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Cholera

Recommendations for prevention in travellers

This article about cholera is part of our travel medicine series for 2010, providing a summary of prevention strategies and vaccination for infections that may be acquired by travellers. The series aims to provide practical strategies to assist general practitioners in giving travel advice, as a synthesis of multiple information sources which must otherwise be consulted.
Cholera is a severe diarrhoeal disease associated with worldwide pandemics. It affects vulnerable populations who lack adequate quality drinking water and sanitation. Travellers are generally at low risk of contracting cholera, even in endemic areas. It is prevented with general water and food precautions (also advisable for prevention of traveller's diarrhoea). In some situations, the oral killed whole cell B subunit vaccine may be recommended for travellers considered at risk.

Keywords: general practice, immunisation, preventive medicine; gastrointestinal diseases; travel

Cholera is an acute diarrhoeal infection caused by ingestion of the enterotoxin producing, motile, curved Gram negative bacillus Vibrio cholerae, first isolated by Koch in the late 19th century. Sudden onset of painless, profuse, watery ('rice water'), secretory diarrhoea,[1] with or without nausea and vomiting,[2] can cause death due to dehydration in more than 50% of untreated severe cases,[1] sometimes within hours of onset.[3] Milder cases of diarrhoea without associated symptoms or complications are common. Approximately 75% of infections are asymptomatic,[2–4] but pathogens are shed in the faeces for 7–14 days.[3]

Transmission occurs via ingestion of contaminated water – as famously shown by John Snow in London in 1855[4] – or food, or direct faecal oral contamination. Person-to-person transmission is rare. Raw or undercooked fish and shellfish, and poorly reheated leftover cooked grains, are considered high risk.[5] As with all diarrhoeal illnesses, those with lower immunity are at higher risk of death; however, cholera can kill even healthy adults.

The risk to travellers while in affected areas is low, less than 1:500 000 (0.001–0.01% per month of stay).[6] Cholera is essentially a disease of vulnerable populations living in unsanitary conditions with inadequate basic environmental infrastructure. The risk of illness increases with gastric hypochlorhydria and in childhood.

There were 236 896 cases reported to the World Health Organization (WHO) during 2006, a 79% increase from 2005; although, it is estimated that less than 10% of actual cases are reported to WHO.[3] A predominance of cases occur in sub-Saharan Africa and Asia[7] (*Figure 1*). Approximately 2–6 cases of cholera are reported in Australia each year, almost always in travellers returned from endemic areas. A small cluster of cases reported in Sydney in 2006, the first reported cluster for more than 30 years, was linked to consumption of raw imported whitebait.[8]

Serogroups, serotypes and biotypes

Serogroups and serotypes are based on cell wall O antigens, while biotypes are based on phenotypic differences. Approximately 150 serogroups of *V. cholerae* are known to exist, but only serogroups O1 and O139 (also known as the 'Bengal' strain) cause epidemic cholera, both producing identical cholera toxin.[4]

Serogroup O1 is the main cause of epidemic cholera.[7] Serogroup O1 includes two biotypes: 'classic' and 'El Tor'. Infections with the El Tor biotype are more likely to be asymptomatic or cause only mild illness.[5,9] Each biotype has three serotypes: Inaba, Owaga and Hikojima (rare).

As the O antigens of the two serogroups are not crossreactive, previous infection with *V. cholerae* O1 does not protect against disease caused by O139.[4]

Many other *V. cholerae* serogroups, with or without the gene for cholera toxin, can cause a cholera-like illness, as can nontoxigenic strains of the O1 and O139 serogroups,[5] but they do not develop into epidemics.[3]

Cholera pandemics

Six pandemics have occurred worldwide over the past 170 years, associated with increasing population density in urban areas and inadequate water and sanitation standards.[4] The current seventh pandemic is caused by the serogroup O1 of biotype El Tor.[4,5] It began in Indonesia in 1960, and had reached Africa in 1971 and the Americas in 1991, when an epidemic occurred in Peru and neighbouring countries.[3,5]

Serotype O139 is less widespread. It caused extensive outbreaks in southeast and east Asia[3] in the early 1990s, but currently remains localised in specific areas of Bangladesh and India. However, there is potential for further spread and an 'eighth pandemic'.[4,5]

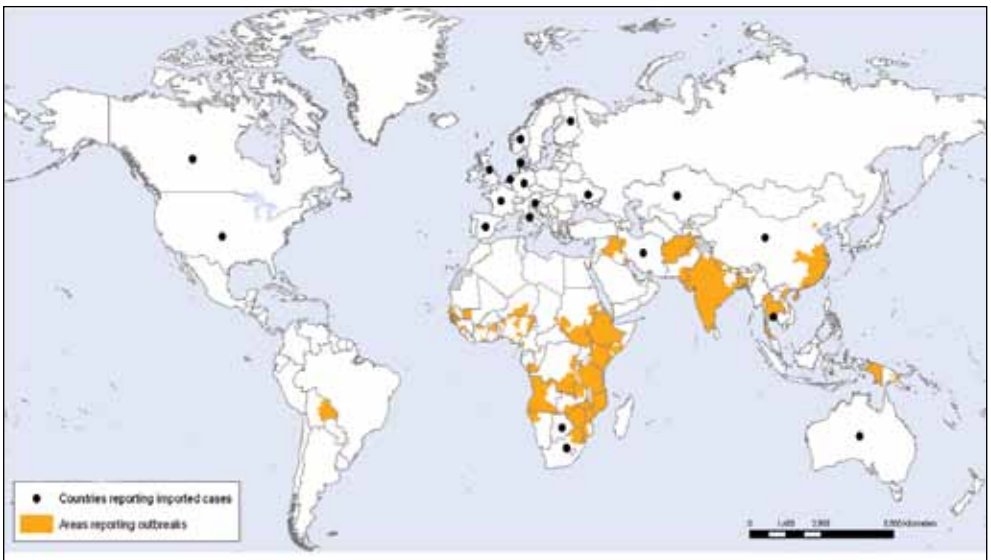

Figure 1. Cholera cases reported to WHO in 2008[19]
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The effects of climate change on epidemiology

Cholera is an ancient disease assumed to be native to the Indian subcontinent. V. cholerae has been shown to be a normal inhabitant of brackish/estuarine surface water. It multiplies in association with plankton ('algal blooms'),[3] shellfish and aquatic plants, independently of infected humans.[4,5] *V. cholerae* survival depends on water temperature, pH, salinity and nutrient availability, but it can remain dormant under unfavourable conditions.[1] It is possible that climate change and its effect on plankton growth has influenced the growth of associated *V. cholerae* bacilli and may affect the epidemiology of cholera.[3,4] *V. cholerae* was found to occur naturally in Australia in river water in some areas of Queensland after a locally acquired case was investigated in 1977.[1]

Prevention of cholera in travellers

General preventive measures

Cholera can be prevented by safe water and food precautions, as usually advised for prevention of travellers' diarrhoea, including adequate food hygiene and hand washing. Specifically, consumption of unboiled water or raw or undercooked seafood should be avoided.[5,6] Breastfeeding is protective for infants.

While antibiotic prophylaxis with tetracycline or chloramphenicol has in the past been used for close household contacts during epidemics in developing country settings,[9] the WHO does not recommend mass chemoprophylaxis in outbreak situations. It also does not recommend preventive chemoprophylaxis to travellers.[3,10]

Vaccination

Travellers rarely need to be vaccinated against cholera. Food and water hygiene and hand washing precautions are the best way to avoid acute diarrhoeal illness, which, even if contracted, is usually mild and self limiting.[4]

Vaccines

WC/rBS

The oral killed whole cell B subunit (WC/rBS) cholera vaccine, composed of killed *V. cholerae* O1 organisms and the nontoxic B subunit of cholera toxin, is the only cholera vaccine currently available in Australia (Dukoral®). Each dose contains heat and formalin inactivated Inaba and Ogawa strains of classic and El Tor *V. cholerae* 01. It provides 85% protection against El Tor cholera for 6 months in adults and in children aged 2 years and over, with 78% ongoing protection in the over 5 years age group at 3 years.

It is not effective against the O139 serogroup. Because of the requirement for two doses and relatively long onset of action (10 days after the second dose), WC/rBS is not recommended for outbreak control.[11] However, an added benefit of this vaccine is the approximately 60% reduction in the incidence of enterotoxigenic *Escherichia coli* (ETEC) diarrhoea. Potentially this could prevent up to 7–12% of all travel related diarrhoea.[1,6,7] Protection is only against heat labile toxin producing ETEC.[7] It is not registered for this use in Australia.

The WC/rBS vaccine can be considered for:

- long term travellers to cholera endemic areas, especially those visiting relatives and friends[4]
- humanitarian workers in epidemic or refugee settings[1,6,7]
- travellers visiting endemic areas who have achlorhydria, are at greater risk of developing severe disease, or have conditions which may be aggravated by cholera. These include inflammatory bowel disease and malabsorption, HIV/

AIDS, immune impairment due to other causes, poorly controlled or complicated diabetes, and severe cardiovascular disease.[1,6] However, data on effectiveness in immunocompromised individuals including those with HIV is limited.[1]

Additionally, oral cholera vaccine may be considered for the prevention of ETEC diarrhoea in individuals at greater risk of severe or complicated diarrhoea,[6,12] although it is not recommended for routine travel.[4,5] The vaccine is registered in Australia only for cholera prevention.[1] Short term travellers who cannot afford to be ill, such as business travellers or athletes, may benefit from partial ETEC protection, although preventive strategies such as food and water hygiene remain of greatest importance.

Vaccination against cholera is not currently an official entry requirement of any country.[3]

Other vaccines

The now outdated parenteral killed whole cell cholera vaccine, developed in 1894 in India,[13] offered only limited short term protection and had unpleasant side effects. It is no longer available.[14] Manufacture of a live attenuated, single dose cholera vaccine, CVD 103-HgR (Orochol-E®), ceased in 2004.[7,15]

A bivalent (O1 and O139) vaccine is available in Vietnam[1,16] and under trial in India and Indonesia.[13] Numerous other vaccines are in development in different parts of the world.[13]

Dosage and administration of WC/rBS

WC/rBS is given in two doses, 1–6 weeks apart, on an empty stomach, with no food or drink 1 hour either side of the dose, in 150 mL of water containing dissolved alkaline buffer.[1,6] Children aged 2–6 years should receive three doses, each 1–6 weeks apart, using only half of the water with dissolved buffer.[1] Administration must be separated from the oral live attenuated typhoid Ty21a vaccine by at least 8 hours. Administration should be postponed during an acute febrile or gastrointestinal illness until recovered.[1] The vaccine is safe and well tolerated, with no significant adverse effects.[6] Gastrointestinal side effects are uncommon (<1%).[1] Further details are listed in *Table 1*.

Treatment of cholera

Mortality due to cholera is low if fluids are maintained,[6] so advice regarding rehydration in cases of acute diarrhoeal illness is important. Treatment of cholera is with rehydration and antibiotics.

Antibiotic therapy

Antibiotic therapy in a confirmed or suspected case reduces the volume and duration of diarrhoea. Recommended treatment is with:

- doxycycline 100 mg (child >8 years of age: 2.5 mg/kg up to 100 mg) orally, 12 hourly for 3 days, or
- ciprofloxacin 1 g (children >12 years of age[17] and >40 kg, and adults) orally, as a stat dose
- pregnant women and children <8 years of age should be treated with amoxycillin 250 mg (child: 10 mg/kg up to 250 mg) orally, 6 hourly for 5 days (category A).[18]

Summary

Most travellers are at low risk of contracting cholera, even in endemic areas. Water and food hygiene and hand washing are usually sufficient for its prevention.

An oral killed whole cell B subunit (WC/rBS) vaccine is available in Australia for use in

Table 1. Vaccination with WC/rBS

Commercial name	Dukoral®
Number of doses required for full immunisation	Two doses, at least 7 days apart
Administration	Oral
Earliest onset of protection after full immunisation	10 days after second dose (against *V. cholerae* 01 only)
Protective efficacy	50–86%
Protective duration	3 years for adults; 6 months for children <5 years of age[4]
Use in pregnancy and breastfeeding	Not recommended as inadequate information is available[1,4]
Simultaneous administration with other vaccines	Possible, except for orally administered vaccines; 8 hour interval with typhoid vaccine (Ty21a)
Exclusion criteria/contraindications	Children <2 years of age; previous anaphylaxis[1]
Side effects	Gastrointestinal symptoms uncommon[1,4]
Precautions	Postpone vaccination in case of acute febrile or gastrointestinal illness; do not eat or drink for 1 hour before and 1 hour after the vaccine as it is acid labile
Presentation	Vial with oral suspension (vaccine) plus sachet with effervescent granules (buffer)
Amount of drinkable water needed	150 mL; for children 2–6 years of age, pour away half the buffer before adding the vaccine

selected travellers. This vaccine also provides limited short term protection against heat labile toxin producing ETEC diarrhoea.

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