

Help protect at-risk travellers against DIARRHOEA caused by CHOLERA^{1,2}

Profuse watery diarrhoea associated with cholera can result in severe dehydration^{1,3} and can cause disruption to a holiday or business trip.⁴ Mild cholera is often clinically indistinguishable from other causes of acute diarrhoea, including traveller's diarrhoea.^{5,6} Associate Professor Bernard Hudson provides some insight into cholera and what can be done to help prevent it.



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1. Are there many cases of cholera reported in Australia each year? How are the majority of reported cases acquired?

Annually, on average, there are two to six cases of cholera notified in Australia. Usually these are all in travellers returning from cholera endemic areas.¹

Since 1991, all cholera cases notified in Australia have been acquired in countries outside of Australia, except for one laboratory-acquired case, and three cases in 2006, in Sydney, that were associated with consumption of raw imported whitebait.¹

2. Where in the world is cholera considered endemic?

Cholera is endemic in Africa and South and Southeast Asia.⁷ Civil strife, population movements and natural disasters, which lead to breakdown in water and sanitation services, are common settings for cholera outbreaks.¹

3. What is the risk of cholera to Australian travellers? Is cholera potentially under-reported in travellers and if so, why?

Cases of cholera, as noted above, in travellers returning to Australia, are rare. The risk of cholera for travellers from western countries to endemic areas has been estimated at

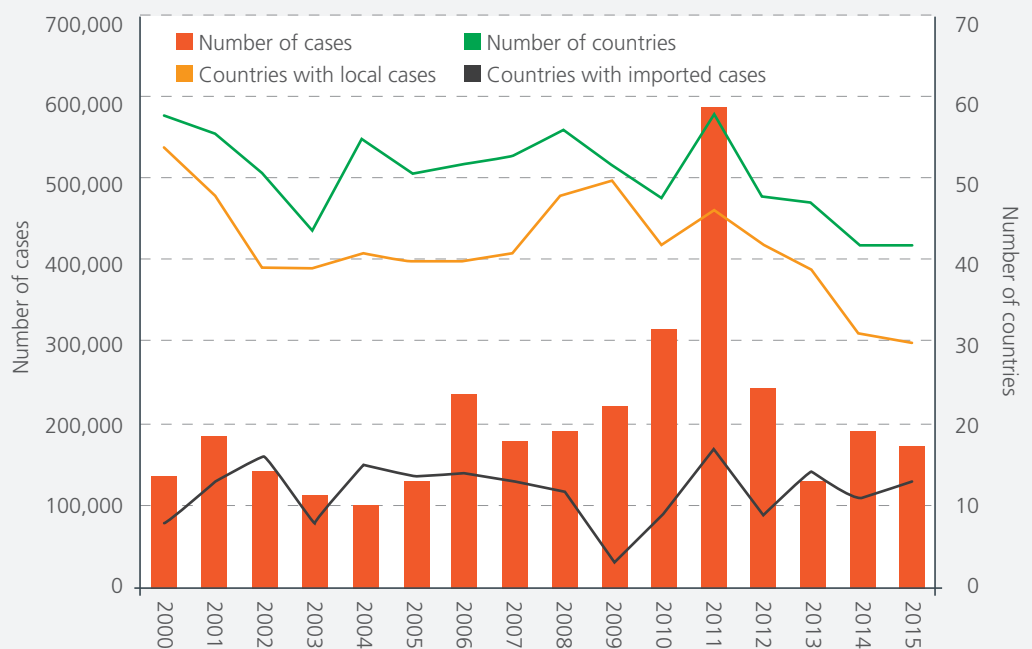
0.2 cases per 100,000, with the risk of severe disease and death being much lower.⁴

Due to the relatively low numbers, most GPs do not consider cholera as a risk for travel even to endemic areas. Whilst this is true to an extent, it is important to also realise that most authorities believe that under-detection and under-reporting of cholera among travellers is likely.^{1,3}

Milder cases almost certainly go unreported as illness may resolve with simple measures such as fluid replacement and without microbiological screening, mild cholera is often clinically indistinguishable from other causes of acute diarrhoea.^{5,6}

Cholera is endemic in Africa, and South and Southeast Asia⁷

Countries/areas reporting Cholera and cases reported by year, 2000–2015.⁸



Adapted from WHO WER no.38⁸

Australian Immunisation Handbook 10th Edition¹ recommends cholera vaccination for at-risk travellers visiting areas epidemic or endemic for cholera, including:

Travellers at increased risk of diarrhoeal disease.

For example, travellers with:

- Achlorhydria
- Poorly controlled or complicated diabetes
- Impaired immunity
- Significant cardiovascular disease

Travellers with considerable risk of exposure to, or acquiring, cholera.

For example:

- Humanitarian disaster workers

Unfortunately, multiple studies have shown that dietary indiscretions are common in travellers,⁹ so additional protection may be of benefit.

4. What are the clinical features of cholera and how do they differ from other causes of acute diarrhoea?

Vibrio cholerae produces a toxin and it is this toxin that causes cholera. Cholera toxin does not cause intestinal inflammation or bleeding (so there are no white or red blood cells in the faeces), but induces secretion of a large amount of electrolytes and fluid into the small bowel lumen, leading to diarrhoea and dehydration.¹ Sometimes diarrhoea may be so severe that it produces rapid dehydration and shock.¹⁰

Cholera is characterised by a sudden onset of painless, profuse, watery diarrhoea.¹ The incubation period ranges from a few hours to five days.^{3,10} Infection is most often asymptomatic or mild. Among those who develop symptoms, around 20% develop acute watery diarrhoea with severe dehydration, leading to death within hours if untreated.⁷ Without treatment, the mortality rate varies between 4 and 50%, and can be higher in more severe cases.⁵

Unlike other bacterial causes of diarrhoea, persistent gut carriage of *V.cholerae* is rare.¹⁰ Other bacterial causes of diarrhoea, such as *Campylobacter*, *Salmonella* and *Shigella* cause inflammation of the bowel and typically have white and red blood cells in the faeces. They can all cause bloody diarrhoea but they may also just cause watery, non bloody diarrhoea, which may also be profuse.¹¹ Without laboratory tests, it may not be possible to determine the microbial cause of the diarrhoea.^{5,6}

5. What can be done to help prevent cholera in travellers?

Cholera is transmitted through the faeco-oral route via consumption of contaminated food and water, especially in areas with poor sanitation.

Outbreaks associated with consumption of seafood, especially shellfish, are well-recognised.¹ Safe eating and drinking practices are paramount to prevent infection, with the aphorism “boil it, cook it, peel it, or forget it” a simple one for travellers to remember. Unfortunately, multiple studies have shown that dietary indiscretions are common in travellers,⁹ so additional protection may be of benefit. For certain travellers, cholera vaccination may be considered in addition to the food and water precautions.

The only cholera vaccine currently registered in Australia is Dukoral®. Dukoral® is an oral vaccine containing inactivated whole-cell *V.cholerae* O1, in combination with a recombinant cholera toxin B subunit. Clinical trials have demonstrated a protective efficacy against cholera of 85% for the first six months in all age categories. The primary vaccination schedule for Dukoral® comprises two doses for adults and children over the age of 6 and three doses for children 2–6 years of age. Doses should be spaced 1–6 weeks apart. For those at ongoing risk, booster doses may be required.² Dukoral® is not recommended for use in children aged less than 2 years.² Overseas, the vaccine has been used to help control epidemics,

in concert with the primary measures of water and sanitation control.¹²

6. When should travellers begin their course of cholera vaccination?

The primary course of Dukoral® should preferably be completed at least two weeks before travel to cholera endemic areas.² This allows adequate time for immunity to develop.

7. Who would you consider as appropriate candidates for cholera vaccination?

In addition to the types of travellers for whom cholera vaccination is usually recommended (see Australian Immunisation Handbook recommendations on the previous page), vaccination against cholera should be considered for travellers to endemic areas who may be unable to guarantee safe food and water, especially those going to remote areas. Remote and/or rural travel in cholera endemic countries may leave little or no time for life-saving treatment as death can occur within 24 hours.^{4,5,12} Achlorhydria e.g. caused by some medications, should always be borne in mind when assessing travellers who may be candidates for cholera vaccination.^{13,14}

DUKORAL®
Oral, Inactivated Cholera vaccine



PBS Information: This product is not listed on the National Immunisation Program (NIP) or the PBS.

Before prescribing, please review the Product Information available at www.Seqirus.com.au/PI

MINIMUM PRODUCT INFORMATION. DUKORAL® Oral Inactivated Cholera Vaccine. **INDICATIONS:** Cholera caused by serogroup O1 *Vibrio cholerae*: Active immunisation of adults and children ≥ 2 years of age, who will be visiting areas epidemic or endemic for cholera and who are at high risk of infection. **CONTRAINDICATIONS:** Hypersensitivity to active substances, excipients or formaldehyde. Acute gastrointestinal or febrile illness. **PRECAUTIONS:** Does not protect against species other than O1 *V. cholera*; does not necessarily prevent spread of cholera via a vaccinee exposed to *V.cholerae* bacteria; not a sole measure in prevention of cholera outbreaks - clean hygiene practices still required; HIV patients; endogenous or iatrogenic immunosuppression; patients on controlled sodium diet. **Pregnancy Category B2. Use in Lactation:** Following careful benefit/risk assessment, DUKORAL may be administered to lactating women although no studies conducted. **INTERACTIONS:** Avoid food or drink 1 hour before or after vaccination. Administration of encapsulated oral typhoid vaccine should be separated by ≥ 8 hours. Other oral vaccines and medicines avoided 1 hour before or after vaccination. **ADVERSE EFFECTS:** In clinical trials, most frequently reported were abdominal pain, diarrhoea, loose stools, nausea and vomiting, at similar frequencies in vaccine and placebo groups (see full PI) **DOSAGE & ADMINISTRATION:** Dissolve effervescent granules in 150mL cool water to make buffer solution (pour away 75mL for children 2–6 years). Shake vaccine vial gently and add to buffer solution; mix well and drink. Adults & children > 6 years: 2 doses; Children 2–6 years: 3 doses; administer doses at intervals ≥ 1 week. Re-start basic immunisation if > 6 weeks elapse between doses. Booster: Adults and children > 6 years: after 2 years; Children 2–6 years: after 6 months **PRESENTATION:** Whitish oral liquid suspension (vaccine) in a single dose glass vial with effervescent granules (buffer), in an accompanying sachet. **STORAGE:** Store at 2°C to 8°C. Refrigerate, do not freeze. Based on TGA approved PI dated 9 September 2003, last amended 6 August 2015.

REFERENCES: 1. NHMRC. The Australian Immunisation Handbook, 10th Edition, 2013. 2. DUKORAL® Approved Product Information, August 2015. 3. World Health Organisation, Cholera Fact Sheet No. 107, February 2014. Accessed online April 2017. 4. Jelinek T *et al. Expert Rev Vaccines* 2008; 7:561–7. 5. Steffan R *et al. Trav Med Infect Dis* 2003; 1:80–8. 6. Zuckerman J *et al. Lancet Infect Dis* 2007; 7:521–30. 7. Centers for Disease Control and Prevention. 2018 Yellow Book. Ch.3 Infectious Diseases Related to Travel. 8. WHO WER No. 38, 2016; 91:433–440. 9. Mattila L *et al. J Travel Med* 1995; 2:77–84. 10. Sack *et al. Lancet* 2004; 363:223–33. 11. Kelly P. *Clin Med* 2011; 11:488–91. 12. WHO WER No. 13, 2010; 85:117–128. 13. Jensen RT. *Basic Clin Pharmacol Toxicol* 2006; 98:4–19. 14. Nalin DR *et al. Lancet* 1978; 2:856–9.

Product Information is available from Seqirus (Australia) Pty Ltd. 63 Poplar Road, Parkville, VIC 3052. ABN 66 120 398 067. Medical Information: 1800 642 865. ® DUKORAL is a registered trademark of Valneva Sweden AB. Seqirus™ is a trademark of Seqirus UK Limited or its affiliates. Date of preparation: June 2017. AUS/DUKO/0914/0001(1). 14245.

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