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New preventive tool for endemic countries

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Cholera vaccine

New preventive tool for endemic countries

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Cholera is a major global public health problem and remains an important threat in almost every developing country, especially in areas where population overcrowding and poor sanitation are common, such as slums and refugee camps. Cholera is one of the most dreaded diseases in the world, in some cases leading to death within 24 h if left untreated. Without treatment, severe infection has a mortality rate of 30–50%. In 2007, WHO recorded 177,963 cholera cases and 4,031 deaths worldwide. However, the estimated actual burden of cholera is in the vicinity of 3 to 5 million cases and 100,000 to 130,000 deaths per year. The disease is endemic to parts of Africa, Asia, the Middle East and South America.¹ Large outbreaks are common after natural disasters or in populations displaced by war, where there is inadequate sewage disposal and contaminated water. In India, during the 10-y period (1997–2006) studied, the states having the highest number of reported outbreaks were West Bengal, Orissa, Maharashtra and Kerala, which together accounted for 60% of all reported outbreaks. A review of cholera cases in India reported to WHO from 2003–2007 showed that the numbers were in the few thousands with a case fatality rate of < 1%. However, it is believed that the number of cholera cases and deaths occurring annually in India is much greater than the number reported. A literature review covering a four-year period from 2003 to 2006 found reported cholera outbreaks in 18 of the 35 States and Union Territories of India. Of these, 11 had cholera outbreaks reported for multiple

years. Vietnam has produced a cheaper variant of killed whole-cell vaccine devoid of the B subunit. This vaccine contains both *Vibrio cholerae* O1 and O139, and provides 50% protection for at least three years after vaccination. For endemic cholera, population-level immunity is relatively high, making control possible with relatively low vaccine coverage levels. This vaccine should be used in areas where cholera is endemic, particularly in those at risk of outbreaks, in conjunction with other prevention and control strategies.

Cholera is a major global public health problem and remains an important threat in almost every developing country, especially in areas where population overcrowding and poor sanitation are common, such as slums and refugee camps. Cholera is an acute water-borne diarrheal infection caused by the enterotoxin subunit-A of *Vibrio cholerae*.² Transmission occurs through direct faeco-oral contamination or through ingestion of contaminated water and food. The disease is characterized in its most severe form by a sudden onset of acute watery diarrhea that can lead to death by severe dehydration and kidney failure within hours.³ Individuals with lower immunity, such as malnourished children or people living with HIV, are at greater risk of death if infected by cholera. Cholera is one of the most dreaded diseases in the world, in some cases leading to death within 24 h if left untreated. Without treatment, severe infection has a mortality rate of 30–50%.¹

A cumulative total of 838,315 cases had been notified to the World Health

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Organization (WHO) for the period of 2004 to 2008, and 676,651 cases were reported from 2000 to 2004. This represents a 24% increase in the number of cases reported with respect to the previous 5-y period (2000–2004).⁴ In 2007, WHO recorded 177,963 cholera cases and 4,031 deaths worldwide. However, the estimated actual burden of cholera is in the vicinity of 3 to 5 million cases and 100,000 to 130,000 deaths per year.⁵

The disease is endemic to parts of Africa, Asia, the Middle East and South America.¹ Large outbreaks are common after natural disasters or in populations displaced by war, where there is inadequate sewage disposal and contaminated water.² Two serotypes of *V. cholerae* cause epidemic cholera (serotype O1 and serotype O139). Serotype O1 is further divided into classical and El Tor biotypes. Outbreaks caused by the classical biotype are infrequent whereas *V. cholerae* El Tor now predominates and is responsible for the current seventh cholera pandemic.⁶ Serotype O139 emerged in 1992 and quickly spread through Asia. It is now responsible for almost 60% of recent cholera cases in developing countries and the threat of pandemic remains.¹

In India, during the 10-y period (1997–2006) studied, the states having the highest number of reported outbreaks were West Bengal, Orissa, Maharashtra and Kerala, which together accounted for 60% of all reported outbreaks. Of the cholera cases that occurred during outbreaks, 91% were identified in the states or union territories of Orissa, West Bengal, Andaman and Nicobar Islands, Assam and Chhattisgarh. The number of affected individuals ranged from a low of 4 in Himachal Pradesh to a high of 102,778 in Orissa. In the 10-y period, 823 deaths were reported, and the overall case fatality rate was 0.37%.⁷

A review of cholera cases in India reported to WHO from 2003–2007 showed that the numbers were in the few thousands with a case fatality rate of < 1%. However, it is believed that the number of cholera cases and deaths occurring annually in India is much

greater than the number reported. A literature review covering a four-year period from 2003 to 2006 found reported cholera outbreaks in 18 of the 35 States and Union Territories of India. Of these, 11 had cholera outbreaks reported for multiple years. These States and Territories are spread across India, showing that cholera is a country-wide cause of diarrheal illness.⁸

According to National health profile 2008, 11,231,039 cases of acute diarrhea were recorded that year, of them, 2,680 were cholera cases.⁹ These were the national figures conveyed to WHO. According to data from population-based diarrhea surveillance in an endemic area of Kolkata, the incidence of cholera was 2.2 cases per 1,000 person/years.¹⁰ If this data were extrapolated to all endemic areas in the country, the total number of cases would far exceed the numbers quoted above. This continuing high burden highlights the need for interventions to prevent cholera. While improved water and sanitation constitute the ultimate basis for the prevention of cholera, this is a far-off goal for the impoverished settings in which cholera thrives.

New-generation OCVs have been available for more than two decades.¹¹ The WHO had recommended their use in the control of endemic and epidemic cholera since 2002,¹² but they have not been extensively adopted. The only WHO-prequalified OCV to date is the Swedish recombinant B-subunit killed whole-cell vaccine (rBS-WC).⁸ Up to that point cholera vaccines were recommended for individual travelers to endemic countries but not for public health use in endemic countries. Far from embracing vaccinations for cholera control, WHO experts recommended gaining more experience through demonstration projects. Since then, mass oral cholera vaccinations have been conducted in Beira, Mozambique, in Darfour, Sudan, and in Aceh, Indonesia. These projects demonstrated the feasibility and effectiveness of vaccination under actual public health conditions.¹³

Vietnam has produced a cheaper variant of killed whole-cell vaccine devoid of

the B subunit. This vaccine contains both *Vibrio cholerae* O1 and O139, and provides 50% protection for at least three years after vaccination.¹⁴ This inexpensive vaccine costs less than a dollar a dose. This vaccine has been used in Vietnam's public health sector in high risk cholera areas and more than 9 million doses have been administered. Since the vaccine does not require any buffer, it is easier to administer. However, an analysis of the Vietnamese vaccine showed that to comply with WHO guidelines, the vaccine needs to be reformulated and its production technology modified. The International Vaccine Institute (IVI) worked with the Vietnamese producer and developed a killed whole cell cholera vaccine that meets quality standards.⁸ The Seoul, Korea-based international organization transferred the production technology to India.

This improved, low-cost oral whole-cell (WC) cholera vaccine that meets international good manufacturing practice (GMP) and WHO standards for production has been licensed in India after studies in Kolkata and Vietnam showed the vaccine to be extremely safe and effective, the National Technical Advisory Group on Immunization (NTAGI) should consider recommending the introduction of the vaccine into public health programs targeted to appropriate populations in India. The oral cholera vaccine (OCV) is an orally administered, inactivated whole cell vaccine, has an overall efficacy of about 52% during the first year after being given and 62% in the second year, with minimal side effects.⁸

For endemic cholera, population-level immunity is relatively high, making control possible with relatively low vaccine coverage levels. This vaccine should be used in areas where cholera is endemic, particularly in those at risk of outbreaks, in conjunction with other prevention and control strategies.¹⁵ The OCV (given in two doses with a minimum inter-dose interval of 14 d) has been licensed on February 24, 2009 by the Drugs Controller General of India.⁸

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