

## 3.2 CHOLERA

### Bacteriology

*Vibrio cholerae* is a motile, curved Gram-negative bacillus and differences in the O antigens have led to the description of more than 150 serogroups, only two of which have been found to cause cholera. Cholera is caused by enterotoxin producing *V. cholerae* of serogroups O1 and O139 (sometimes referred to as the 'Bengal' strain). Serogroup O1 includes 2 biotypes (classical and El Tor), each of which includes organisms of Inaba, Ogawa and Hikojima serotypes. The ability of *V. cholerae* to persist in water is determined by the temperature, pH, salinity and availability of nutrients; it can survive under unfavourable conditions in a viable dormant state.<sup>1</sup> Transmission predominantly occurs when people ingest faecally contaminated food or water.

### Clinical features

Cholera is an acute bacterial infection that is generally characterised by the sudden onset of painless, profuse, watery diarrhoea. If untreated, more than half the severe cases will die. Mild cases also occur, as does subclinical infection.<sup>1</sup>

The cholera toxin does not produce intestinal inflammation. The cholera toxin induces secretion of increased amounts of electrolytes into the intestinal lumen, resulting in mild to severe dehydration and, in some cases, metabolic acidosis.

### Epidemiology

Cases of cholera in Australia (about 2 to 6 cases a year) almost always occur in individuals who have been infected in endemic areas of Asia, Africa, the Middle East, South America or parts of Oceania.<sup>2-4</sup> The disease is usually transmitted via food and water contaminated with human excreta. Shellfish obtained from contaminated waters have also been responsible for outbreaks.<sup>1</sup>

In 1977, a locally acquired case led to the discovery of *V. cholerae* in some rivers of the Queensland coast.<sup>5</sup> Because of this, health workers should be aware that sporadic cases of cholera may, on rare occasions, follow contact with estuarine waters.

As the incubation period of the disease may extend up to 5 days, surveillance of household contacts or those exposed to a possible common source should be maintained for 5 days from the date of last exposure. Stool cultures (cultured using specific media) may be taken from close contacts if required. Food handlers should not be allowed to return to work until 2 consecutive stool samples, taken at least 24 hours apart, are negative. Contacts should also be advised to maintain high standards of personal hygiene to avoid becoming infected. Cases should be reported immediately to the public health authorities (for contact details, refer

to Appendix 1, *Contact details for Australian, State and Territory Government health authorities and communicable disease control*).

## Vaccines

- **Dukoral** – Sanofi Pasteur Pty Ltd (inactivated whole-cell *V. cholerae* O1 in combination with a recombinant cholera toxin B subunit (rCTB)). Each 3.0 mL liquid vaccine dose vial contains heat and formalin inactivated Inaba, Ogawa, classic and El Tor strains of *V. cholerae* O1,  $2.5 \times 10^{10}$  vibrios of each, combined with 1.0 mg rCTB. The buffer consists of a sachet of effervescent granules of anhydrous sodium carbonate, sodium bicarbonate, anhydrous citric acid, sodium citrate, saccharin sodium and raspberry flavour.

Trials of the safety, immunogenicity and efficacy of oral vaccines, both killed and live attenuated, have been carried out in the United States, Bangladesh, Thailand, Indonesia, Chile, Peru and Switzerland.<sup>6-12</sup>

Trials of the inactivated vibrio combined with rCTB vaccine have been done mainly in Bangladesh and Peru.<sup>9,13-16</sup> In Bangladesh, a 2-dose regimen showed protective efficacy of 44% in children 2 to 6 years of age and 76% in adults at the end of 1 year, and 33% and 60%, respectively, after 2 years. The studies in Peru showed an overall efficacy of 61% in 2–65-year-olds. A recent study undertaken during a mass oral cholera vaccination program in Mozambique concluded that 1 or more doses of the inactivated oral cholera vaccine was 78% protective.<sup>17</sup>

To date, there is no vaccine marketed to protect against infection with *V. cholerae* O139. A killed oral whole cell cholera bivalent vaccine (against both serogroups O1 and O139) is currently being evaluated in Vietnam.<sup>18,19</sup>

A study in short-term Finnish tourists<sup>20</sup> showed that the inactivated oral cholera vaccine also provided a 60% reduction in diarrhoea caused by heat-labile toxin producing enterotoxigenic *E. coli* (LT-ETEC). A study in Bangladesh, an endemic area, showed 67% protection against LT-ETEC for 3 months only.<sup>21</sup> It can be expected that the inactivated vaccine will reduce the proportion of travellers' diarrhoea that is caused by LT-ETEC. Approximately 30 to 40% of travellers to developing countries contract travellers' diarrhoea, with an average of 20% of cases caused by LT-ETEC; hence, the 60% efficacy of the oral inactivated vaccine against LT-ETEC could be expected to prevent around 10 to 12% of travellers' diarrhoea.<sup>22</sup> However, in Australia this vaccine is only registered for the prevention of cholera.

## Transport, storage and handling

Transport according to *National Vaccine Storage Guidelines: Strive for 5*.<sup>23</sup> Store in a refrigerator at +2°C to +8°C. Do not freeze. Protect from light.

## Dosage and administration

For adults and children over the age of 6 years, Dukoral is administered orally after dissolving the buffer granules in 150 mL of water and adding the vaccine to the solution. Two doses are required, given a minimum of 1 week and up to 6 weeks apart. If the second dose is not administered within 6 weeks, re-start the vaccination.

For children aged 2–6 years, Dukoral is administered orally after dissolving the buffer granules in 150 mL of water. Half the solution is then poured away and the entire content of the vaccine vial is mixed with the remaining 75 mL. Children aged 2–6 years should receive 3 doses of the vaccine. Doses are to be administered with a minimum interval of 1 week between doses up to a maximum interval of 6 weeks. If an interval of more than 6 weeks occurs between any of the doses, re-start the vaccination.

Food and drink should be avoided for 1 hour before and 1 hour after administration of the inactivated cholera vaccine, as it is acid labile.

The inactivated oral cholera vaccine can be given at the same time as other travel vaccines. However, there should be an interval of at least 8 hours between the administration of the inactivated oral cholera and oral typhoid vaccines, as the buffer in the cholera vaccine may affect the transit of the capsules of oral typhoid vaccine through the gastrointestinal tract.

Adults and children >6 years of age should receive a single booster dose after 2 years and children 2–6 years of age should receive a booster dose 6 months after completion of the primary course.

## Recommendations

Despite the endemicity of cholera in some countries often visited by Australians, routine cholera vaccination is not recommended as the risk to travellers is very low. Careful and sensible selection of food and water is of far greater importance to the traveller than vaccination.

Immunisation should be considered for people at increased risk of diarrhoeal disease, such as those with achlorhydria, and for people at increased risk of severe or complicated diarrhoeal disease, such as those with poorly controlled or otherwise complicated diabetes, inflammatory bowel disease, HIV/AIDS or other conditions resulting in impaired immunity, or significant cardiovascular disease. It could also be considered for humanitarian disaster workers.

Vaccination against cholera is not an official requirement for entry into any foreign country.

## Contraindications

The only contraindications to the use of cholera vaccine are:

- anaphylaxis following a previous dose of the vaccine,
- anaphylaxis following any component of the vaccine,
- inactivated oral cholera vaccine is *not* recommended for children <2 years of age.

## Precautions

- Postpone administration during either an acute febrile illness or acute gastrointestinal illness with persistent diarrhoea or vomiting, until recovered.
- Although the vaccine is not contraindicated in immune impaired individuals, including HIV-infected individuals, data on effectiveness in this population is limited.
- There should be an interval of at least 8 hours between the administration of the inactivated oral cholera and oral typhoid vaccines, as the buffer in the cholera vaccine may affect the transit of the capsules of oral typhoid vaccine through the gastrointestinal tract.

## Adverse events

The inactivated oral vaccine is uncommonly (<1%) associated with mild gastrointestinal disturbances.

## Use in pregnancy

There is inadequate information on the use of inactivated oral cholera vaccines during pregnancy and breastfeeding.<sup>24</sup>

## Variations from product information

None.

## References

Full reference list available on the electronic *Handbook* or website <http://immunise.health.gov.au>.