Summary of the Fourteenth Meeting of the
International Task Force for Disease Eradication (II)
June 4, 2009

The Fourteenth Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 3:30pm on June 4, 2009 to discuss the potential eradicability of measles (rubeola). The Task Force members are Sir George Alleyne, Johns Hopkins University; Mr. Ekkehard Betsch, The World Bank; Dr. Donald Hopkins, The Carter Center (Chair); Dr. Adetokunbo Lucas, Harvard University; Professor David Molyneux, Liverpool School of Tropical Medicine (Rtd.); Dr. Mark Rosenberg, Task Force for Global Health; Dr. Peter Salama, UNICEF; Dr. Lorenzo Savioli, World Health Organization (WHO); Dr. Harrison Spencer, Association of Schools of Public Health; Dr. Dyann Wirth, Harvard School of Public Health; Dr. Yoichi Yamagata, Japan International Cooperation Agency (JICA), and Representative (TBD), Centers for Disease Control and Prevention (CDC). Six of the Task Force members (Hopkins, Alleyne, Betsch, Lucas, Rosenberg, Yamagata) attended this meeting, and two others were represented by alternates (Dr. Stephen Blount for CDC, Dr. Edward Hoekstra for Salama).

Presenters at this meeting were Dr. M. Carolina Danovaro-Alfaro of the Pan American Health Organization, Dr. William Moss of Johns Hopkins Bloomberg School of Public Health, Dr. Paul Rota and Dr. Amra Uzicanin of the Centers for Disease Control and Prevention, and Dr. Peter Strebel of the World Health Organization.

Measles Eradication

The ITFDE previously considered this topic in January 2002, when it concluded that "measles eradication is technically feasible, and it is a desirable goal, ultimately".[1] The ITFDE reviewed the current status of global measles control and regional elimination at this meeting, with particular emphasis on the biologic feasibility of measles eradication, at the request of the World Health Organization.

Measles is one of the most infectious diseases known, and it confers life-long immunity on persons who recover from the viral infection. Patients are most infectious during the four-day prodromal period just before the characteristic rash appears and continue to shed virus for another four days after the rash appears. Transmission occurs year-round, but normally peaks in the dry season or late winter/early spring, with major epidemics appearing at 2-4 year intervals. There is no animal reservoir of infection, and no asymptomatic carrier state. Measles virus is monotypic, genetically stable and shows no evidence of virus recombination.

[1] Summary of the 2nd Meeting of the International Task Force for Disease Eradication, 2002. http://cartercenter.org/documents/1182.pdf.

Before live attenuated measles vaccine was licensed in 1963, measles killed more than 2 million children globally each year. With increasing immunization coverage, the number of deaths from measles globally was reduced to about 750,000 in 2000 (estimated immunization coverage of 72%), and to an estimated 197,000 deaths, mostly children, in 2007 (estimated immunization coverage of 82%). The current goal is to raise immunization coverage to 90% or more at national level and to 80% or more in every district and reduce global deaths from measles to below 75,000 (90% below the 2000 level) by 2010. The epidemiology of measles has been complicated in recent years by significant numbers of susceptible teenagers and young adults who have escaped infection with the natural virus as well as missed immunization against measles (before widespread immunization, almost all persons had acquired measles naturally before 15 years of age or so).

The attenuated live measles vaccine is highly effective, yielding serocoversion rates of 95% or more in persons over 12 months old, is administered by subcutaneous or intra-muscular injection, and must be refrigerated. The vaccine is less effective in infants under 12 months of age (e.g., 90% seroconversion in 9 month olds and 70% in 6 month-olds), who become susceptible to the disease at differing times due to the loss of maternal antibodies (which protect younger infants from infection), as well as because of the infants' own immunological immaturity. Hence, some infants are exposed to and infected by the wild measles virus before they are immunized effectively by vaccination. Almost all children who fail to respond to the first dose will respond to the second dose, thus ensuring seroconversion rates after two doses of 95% or more if the first dose is given at 9 months or 99% or more if the first dose is given at 12 months or older. Providing all children with 2 doses of measles vaccine is now the standard for all national immunization programs with the second dose delivered either through campaigns or through routine health services depending on which approach reaches the highest coverage.

Cellular and humoral immunity are both important for protection against measles. There is concern about the high prevalence in some populations of persons whose immune systems are suppressed by HIV infection and might be less responsive to measles vaccine but so far this does not appear to be a major problem. By facilitating person-to-person spread of the highly contagious measles virus, including to very young susceptible children, urbanization and rapid population growth pose a special challenge, which experience shows requires sustained immunization levels of at least 93-95% in order to stop transmission of measles.

As countries reduce the number of cases of measles, more intensive "case-based surveillance," in which programs seek to test every patient who meets a case-definition for measles (rather than only testing one or two patient from each outbreak) becomes appropriate. Laboratory surveillance for measles is less complicated than polio surveillance because laboratory confirmation of suspected cases of measles is achieved primarily by detecting measles-specific IgM antibodies in a single serum sample taken early after infection. A number of sensitive and specific commercial enzyme immunoassays to detect IgM are available at reasonable cost. Measles cases can also be

confirmed by detecting a four-fold rise in IgG antibody in the acute and convalescent phases of infection, or by isolating the virus in cell culture or detecting viral RNA in clinical samples. Use of dried blood spots on filter paper or oral fluid samples for detection of measles antibodies and viral RNA can help to extend surveillance into remote areas. Global laboratory surveillance for measles and rubella is integrated into a single laboratory network that has an organizational structure that is similar to that of the global polio laboratory network. The WHO Global Measles and Rubella Laboratory Network has grown from 80 national, regional reference and global specialized laboratories in 2001 to 679 such laboratories in 164 countries in 2007. These laboratories are testing approximately 300,000 serum samples each year for the presence of IgM to measles and rubella and the number of samples will increase substantially as more countries and regions initiate case-based surveillance. The WHO Network has begun to incorporate molecular techniques that will be used to detect viral RNA in clinical samples and to support molecular epidemiologic studies. Genetic characterization of wild-type viruses is used to trace the transmission pathways of the virus and, in elimination settings, to provide evidence of interruption of transmission of endemic virus.

In 1994, the World Health Organization region of the Americas (AMR) was certified as free of indigenous polio and immediately established a regional goal to eliminate measles by the year 2000. The operational strategy used included "catch-up" mass measles immunization campaigns that initially targeted all children 9 months-14 years of age, regardless of immunization or disease history, in order to quickly raise immunization levels to 90% or more. Programs then sought by means of adequate routine immunization to "keep-up", maintaining high immunization levels in the face of continuing new births (susceptibles). Those efforts were supplemented as needed by "follow-up" campaigns about every four years targeting 1-4 year-olds, in order to ensure first measles immunizations to children who had been missed by routine immunization services, and simultaneously deliver a second dose of measles vaccine to young children who had already received their first dose.

Most American countries conducted "catch up" campaigns between 1989 and 1998, and "follow up" campaigns starting in 1996. Many American countries had already stepped up measles immunization by including it with polio immunization during the latter years of the regional campaign to eliminate polio. The last endemic cases of measles in the Americas occurred in Venezuela in November 2002. High levels of epidemiologic surveillance, laboratory diagnosis, performance indicators, "keep up" and "follow up" immunizations have been required in order to prevent the numerous cases of measles imported from other regions from re-establishing endemic transmission in the Americas. Other noteworthy elements of the success in the Americas include high levels of political support and relatively high routine immunization levels in the countries, vaccine laws to ensure funding of a line item for immunization in national budgets, and a special Vaccine Revolving Fund that the Pan American Health Organization (PAHO) established to facilitate advantageous procurement and timely availability of measles vaccine. Since 2003, PAHO has urged its member states to combine on-going measles immunization with immunization against rubella, with a new goal of eliminating rubella and congenital rubella syndrome from the Americas by 2010.

Spurred by the adverse effects of measles and also by the success in the Americas, all other regions of WHO have established target dates for eliminating measles transmission or for reducing measles mortality.

- In 1997 the Eastern Mediterranean Region (EMR) established a goal to eliminate measles (defined as incidence <0.1 per 100,000) by 2010. By 2007 this region had reduced incidence to 2.8 per 100,000, but EMR faces significant challenges of insecurity in parts of Afghanistan, Iraq, Pakistan, Somalia and Sudan.
- In 2002 the European Region (EUR) established a target date of 2010 for eliminating measles. EUR achieved a rate of 0.6 cases per 100,000 by 2007, with special challenges posed by misperceptions of measles as a mild disease and resistance to immunization because of misplaced fears about measles-containing vaccines in parts of Germany, Romania, Russia, Switzerland, Ukraine and the United Kingdom.
- In 2005 the Western Pacific Region (WPR) established a target date of 2012 for eliminating measles. WPR attained a rate of 6.3 per 100,000 in 2007, with a major challenge in China (about 1 million infants not receiving a first dose of measles vaccine each year, measles in migrant populations, and increasing proportion of cases among adults).
- The Southeast Asia Region (SEAR) has not established a measles control goal through its Regional Committee but, in 2005, adopted the global goal to reduce measles mortality by 90% (compared to 2000 levels) by 2010. SEAR had reduced the level by 42% in 2007, with the major challenge by far being India, with an estimated 8.5 million infants not receiving a first dose of measles vaccine each year and about 204 million children needing catch up immunizations.
- The African Region (AFR) established a goal in 2006 to reduce measles deaths by 90% (compared to 2000 levels) by 2009. AFR had reduced the level by 89% in 2007, with major challenges remaining in Nigeria (over 2 million un-immunized infants) and Ethiopia (about 1 million un-immunized infants). Seven contiguous countries in southern Africa that began implementing the recommended strategy over ten years ago have continued to make progress, but experienced deterioration of coverage and a transient resurgence of measles in some areas recently. In 2008, the African Task Force for Immunization recommended establishing a "pre-elimination target of a 98% reduction in measles mortality by 2012 compared with the 2000 level.

Programs are faced with several operational challenges. Clinical surveillance and reporting of measles is still poor (under-reporting), vaccination coverage levels are often over-stated, and age specific immunity is usually not known when decisions have to be made about the timing of remedial mass immunization for measles and what age groups to target. Burkina Faso was cited as an example of a country that currently is experiencing a substantial resurgence of measles with a high proportion of cases among unvaccinated children that is incompatible with the reported immunization coverage. Other operational challenges include weak health infrastructures and insufficient human

resources in many countries, especially in Africa, as well as inadequate supervision, funding and political support. Several countries have, however, used mass measles vaccination campaigns as platforms for providing additional child survival interventions such as polio immunization and distribution of bed nets, vitamin A capsules and de-worming tablets. It was suggested that immunization against polio and measles should perhaps be combined in India and Nigeria, which are high priority countries for both programs, although the fact that donors fund the two initiatives separately was felt by some to be an impediment to doing so.

The successful elimination of measles in the Americas, and the achievements in southern Africa and elsewhere over the past seven years since the ITFDE last considered this topic were discussed at length, with emphasis on lessons and implications for the global eradication of measles. Participants stressed the favorable advantages enumerated above that contributed to success in the American Region, but which are not as strong or lacking altogether in some other regions. It was agreed, however, that the successes prove that measles transmission can be interrupted in densely populated urban areas (e.g., Sao Paulo, Brazil; Mexico City, Mexico), and that prevalent HIV infected persons also are not a barrier to interrupting transmission of measles virus.

Great concern was expressed about recent decreases in funding for measles immunization and related efforts. One participant likened the current shortfall in resources of about US$100 million per year globally to advance warning of a "tsunami" of preventable deaths from measles that is sure to follow if funding to help sustain effective programs is not made available.

Conclusions and Recommendations

1. Much has been accomplished to reduce measles mortality and eliminate measles transmission in the Americas and in parts of Africa and other regions since 2002. These experiences also demonstrate that large urban centers and prevalent HIV infection are not insurmountable barriers to interrupting measles transmission, using currently available tools. These hard-won gains are fragile however, and will require substantial efforts to maintain and secure.
2. The ITFDE concludes, with even greater confidence than seven years ago, that measles eradication is biologically possible, using tools that are currently available, as already demonstrated in the Americas, although implementation challenges remain in each of the remaining five regions.
3. The delay in eradication of polio is a special obstacle to global measles eradication. Both goals might be advanced by an effort to combine forces in India and Nigeria, where both countries pose serious challenges to both initiatives. Donors should consider supporting such an approach.
4. The projected global shortfall of about US$100 million per year for measles programs, starting in 2010, is a very big concern, and risks the danger of measles recrudescing in areas where measles has already been controlled (as is happening now

in Burkina Faso) and the consequent costs in lives and medical expenses. Countries, donors and all others concerned should be aware that allowing such recrudescence would be more costly than preventing it.

5. Other regions should seriously consider certain aspects that contributed to elimination of measles in the Americas, especially the Vaccine Revolving Fund, strong political support, and laws to ensure that funds for measles programs are included in national budgets.

6. The crucial role of effective routine immunization services to help maintain high coverage levels of measles immunization deserves special attention, although even that alone is not enough. Regular "follow up" campaigns are also required until routine services are able to reach very high coverage with two doses.

7. Additional efforts are needed to improve surveillance (reduce under-reporting), accurate and timely knowledge of vaccine coverage, and to obtain country-specific data on age-specific immunity.

8. As more countries and regions initiate case-based surveillance for measles, additional support will be needed to expand the capacity of the WHO Measles and Rubella Laboratory Network. In addition to the increased workload, more training will needed to maintain competence, to introduce new laboratory methods especially molecular techniques, and to strengthen data management and quality control.

9. Though WHO has established a database for recording information about circulating genotypes of measles viruses, there is an urgent need to develop a global sequence database to support the molecular epidemiologic investigations being conducted by the WHO Measles and Rubella Laboratory Network.

10. Research to discover new tools or to improve existing ones is indicated in order to strengthen the armamentarium against this highly contagious disease, the above-mentioned successes notwithstanding. Any practical break-through in ways to mitigate any one of the current requirements to inject, provide two doses, and refrigerate measles vaccine, and to improve vaccine efficacy in young infants would be a major contribution to measles eradication, as would development of field tests to confirm measles infection and rapidly assess population immunity.

11. A study comparing the projected costs of eradicating measles versus indefinite control of measles, has recently been commissioned by the World Health Organization and funded by the Bill & Melinda Gates Foundation and should provide useful information.

12. The experience with polio eradication suggests northern Nigeria and northern India may prove extremely challenging for any future measles eradication effort. Operational research should be conducted now to determine how to conduct high quality campaigns in Nigeria while strengthening routine service delivery. In India, the challenges of extremely high birth rates and population density require both immunogenicity and vaccine effectiveness studies as well as studies of transmission dynamics to determine how the current vaccine can best be used to stop measles transmission in this setting.

13. Other potential biological barriers to eradication that may require further investigation include the effect of the HIV pandemic on measles disease and protection afforded by measles vaccination.