organization; Dr. Yves Bergevin, UNICEF; Dr. Mariam Claeson, The World Bank; Dr. Julie Gerberding, Centers for Disease Control and Prevention; Dr. David Heymann, World Health Organization; Dr. Donald Hopkins, The Carter Center; Dr. Adetokunbo Lucas, Nigeria; Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Mark Rosenberg, Task Force for Child Survival and Development; 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. Six of the Task Force members (Heymann, Hopkins, Lucas, Molyneux, Rosenberg, Wirth) attended this meeting, and three others were represented by alternates (Dr. A. David Brandling-Bennett for Dr. Alleyne, Dr. Maria O. Costales for Dr. Bergevin, Dr. David W. Fleming for Dr. Gerberding).

Lymphatic Filariasis

The presentations on lymphatic filariasis were given by Prof. David Molyneux (in collaboration with WHO), and by Dr. Anne Haddix and Dr. Eric Ottesen of Emory University. Dr. David Addiss of CDC assisted in the preparation of Dr. Ottesen's presentation.

Most (~95%) cases of lymphatic filariasis are caused by infection with *Wuchereria bancrofti*; other related parasites that infect humans are *Brugia malayi* in southeast Asia and *Brugia timori* in Indonesia. There is no animal reservoir of *W. bancrofti*, and potential reservoirs of the two other infections do not appear to be significant for humans. The infection is transmitted to humans by bites of infected mosquitoes (*Anopheles*, *Culex*, *Aedes*, *Mansonia*). Lymphatic filariasis is estimated to infect 120 million persons (40 million of them with symptoms) in more than 80 countries of Asia, the Pacific, Africa and the Americas. At least one billion people are at risk of this disease, and combating it would contribute greatly towards poverty alleviation in endemic areas.

The conclusion by the previous ITFDE in 1993 that lymphatic filariasis was one of only six eradicable or potentially eradicable diseases was the original stimulus that led to the

current global campaign against lymphatic filariasis. There have been several notable advances since then.

Technical advances include more effective tools for diagnosing and treating the disease. A new Immunochromatographic antigen card test (ICT) allows accurate rapid diagnosis based on a finger-stick sample of blood, which does not have to be taken at night. The safety and efficacy of two different two-dose drug combinations (Mectizan and albendazole; DEC and albendazole¹) suitable for annual mass treatment of at risk or infected populations have been well established, as well as new antibacterial techniques for better home management of swollen limbs (daily washing of affected limbs with soap and water, thorough drying between digits, application of emollients, antibacterial/anti-fungal creams, limb elevation and appropriate exercise). Potentially powerful synergies in combining interventions against lymphatic filariasis with control measures against other infections (e.g., malaria, onchocerciasis, schistosomiasis, intestinal parasites) are also being recognized. More is now known about the successes of earlier efforts against the disease (e.g., in China, Solomon Islands, Suriname, Trinidad and Tobago). There is increasing evidence that longstanding mass treatment with Mectizan for onchocerciasis in Burkina Faso has also reduced the prevalence and intensity of *W. bancrofti* (unpublished observations). Studies in Tanzania and elsewhere suggest that mass administration of a two-drug combination annually for as little as two years can reduce existing lymphedema and hydrocele in some patients (unpublished). The clinical and economic burdens of the disease are also better understood. It is now realized that children often acquire the disease early, manifest signs of infection only later, but are blighted for life. Medical treatment of infected individuals costs an estimated US\$30 million annually in India alone, and global costs in lost productivity are estimated to exceed US\$3 billion per year. The provisionally estimated Economic Rate of Return (ERR) for investment in efforts to control lymphatic filariasis over the period 2000-2029 is 27%. (Targeting the highest endemic areas to receive control measures first will tend to increase the ERR.)

Since the previous ITFDE's conclusion, significant global political will to fight lymphatic filariasis is manifest in the 1997 resolution by the World Health Assembly (WHA50.29, "Elimination of lymphatic filariasis as a public health problem"), by the decisions of GlaxoSmithKline (then SmithKline Beecham) and Merck, in 1997 and 1998 to donate albendazole for the global campaign, and Mectizan for programs in Africa, respectively; and by formation of the Global Alliance for Elimination of Lymphatic Filariasis in 2000. In 1999, over 200,000 persons at risk were treated in mass campaigns in 3 countries. More than 3.2 million were treated in 14 countries in 2000, 25.5 million in 22 countries in 2001, and 82 million are expected to be treated in 34 countries in 2002.

The goal of the current campaign is to "eliminate lymphatic filariasis as a public health problem" by 2020, with the period 2016-2020 being anticipated for surveillance only. The current strategy is to use annual mass treatment (and health education) with a two-

¹ The DEC/albendazole combination is not safe in areas where onchocerciasis is also endemic. Merck has facilitated use of Mectizan with albendazole in the latter areas, by expanding their donation of Mectizan to include the control of lymphatic filariasis in onchocerciasis endemic areas. The optimal dosage of albendazole for mass administration in this program has not been fully optimized.

drug regimen to reach at least 70% of all endemic populations for 4-6 years, in order to interrupt transmission of the infection and allow time for pre-existing adult worms to die. (A strategy adapted specifically for use in endemic urban areas is not yet in place.) Prevention and alleviation of disability by education of patients and health care workers is also part of the current strategy. Mapping is expected to be completed by 2005; it is already finished in 29 endemic countries. An estimated \$80 million more is needed between 2002-2005 in order to reach 350 million persons targeted in all the necessary areas. Global activities are being regionalized to better reflect the different settings and epidemiologic patterns. The weakness of primary health care systems in Africa is an important constraint in the global campaign.

In discussing promising on-going research, it was noted that seven countries are now collecting cost data related to this problem, that work is being done to clarify any potential therapeutic role of *Wolbachia* endosymbiont as a target for chemotherapy, as well as work on a PCR diagnostic test to detect infection in vectors, and an antibody assay to monitor first exposure to lymphatic filariasis infections. It was also noted with concern that there are very few young researchers going into this field.

Conclusions and Recommendations

1. The Task Force commended the Global Alliance on the progress being made against lymphatic filariasis. The Task Force acknowledged that evidence from several settings has provided evidence of elimination of lymphatic filariasis as a public health problem. It noted, however, that there is as yet no definite proof that the current strategy will interrupt transmission of lymphatic filariasis (as opposed to “eliminating [it] as a public health problem”) within 4-6 years in larger endemic areas. The Task Force strongly recommends that priority attention be given to documenting achievement of such “proof of principle” in parallel with current efforts to scale up interventions.
2. Endemic countries should be encouraged to take advantage of the benefits of the broad spectrum anthelmintics used in this and other programs (e.g., schistosomiasis, other intestinal helminthiases), as well as possibilities to combine provision of these and other services (e.g., vitamin A supplements). Integration of such services and activities should be actively pursued wherever possible for the sake of greater sustainability and efficiency.
3. The Task Force believes that it would be useful to establish a Lymphatic Filariasis Research Forum, to provide more structure, information exchange, prioritization, and coordinated use of resources for research in this field. Such a forum could also seek to help build or expand capacities for related research in endemic countries. (At present, WHO’s Technical Advisory Group meets annually and makes recommendations on research and policy. WHO’s Program for Research and Training in Tropical Diseases focuses on operational research, MACROFIL and some other areas.)
4. It is highly advisable for this program to monitor for drug resistance.

5. More information is needed on the socio-economic effects of lymphatic filariasis and the costs of interventions.

African Trypanosomiasis

The presentations on African trypanosomiasis were given by Dr. Anne Moore of the Centers for Disease Control and Prevention, Dr. Jean Jannin of the World Health Organization, and Dr. Christian Burri of the Swiss Tropical Institute. (This disease was not discussed by the previous ITFDE.)

Human African trypanosomiasis (African sleeping sickness) is caused by infection with one of two parasites: *Trypanosoma brucei gambiense* (97% of human cases) and *T.b. rhodesiense*. The Gambian form is found in West and Central Africa, and its principal reservoir is humans. The Rhodesian form occurs in East and Southern Africa, and its main reservoir is wild animals and cattle. Both parasites are transmitted to humans by the bite of Tsetse flies (genus *Glossina*). The two infections are epidemiologically and clinically distinct, but both are 100% fatal in humans without treatment. An estimated 300,000 to 600,000 persons are affected, but about 60 million persons are at risk. There has been a sharp resurgence in cases since 1965, affecting especially parts of Sudan, Uganda, Central African Republic, Democratic Republic of Congo (DRC), Congo Republic, and Angola. This resurgence is attributed to deterioration of health and specific programmatic structures and services over the years, and reduced capacity to manage programs, and diagnose and treat patients, largely as a result of wars and other civil disruption, including emergence of HIV/AIDS. It was noted that each of the six countries cited above have experienced civil war or other prolonged armed conflict during all or part of the last decade.

The main control strategies are to reduce the parasite reservoir by active case detection and treatment of infected humans (*T.b. gambiense*), and reduce contact between humans and Tsetse flies through vector control (both parasites). Active case detection is accomplished by mobile teams that screen populations, do microscopic examinations, determine the stage of infection or disease (whether the brain and spinal cord are infected or not), and carry out follow up. Vector control is accomplished by aerial or ground-based spraying, or by using insecticide-impregnated screens or traps, but these methods are difficult to sustain. (Aerial spraying has mainly been used in controlling the disease in animals.) The efficacy of these interventions, when applied consistently, is well demonstrated (e.g., in Angola, Uganda and DRC; local elimination in some West African foci), despite the fact that available tools for detecting the parasite, staging the infection, treating those who need it, and killing the vector flies, each lack one important desirable characteristic or other. A major constraint is inadequate access to treatment for affected populations. Not much data are available on the cost effectiveness of interventions.

Increasing attention is being paid to African trypanosomiasis because of its resurgence, greater appreciation of the clinical and development burdens it imposes on poor persons and communities in endemic areas, and realization of the efficacy of available control

measures when conditions permit them to be applied. Access to affected areas is a major problem, but may improve with some of the recent improvements in security (political settlements of wars). WHO has led the assembling of enlarged partnerships, excellent networks, and much improved coordination aimed at controlling this disease. WHO's strategy emphasizes improving organizational aspects of the program, maximizing scarce human resources (for health care, laboratory services, research) in affected areas, and mobilizing sufficient resources. A WHO Sleeping Sickness Treatment and Drug Resistance Network was established in 1999 to improve access to treatment by the populations concerned. (Even when areas are not involved in conflict, treatment is often still unavailable to those who need it because of lack of drugs, inadequate infrastructure, personnel, need for training, transport, etc.) The group discussed and welcomed the strong political commitment manifest by the Pan African Tsetse and Trypanosomiasis Eradication Campaign, which is endorsed by African heads of state, but greatly regretted the misleading use of the word "eradication" in this instance.

By working with several pharmaceutical companies, Medecins Sans Frontieres, the Gates Foundation, and others, WHO has helped secure donation of the five major drugs now used for treating this disease (pentamidine, suramin, melarsoprol, eflornithine, nifurtimox). Treatment failures are an increasing concern. While seeking to improve the use and availability of existing drugs, the partners are working to promote research on combinations of existing drugs, and on new drugs for first, second, and both stages of the infection. Research on a new oral drug (DB 289) for treating first stage disease is being supported by the Bill & Melinda Gates Foundation. Mention was made also of the Drugs for Neglected Diseases Initiative (DNDi), which includes this disease among its targets (along with American trypanosomiasis and leishmaniasis). A lot of research has been done, and much is known about technical aspects of this group of pathogens, but that knowledge has not been translated into significant improvements in diagnostic or treatment tools, apparently because of inadequate commercial attractiveness. A dipstick diagnostic test would also be very helpful.

Conclusions and Recommendations

1. African trypanosomiasis is a major problem that is getting much worse in some areas. The true burden is difficult to estimate, but there has been a rapid increase in incidence over the past decade. It is an important constraint to development and poverty alleviation in affected areas.
2. *T.b. rhodesiense* is not eradicable, as it is a zoonosis. The zoonotic status of *T.b. gambiense* remains uncertain, but it is likely that humans are the most significant reservoir of infection. Whilst organisms similar to *T.b. gambiense* found in humans are found in pigs and some game animals, the public health significance of this is not known.
3. It is possible to achieve much better control of both diseases, using available tools and strategies, where the tools and strategies are applied consistently.

4. There is urgent need to extend access to existing diagnostic, treatment and other disease control methods to neglected populations who need them, in order to mitigate existing epidemics, and to prevent resurgence of the disease in other populations at risk in (currently) low prevalence areas.
5. The single greatest research goal for this disease is for better treatment; ideally, a drug that is effective against all stages of the infection, non-toxic, relatively inexpensive, and can be administered orally. Having all or most of such characteristics would allow rapid mass treatment of populations at risk even if the methodology for individual diagnosis and staging is not improved.
6. More sensitive, simpler tools for diagnosing and staging this infection are also needed.
7. WHO and interested researchers should develop more data on the cost effectiveness of interventions and promote good health systems research related to this disease.
8. Stronger, sustained advocacy is needed, both for peace in endemic areas, and for extension of effective preventive and curative services for this and other diseases to the neglected populations concerned.
9. The Task Force commends the excellent leadership that WHO is providing for this problem.

The Task Force also agreed unanimously that appropriate representative(s) of the Bill & Melinda Gates Foundation should be invited to each meeting of the Task Force, and that when a representative cannot attend, perhaps the final thirty minutes of the meeting could be set aside for the Task Force to provide a quick summary of its deliberations to Foundation staff by video conference or by conference telephone call.