Summary of the Fifteenth Meeting of the
International Task Force for Disease Eradication (II)
October 30, 2009

The Fifteenth Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 3:30pm on October 30, 2009 to discuss rotavirus infection. The Task Force members are Sir George Alleyne, Johns Hopkins University; Mr. Ekkehard Betsch, The World Bank; 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; Professor David Molyneux, Liverpool School of Tropical Medicine (Rtd.); 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). Five of the Task Force members (Hopkins, Betsch, Lucas, Molyneux, Rosenberg) attended this meeting, and two others were represented by alternates (Dr. Mark Eberhard for Blount, Dr. Maria Costales for Chopra).

Presenters on rotavirus at this meeting were Dr. Duncan Steele of PATH, Dr. Mary Agocs of the Centers for Disease Control and Prevention, Dr. Manish Patel of the Centers for Disease Control and Prevention, and Dr. Umesh Parashar of the Centers for Disease Control and Prevention. Dr. Donald Hopkins also provided a brief update on the status of the Hispaniola Initiative to eliminate malaria and lymphatic filariasis, which the ITFDE first recommended in 2006.

Rotavirus

Dr. Duncan Steele described the disease spectrum and epidemiology of rotavirus infections. Rotavirus is the most common cause of severe diarrhea among young children worldwide, being responsible for an estimated 111 million cases, 25 million outpatient visits, 2 million hospitalizations, and over 520,000 deaths annually. Globally, about 40% of diarrheal hospitalizations are due to rotavirus. Asia and Africa have the largest disease burden from rotavirus infections, but all continents are affected significantly. Six countries (China, Democratic Republic of Congo, Ethiopia, India, Nigeria, Pakistan) account for more than 50% of all rotavirus deaths in children, with India and Nigeria recording 32.7% of all such deaths. This disease is characterized clinically by profuse watery diarrhea, projectile vomiting and dehydration, with fever in about 30% of cases.

Most children are infected by 2-3 years of age, with peak incidence of clinical illness among 6-18 month olds. Transmission is person-to-person; it is not waterborne. Children acquire natural immunity against severe disease that is about 75% effective in re-infections. The average age of first infection is younger among children in developing countries (6-9 months) than in developed countries (9-15 months), while the infection

tends to peak during the winter months in developed countries but occurs year round in most developing countries.

Serotypes of rotavirus are distinguished by two surface proteins (G and P protein) of the virus. There are over 100 combinations of the major G (glycoprotein) and P (protein) types of antigens. Relatively few strains are common globally in humans, but the specific serotypes in circulation vary widely among countries, with striking differences even between some neighboring countries and over time in the same country. Rotavirus strains are also common in pigs, cattle, dogs and other animals, and the strains in animals and people are constantly evolving. Interspecies transmission of rotavirus is uncommon but has been documented.

Dr. Mary Agocs described the World Health Organization (WHO) Network of hospital-based surveillance and laboratory capacity for rotavirus detection and typing. The first network was established in Asia in 1999, and included 9 countries in its first phase, in 2001-2003. Using funding provided primarily by the Global Alliance for Vaccines and Immunizations (GAVI), WHO subsequently coordinated development of surveillance networks via its regional offices, with strong linkages to ministries of health. By November 2007, networks had been established covering all regions of WHO, with six reference laboratories. The main aims of these networks are to determine the burden of disease, establish baseline epidemiological trends, and monitor the impact on those during and after introduction of rotavirus vaccines. 55 member states are currently part of the WHO network for surveillance of rotavirus infections, with other countries conducting surveillance and reporting to the regional offices. Sentinel sites in participating countries and regional reference laboratories report to WHO headquarters quarterly, and WHO will issue a summary report of the data at six monthly intervals. The first six-monthly report is due before the end of 2009, and a global surveillance meeting will be held in 2010.

Dr. Manish Patel summarized the current status of rotavirus vaccines. Two vaccines have been licensed for immunizing infants against rotavirus: Rota Teq®, by Merck, is a live, attenuated pentavalent vaccine administered orally in three doses, given between 6 and 32 weeks of age. Rotarix®, by GlaxoSmithKline, is a live, attenuated monovalent vaccine administered orally in two doses, given between 6 and 24 weeks of age. Both vaccines require refrigeration, and the relatively large per-dose volume of the vaccines is also a challenge for immunization programs. Introduced in 2006, both vaccines have proven to be safe and effective against severe rotavirus gastroenteritis when given as recommended after introduction in North and South America and without increased rates of intussusception that followed introduction of an earlier rotavirus vaccine. Efficacy trials in Asia and Africa demonstrated significant public health benefit of the vaccines. Both vaccines also provide cross-protection against other strains of rotavirus besides the specific serotype(s) in the vaccine. Average efficacy has tended to be better (85-100%) against severe rotaviral diarrhea in high and middle-income countries as compared to in low-income countries (50-70%), but there is no interference when vaccine against rotavirus is administered simultaneously with vaccine against polio virus. Data from the United States, Mexico and Australia have shown a dramatic impact in reduced

hospitalizations and/or deaths due to diarrhea after introduction of rotavirus vaccine. Early studies also suggest a possible "herd immunity" effect, with un-immunized children also benefiting when other children are immunized.

A full series of rotavirus vaccine costs about US$70-$200 per child in the private sector in high and middle income countries. In Latin America, the PAHO Revolving Fund procures the vaccine at about $16 per child immunized for the public sector. 72 low income countries (gross national income equal to or less than US$1,000 per capita) are eligible for vaccine subsidies from the GAVI Alliance that would cover most of the cost of the vaccine, leaving the countries with a co-pay of about 30 cents per child. The World Health Organization now "strongly recommends the inclusion of rotavirus vaccination into the national immunization programmes of all regions of the world."[1]

Dr. Umesh Parashar summarized remaining challenges in preventing morbidity and mortality from rotavirus infections. The observed reduced immunogenicity of the existing vaccines in developing countries deserves further study, even though use of the vaccines is still very cost effective in low-income settings. Given the presence of maternal antibodies in infants and of neutralizing antibodies against vaccine strains in breast milk, there is need to consider the efficacy of vaccine schedules, and other possible strategies that may help to improve vaccine performance in such settings. Other challenges include the relative bulk, cold chain requirements, and costs of the current vaccines. Manufacturers in Brazil, China, India, and Indonesia are developing rotavirus vaccines, which may reduce the cost of vaccine. Whether introduction of vaccine into wide use will cause significant changes in diversity of patterns of rotavirus strains in the future is currently unknown, but deserves monitoring. Another possibility is that use of the vaccine will alter the age-specific patterns of disease in humans, as measles vaccine did, so that previously uninfected and un-immunized teenagers may become vulnerable to first encounters with rotavirus in future.

Conclusions and Recommendations

1. Although the full significance of the apparently substantial reservoir of rotavirus strains in animals is not understood, it is unlikely that rotavirus infection can ever be completely eradicated in humans.
2. The burden of disease caused by rotavirus is very large, as the infection is the cause of much severe illness, many deaths, numerous outpatient visits and frequent hospitalizations. The goal of mass vaccination against rotavirus is to reduce severe illness and death, not to interrupt transmission.
3. Monitoring of the two rotavirus vaccines now in use has shown them to be safe and highly effective against severe rotavirus disease and consequent hospitalization, in middle income and high income countries. Although they show moderate efficacy in

[1] World Health Organization, 2009. Meeting of the immunization Strategic Advisory Group of Experts, April 2009 – conclusions and recommendations. *Weekly Epidemiological Record* 84(23):232—236.

low-income countries with high burden of disease, use of the vaccines there still provides a significant public health impact.

4. The Task Force joins the World Health Organization in urging introduction of routine immunization against rotavirus in all countries, including in Africa and Asia, as quickly as possible. The current vaccines offer an opportunity to save many lives and resources, in industrialized and in developing countries, and GAVI is prepared to assist many low income countries, but additional resources are needed urgently for what could be a huge impact, at a small fraction of the costs for some other programs. The challenge of improving the capacity for implementing routine immunizations, especially in many low-income countries, is acknowledged, and must be addressed.
5. Utility of the two current rotavirus vaccines is constrained by their requirement for refrigeration, their relative bulk, and cost. Vaccine manufacturers are encouraged to investigate ways to eliminate the need for refrigeration, to reduce the volume per dose, and to reduce the cost of vaccine.
6. The WHO surveillance and laboratory network is well established, and has an important role to play in monitoring patterns of serotypes in various countries and regions as vaccination against rotavirus is introduced, including the impact of vaccination in Asia and Africa.
7. More research is needed to assess the duration of vaccine protection in the second and subsequent years of life, and to develop additional data on issues related to vaccine performance in the developing world, such as the immunization schedule and impact of additional doses.
8. Although improved sanitation and hand washing are not specifically effective in preventing rotavirus infection, they are still useful and very much advisable to be included in health education programs, because of their effectiveness against other important infections.