Summary of the Eleventh Meeting of the ITFDE (II)
October 11, 2007

The Eleventh Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 4:00pm on October 11, 2007. The Task Force reviewed the problems of Buruli ulcer and yaws, and discussed a brief update on the status of cooperative efforts to eliminate malaria and lymphatic filariasis in Haiti and the Dominican Republic, as recommended at the previous Task Force meeting.

The Task Force members are Dr. Olusoji Adeyi, The World Bank; Sir George Alleyne, Johns Hopkins University; Dr. Julie Gerberding, Centers for Disease Control and Prevention (CDC); Dr. David Heymann, World Health Organization (WHO); Dr. Donald Hopkins, The Carter Center (Chair); Dr. Adetokunbo Lucas, Harvard University; Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Mark Rosenberg, Task Force for Child Survival and Development; Dr. Peter Salama, UNICEF; 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). Four of the Task Force members (Hopkins, Adeyi, Lucas, Yamagata) attended this meeting, and four others were represented by an alternate (Dr. Walter Dowdle for Rosenberg, Dr. Mike St. Louis for Gerberding, Dr. Robin Nandy for Salama, Dr. Kingsley Asiedu for Heymann).

Presenters at this meeting included Dr. Kingsley Asiedu of the World Health Organization; Dr. Jai Narain, South East Asia Office of the World Health Organization; Dr. Pamela Small, University of Tennessee; Ms. Ellen Whitney, Emory University; Ing. Angel Solis, Dominican Republic, and Dr. Claudel Bois, Haiti.

Buruli Ulcer Disease

This disabling, disfiguring and sometimes fatal infection, caused by *Mycobacterium ulcerans*, generally affects poor populations in rural areas or urban slums in the tropical areas of Africa, Asia and Latin America, but is not exclusively confined to them. It is one of the "Neglected Tropical Diseases" officially designated by the World Health Organization. It primarily affects the skin, producing ulcerative and/or non-ulcerative lesions most commonly on the extremities, but the infection may affect any external part of the body and also the bones. Sequelae may include disabling contractures and squamous cell carcinoma. Most patients are children, living near rivers or swampy areas, where the bacterium may be associated with biofilms, aquatic plants, insects and snails. All ages, genders and races can be affected. It is not spread between humans. Distribution is focalized within countries. Known prevalence is particularly high and apparently increasing in four adjacent West African countries: Cote d'Ivoire, Ghana, Togo, and Benin, but several other countries in Africa, Latin America, and Asia, as well

as Australia, have reported cases. Some animals (e.g., koalas, possum) are also naturally infected.

M. ulcerans is a slow growing mycobacterium which can be cultured at 30-33 degrees centigrade, and produces a unique toxin: mycolactone. Specimens are collected by swab, biopsy, or (recently) fine needle aspiration. Early diagnosis and treatment with antibiotics (rifampicin and streptomycin) provide the best outcomes, and can prevent the disfiguring scarring and need for extensive surgery that was required in the past. Health education of people in communities at risk and training of health workers and community agents are keys to improving early case-finding and treatment. Wearing long pants and long-sleeved shirts appear to be protective, as may be the use of bednets and insect repellants (the latter suggestions based on very preliminary data from one study).

The World Health Organization established its Global Buruli Ulcer Initiative in 1998, and has realized a rapid rise in participation at its annual meetings on this disease since then; a rise which has been mirrored by increased studies and related publications. The World Health Organization's current priorities for Buruli ulcer research include identification of transmission pathways from the environment to people; understanding the roles of changes in the environment on increasing incidence of the disease; development of a rapid, inexpensive, low-tech field test for diagnosing early disease; development of an effective completely oral antibiotic treatment regimen (such as rifampicin and clarithromycin); and improving availability of physical therapy for rehabilitation.

Conclusions and Recommendations

1. It is unlikely that Buruli ulcer disease can be eradicated, because of the presence of sources in the environment.
2. The World Health Organization is providing effective leadership on this issue, including annual reports in the *Weekly Epidemiological Record*. However, there is need to increase surveillance and mapping of the disease's distribution. Annual joint Program Reviews for clusters of neighboring endemic countries such as Cote d'Ivoire, Ghana, Togo, and Benin; and monitoring of a few indices of key interventions could also be very helpful.
3. Efforts to seek synergies for practical integration of efforts with those of other programs should continue.
4. Early detection and treatment of patients is more effective and less expensive than allowing patients' lesions to progress to extensive ulceration and more complicated disease.
5. More funding is needed for research, especially for a better and faster field diagnostic test and orally administered treatment.

Yaws

This discussion included consideration of all three non-venereal endemic treponematoses: yaws (caused by *Treponema pallidum* subspecies *pertenue*), endemic syphilis (subspecies *endemecium*) and pinta (subspecies *carateum*), but focused mainly on yaws, as the most widespread of the three related diseases. Yaws is transmitted by direct skin-to-skin contact among people with poor hygiene in certain warm and humid tropical areas of Africa, the Americas and Asia. Children age 2-15 years old are most highly affected, and persons with florid papillomatous lesions are the most infectious. Late lesions, which may occur 2-5 years after the infection begins, can cause destruction of bones and cartilage. Latent periods during which patients show no signs of infection but are sero-positive occur commonly throughout the acute and chronic stages of infection. Endemic syphilis occurs mainly in some drier parts of Africa and Asia, and may be transmitted by shared eating and drinking utensils as well as skin-to-skin contact. Pinta only occurs in parts of Latin America and its pathogenic effects mainly involve hypopigmentation of the skin. Serologic tests for all three diseases are identical (serology may be performed using a fingerstick blood sample in the field), and are indistinguishable from those of persons infected with venereal syphilis.

Yaws may be cured by a single injection of long-acting penicillin. This magical intervention can reduce the active lesions dramatically and enhance the credibility of health care workers. More than 50 million treatments were administered in 46 countries with the support of the World Health Organization and UNICEF during a global campaign from 1952 to 1964 that reduced the prevalence of the diseases by about 95% (to ~2.5 million cases). Subsequent integration of control efforts into weak basic health systems was not successful, and yaws especially resurged in several areas during the 1970s, in parts of Africa (e.g., Ghana, Cote d'Ivoire, Congo), Southeast Asia (e.g., India, Indonesia) and the Americas (e.g., Haiti). A resolution by the World Health Assembly in 1978 called for increased control efforts, but was largely ignored. When the previous International Task Force for Disease Eradication published its report on this subject in 1993, it concluded that political and financial inertia were the biggest obstacles to interrupting transmission of yaws, and that the potential for emergence of penicillin resistance, the possible existence of an animal reservoir of the infection, and the inability to distinguish the treponemes serologically from one another were also significant considerations. Since then, no penicillin resistance has been proven, but yaws lesions have been identified recently in 17% of wild gorillas in the Republic of Congo.[1] Although a single injection of penicillin is effective in curing yaws, the obvious potential advantages of a single-dose oral drug for yaws was articulated and suggested to be explored.

India launched a renewed effort to eliminate yaws beginning in 1996 when it reported almost 3,571 cases from 10 states and 49 districts. India's last yaws case was reported in 2003. In September 2006, India declared that it had eliminated yaws from the country,

[1] Levréro, F., S. Gatti, A. Gautier-Hion, & N. Ménard, 2007. Yaws disease in a wild gorilla population and its impact on the reproductive status of males. *American Journal of Physical Anthropology*, 132(4):568-575.

following confirmation by independent appraisals in 2004-2006. The South-East Asia Region of the World Health Organization has set a goal of eliminating yaws from the entire region (which includes Indonesia and Timor-Leste) by 2012. The World Health Organization convened an informal consultation on yaws in Geneva on January 24-26, 2007, to review the current situation and launch a new initiative on yaws as part of the Neglected Tropical Diseases Initiative.

Conclusions and Recommendations

1. The ITFDE commends the strong example set by India recently, for demonstrating the possibility of interrupting transmission of yaws nationwide, given sufficient political will, despite the biologic constraints associated with the pathogen. India's example and the recent efforts underway in the South East Asia region of the World Health Organization deserve much greater attention and should be published in an appropriate journal.
2. The continued occurrence of yaws and other endemic treponematoses, despite availability of an effective, stable and inexpensive treatment and a simple means of diagnosis in the field, is lamentable testimony to lack of political will, inadequate funding, and persistent weaknesses in primary health care systems of affected countries.
3. The current status of knowledge of the extent of yaws is very poor. The World Health Organization should publicize the currently known and unknown status of surveillance for this disease in each of the remaining suspected endemic countries, and encourage mapping and more detailed reporting of surveillance data.
4. The World Health Organization and UNICEF are the best hopes for strong global advocacy to address this eminently curable and preventable Neglected Tropical Disease.

Elimination of Malaria and Lymphatic Filariasis on Hispaniola

Hispaniola is the only Caribbean island where malaria still exists, and it also contains more than 90% of the lymphatic filariasis cases remaining in the Americas. Haiti is affected more than the Dominican Republic for both diseases. Since this subject was first reviewed at the May 2006 meeting of the International Task Force for Disease Eradication, Hispaniola has been the source of outbreaks of *P. falciparum* malaria in the Bahamas and Jamaica; Haiti has added the gametocytocidal drug primaquine to its regimen for case management to help decrease transmission of malaria; the report and recommendations of the previous ITFDE review were published in WHO's *Weekly Epidemiological Record* and shared with both heads of state of the two countries; two bi-national meetings were held in July and September 2006; localities have been selected to begin implementing elimination efforts (including integrated vector control for both diseases) over the next 2-3 years in 14 border areas (7 in each country); mapping of the two diseases is being coordinated; and the two ministers of health have conducted a bi-national agreement to facilitate cooperation between the two sides. This agreement

includes formation of a bi-national committee, and the mutual goal of eliminating lymphatic filariasis and malaria from Hispaniola by 2016-2017.

Conclusions and Recommendations

1. The International Task Force for Disease Eradication commends the progress made over the past year and a half by the Dominican Republic and Haiti (with the assistance of the Pan American Health Organization and the Centers for Disease Control and Prevention) to increase their cooperation towards eliminating lymphatic filariasis and malaria.
2. The ITFDE emphasizes the urgency of both countries completing a joint plan, proposal and budget with which to seek external funding to help implement this important bi-national effort.