

PAHO TECHNICAL ADVISORY GROUP ON VACCINE-PREVENTABLE DISEASES

Meeting Report on Cholera Vaccination

PAHO/HQ, Washington DC, August 14, 2012

Background

Since October 2010, when cholera emerged in the Island of Hispaniola, 584,683 and 26,056 suspect cases were reported as of July 28, 2012, in Haiti and the Dominican Republic, respectively. During the same period, 7,472 cholera-related deaths (case-fatality rate [CFR] = 1.28) were reported in Haiti and 402 (CFR = 1.58) in the Dominican Republic. Although incidence is lower in 2012 (January 1–July 28) compared to previous years, cholera still remains a significant public health problem in the Island: 64,491 suspect cases and 454 cholera-related deaths (CFR = 0.70) were reported in Haiti and 3,809 cases and 32 deaths (CFR = 0.84) in the Dominican Republic. In 2010–2011, eight countries in the Americas reported 92 cases imported from the Island of Hispaniola (38 confirmed and 54 epidemiologically linked cases). Since early July 2012, an outbreak has been reported in Cuba, where 236 patients have been confirmed.

The presidents of Haiti and the Dominican Republic, together with representatives of PAHO/WHO, UNICEF, and the CDC, issued in January 2012 a call to action to eliminate cholera transmission from both countries through new investments in water and sanitation infrastructure. This call led in June 2012 to the creation of the Regional Coalition on Water and Sanitation for the Elimination of Cholera Transmission in the Island of Hispaniola, which will bring together the necessary technical expertise, raise new funds, and mobilize previously committed pledges.

Deployment of oral cholera vaccine (OCV) has been considered since October 2010. At that time, also considering the rapidly spreading epidemic and the limited vaccine supplies, PAHO recommended to focus emergency efforts on time-tested measures for cholera outbreak response, namely on treatment to prevent deaths and traditional preventative actions to halt transmission (i.e. delivery of safe potable water, provision of supplies for hand washing and other hygienic measures, sanitation, and proper waste disposal). An expert consultation convened by PAHO in December 2010 recommended that the limited vaccine supply be used for demonstration projects and that efforts be initiated to increase OCV availability.

Two oral cholera vaccines are marketed globally under the names of Dukoral and Shanchol and are now WHO-prequalified. When compared to Dukoral, Shanchol offers operational advantages, because it does not require administration with a buffer solution, requires significantly less cold chain volume, can be administered from 1 year of age (versus 2 years of age), and costs one third per dose at current prices. As published in October 2011, results of Shanchol clinical trials show a 66% overall efficacy at three years of follow-up. Within a community, vaccination with OCV may also provide herd protection and thus reduce cholera burden among persons who remain unvaccinated. Shanchol's manufacturer has indicated the immediate availability of up to 800,000 doses and the capacity to scale up production to 5 million doses in 2013 and to >10 million doses in 2014 and thereafter; this availability is not exclusively reserved for the Americas.

Following the above-mentioned recommendation of a PAHO-convened expert consultation, the two non-governmental organizations GHESKIO and Zanmi Lasante/Partners in Health conducted between April and June 2012 separate but coordinated cholera vaccination in one urban and one rural area of Haiti. Overall, 97,725 persons received at least one vaccine dose and completion rate for the two-dose immunization series was 91%. Key lessons from these cholera vaccination demonstration projects in Haiti were community acceptance of cholera vaccination and feasibility of administering the vaccine on a large scale in both rural and urban settings. At the same time, the demonstration underscored the need for substantial planning prior to vaccination, for a reliable cold chain and other logistic resources, for an ongoing monitoring of vaccination activities, and for communication activities involving the community, opinion leaders and the media. Impact evaluation is now being planned.

National immunization programs throughout the Region remain committed to maintaining the elimination of polio, measles and rubella, to reducing within-country inequalities in vaccination coverage, and to advancing in the evidence-based and sustainable introduction of new vaccines. For instance, the local Ministry of Health, PAHO, and partners made significant progress in Haiti during the first semester of 2012 to improve routine vaccination and to carry out a nationwide intensification of measles/rubella/polio vaccination. In Haiti, vaccination with pentavalent vaccine (DTP-HepB-Hib vaccine) should begin in September 2012 and introduction of rotavirus and pneumococcal conjugate vaccines is planned for 2013.

At least four elements warrant a reconsideration of OCV deployment in the Island of Hispaniola: The ongoing occurrence of cholera now almost two years after the epidemic began; the WHO-prequalification in September 2011 of a second OCV (Shanchol) that eases some operational challenges; the immediate availability in principle of up to 800,000 OCV doses; and the demonstration that, with substantial planning and logistic resources, OCV deployment is feasible on the Island.

Most important, interventions to decrease cholera transmission through improvements in water and sanitation, the provision of clean water and sanitation to every household will take years to accomplish and will require the mobilization of billions of dollars, while immunization against cholera requires a significantly lower investment in the short term.

Recommendations

- Elimination of cholera transmission in the Island of Hispaniola, defined as cholera no longer being a public health burden, will only be achieved in the long run through considerable investments towards significant and sustained improvements in access to potable water and sanitation. To achieve the overarching goal of cholera transmission elimination, several short-term actions should also be considered, including the expanded use of OCV. However, if water and sanitation are not improved in the long run, the Island will likely remain vulnerable to repeated epidemics, even though a large-scale cholera vaccination program is in place.
- Ultimately, OCV should be offered universally in Haiti, also leveraging its delivery to strengthening the provision of other cholera prevention measures (such as, social mobilization and active case-finding) and national immunization services. To reach this objective,

incremental advances are needed in the integration of OCV use with WASH development plans, in assuring sufficient OCV availability and financial sustainability of its purchase and delivery, and in developing operational and monitoring immunization capacities. These advances need to build national and local capacity of immunization programs and the health system as a whole. The timeframe during which vaccination will be needed depends on the advances in access to potable water and provision of sanitation and on the evolution of natural and vaccine immunities at population level. Regardless of the time and eventual scope of a cholera vaccination program, additional resources and funds will be needed for the program to be successful.

- Up to 800,000 OCV doses are currently available; global production capacity could be scaled up to 5 million doses in 2013 and to >10 million doses in 2014 and thereafter. Therefore, a phased introduction based on global supply will need to be used in the Island of Hispaniola. To begin OCV should be given on a targeted basis to the persons most at risk and to those who will benefit most based on an analysis of the surveillance data and an understanding of local conditions. For instance, at the start vaccination could be prioritized to urban areas with high population-density and WASH insecurity and to rural areas with difficult access to health care. However, only a detailed analysis of the epidemiologic surveillance data can determine which areas and populations are at highest risk. This analysis should be presented at the next TAG meeting scheduled for October 2012.
- To solve global OCV availability, international partners should renew efforts to establish why OCV remains in short supply and to communicate clearly to manufacturers the expected demand. A global OCV stockpile continues to be encouraged.
- TAG would like to better understand manufacturers' needs. The PAHO Secretariat should gauge these needs and present them at the next TAG meeting.
- As some knowledge gaps persist, evaluation and research should be an integral part of the plan to expand OCV use. In particular, research should focus on development of a single-dose vaccine, efficacy proof of a single dose of current two-dose vaccines, safety studies of OCV use in pregnant women, occasional environmental bacteriology testing, serosurveys to determine which fraction of the population is already immune to cholera, and effectiveness studies of vaccine (including nested case-control studies). A proposal for a comprehensive research agenda should be presented at the next TAG meeting.
- The cholera epidemiology in the Island of Hispaniola should be better described and understood. Surveillance system and data should be reviewed and, if necessary, surveillance should be improved with a more systematic bacteriological confirmation of cases.
- TAG welcomes an expanded United Nations role and support for both the short and the long term in achieving the elimination of cholera transmission in the Island of Hispaniola.