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A National Cholera Vaccine Stockpile — A New Humanitarian and Diplomatic Resource

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Cholera is a severe and often rapidly fatal diarrheal disease caused by the bacterium *Vibrio cholerae*. People die from cholera because the pathogen elicits the secretion of large quantities (up to 20 liters daily) of bacteria-laden fluid from the intestine, resulting in extreme dehydration. If supplies of drinking water or food become contaminated with *V. cholerae*, the disease can spread through a population very rapidly.

Cholera has afflicted humans for thousands of years and has led to millions of deaths. It is endemic in many parts of South Asia, and it can cause epidemics both in areas where it is endemic and in those where it is not, often as a result of man-made or natural disasters. The threat of cholera has largely been eliminated in regions that can maintain provision of clean water, adequate hygiene, and proper sanitation for all residents. However, refugees, who often live in overcrowded and unsanitary conditions, are at extremely high risk for contracting cholera, and outbreaks in such environments can be devastating. In 1994, cholera caused the deaths of more than 10,000 Rwandan refugees in Goma, Zaire, and last year there were reportedly 4000 deaths during Zimbabwe's protracted epidemic, which was made worse by a general breakdown of that country's public health and health care infrastructure.¹ The World Health Organization (WHO) estimates that the annual global burden of cholera is 3 million to 5 million cases and 100,000 to 130,000 deaths, with no evidence of a global decline, despite major efforts to ensure the provision of clean water and adequate sanitation.¹

Treatment for cholera is straightforward. Replacement of lost fluid with oral or intravenous rehydration solution is usually lifesaving. Antibiotics can be used to shorten the duration of illness. However, these interventions can be difficult to administer when there are inadequate medical facilities available, as is often the case in complex humanitarian emergencies, and the rapid progression of the disease means that there is only a narrow therapeutic window. Provision of clean water and temporary sanitary facilities are also mainstays of epidemic control, yet as recent events in Africa and Asia have shown, cholera epidemics can be protracted despite such efforts. Clearly, it is time to consider additional preventive interventions that would complement existing approaches.

Efforts to create safe and effective vaccines for the prevention of cholera have a long history. Parenteral vaccines have not proved to be effective, but there are several oral vaccines for cholera that have proved to be safe and reasonably effective in parts of the world where cholera is endemic and that even provide some degree of herd immunity.¹

Three oral cholera vaccines are the most widely used. One consists of killed *V. cholerae* cells formulated with recombinant cholera toxin B (Dukoral, Crucell). Since 1991, Dukoral has been licensed in more than 60 countries, and it is prequalified by the WHO for United Nations purchase and has been used previously in crisis or refugee situations in Indonesia, Sudan, and Uganda, as well as in densely populated urban slums in Mozambique.^{2,3} The two other vaccines consist of killed *V. cholerae* cells without added toxin (Shanchol, Shantha Biotechnics; and mORC-VAX, VaBiotech). Both vaccines were licensed in 2009, and Shanchol is currently awaiting prequalification by the WHO.⁴ All three vaccines are given in two-dose regimens (Dukoral is given in three doses to children under 6 years of age), are relatively cheap, and are simple to administer.

Even though there is no imminent threat of cholera in the United States, we believe that our country should stockpile cholera vaccines for rapid deployment to parts of the world that suddenly find themselves at high risk for this disease. Until recently, Latin America and the Caribbean region were considered to have a negligible risk of a cholera epidemic. Recent events in Haiti, however, force us to reconsider this belief. Other areas of the world where populations are at great risk include sub-Saharan Africa and South and Southeast Asia (see maps). A recent analysis of the global burden of cholera undertaken by the International Vaccine Institute suggests that approximately 1.5 billion people are at risk for cholera globally.

The costs to the United States of creating and maintaining a stockpile of several million doses of cholera vaccine would be low. (The current price of Shanchol to public-sector programs in developing countries is under \$2 per dose.) But the humanitarian benefits of rapid deployment of cholera vaccines to areas at high risk for major cholera outbreaks — such as earthquake-wracked Port-au-Prince, the Haitian capital where 1.3 million people live in unsanitary refugee camps, or the neighboring country of the Dominican Republic, where the epidemic could potentially spread to the slums of Santo Domingo, or flood-ravaged areas of Pakistan, where cholera emerged this past spring — could be enormous. Remarkably, there are fewer than 400,000 total doses of oral cholera vaccines (either Dukoral or Shanchol) available at present for shipment from their manufacturers, making it impossible to consider large-scale vaccination of at-risk populations with the recommended two- or three-dose regimens of either product. The global shortage of cholera vaccine reinforces the urgency of creating a stockpile.

In addition to the obvious health and humanitarian benefits that a national stockpile of cholera vaccine could yield, deployment of such a vaccine to regions of the world that are at high risk for a cholera epidemic offers numerous other benefits. Outbreaks of cholera and other diarrheal diseases impede recovery from disasters. They also destabilize poor communities, promoting poverty by interfering with agricultural productivity and adversely affecting food security, and thereby potentially igniting new conflicts or exacerbating existing ones.⁵ If the vaccine were available now, it could still be delivered to as-yet-unaffected parts of Haiti in time to stabilize the country before its national elections.

Moreover, there is a goodwill argument to be made for providing cholera vaccine to countries, such as Pakistan, with which our country has troubled relationships. And through so-called vaccine diplomacy, the United States could also do its part to promote international stability and peace. For example, on the island of Hispaniola, the use of a cholera vaccine could ease the tensions that are arising between Haiti and the neighboring Dominican Republic. In this way, in addition to saving thousands of lives each year in low- and middle-income countries, the establishment and use of a stockpile of cholera vaccine could advance the U.S. diplomatic aims of promoting peace and stability in the world.

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In South Africa, there was also a cholera outbreak in 2000–2001 that included about 12,000 cases. Data are from the World Health Organization and the ProMed and PubMed databases.

2. . Registered Cholera Cases and Deaths in Haiti, November 2010

As of November 13, 2010, a total of 16,111 cases of cholera and 992 deaths had been reported to the Pan American Health Organization in Haiti.