

Cholera advice prior to travel

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Although cholera is a low risk for most travellers, preventive advice should be offered routinely.

Until the early 1990s it was common practice for intending travellers to be vaccinated against cholera. The vaccine was often administered combined with typhoid vaccine, and despite the frequent incidence of significant side effects, both doctor and traveller would feel somehow satisfied that the risk of any disease was now largely avoided. Certification of cholera vaccination was often required for admission to various countries, a custom that still exists at some borders, yet not officially required by the WHO for any country.

In the last decade, more than 20 new vaccines have become available for travel, the older injectable cholera and typhoid vaccines have been taken off the market, and a new oral cholera vaccine has been introduced. This article reviews information about cholera for GPs, including the advice to give travellers to prevent this disease.

The disease

Cholera is an acute diarrhoeal disease caused by the toxigenic *Vibrio cholerae* bacterium. Ingestion of food or water contaminated with *V. cholerae* results in colonisation of the intestine and consequent secretion of the toxin.

The A subunit of the toxin is the enzymatically active component, which stimulates intestinal cyclic AMP to transfer salts and fluid across the intestinal epithelium. This results in rapid loss of large volumes of water into the intestinal lumen. The B subunit binds the toxin to the gut and is itself nontoxic.

Serogroup O1 has been the main cause of worldwide epidemics (i.e. pandemics), and is divided into biotypes Classical and El Tor, each of which are further divided into serotypes Ogawa and Inaba (Figure 1).

The current (seventh) pandemic began in 1961 in Indonesia and reached Africa in 1970 and South America in 1991. Disease outbreaks in refugee situations have resulted in the deaths of over 20,000 people within one month.

Serogroup O139 has been active throughout Asia since 1992, and, although harmless before that time, has caused severe outbreaks in India, Bangladesh and Thailand.¹ The WHO reported 41 outbreaks in 2001 alone,² and at the time of writing this article, an outbreak had been reported in the Niger, linked to heavy rainfall and population movement.³ Countries reporting cholera cases and those with imported cases in 2002 to 2003 are shown in Figure 2.

One of seven diseases in Australia that are subject to quarantine control, cholera is reported in roughly six people annually in this country.⁴ This equates to a risk for the traveller of just one in 500,000, similar to overseas figures. However, several studies have contrasted sharply with this incidence. A Japanese study reported rates of cholera in Bali at 13 cases per 100,000 people, equivalent to the risk of typhoid.⁵ A survey at the American Embassy in Peru found that five out of 317 people contracted cholera, equivalent to 44 cases per 100,000 people per month of exposure.⁶ An outbreak of cholera aboard a plane affected 74 of the 336 passengers with one death.⁷ Therefore, prevention may be warranted, and certainly travellers at risk need to be offered the choice of vaccination.

For some perspective, cholera is an uncommon cause of diarrhoea and low on the list of vaccine preventable disease in travellers. Since 1973, the WHO has recommended that cholera vaccination is not required for any traveller.¹ However, officials in some countries, notably in Africa, may still ask for official documentation of cholera vaccination. In these situations, a single dose of vaccine will suffice, or a medical waiver can be given.

Cholera is transmitted only from human to human, and

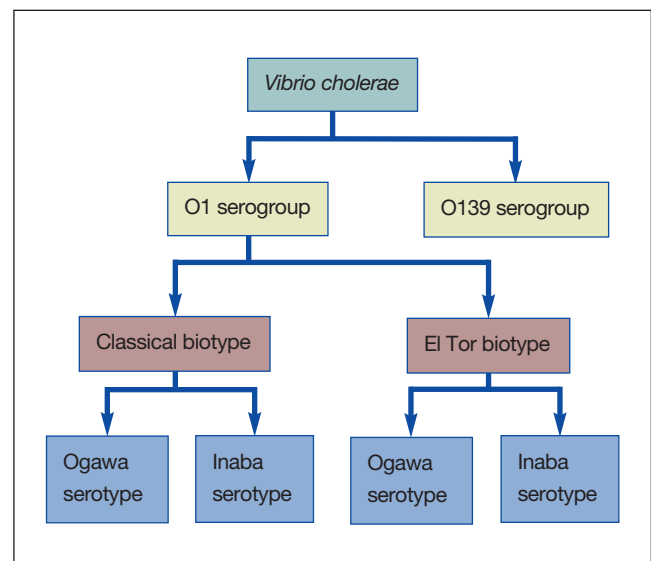


Figure 1. Classification of toxigenic *Vibrio cholerae*. Source: Travel Clinics Australia.

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foods at higher risk of contamination.

Although most cases will be mild or asymptomatic, severe forms make cholera one of the most rapidly fatal illnesses known. Profuse watery diarrhoea, with or without vomiting, may progress to a clear form with mucous, known as 'rice water stool'. The large volume and rapid fluid loss of up to one litre per hour can result in hypotension, metabolic acidosis with hypocalcaemic tetany, renal failure and death, which may occur in hours unless adequate hydration is provided. Diseases such as cholera motivated much of the early research on appropriate rehydration therapy, and modern treatment has reduced the mortality from 50% to 1%.¹

Diagnosis

In the returning traveller, the diagnosis of cholera is made after a patient has had acute diarrhoeal illness and on clinical suspicion. The test to request for confirmation is faecal microscopy, culture and antigen detection. As normal culture may miss the diagnosis, the laboratory needs to be informed so that the specific culture for *V. cholerae* is used. Urea and electrolyte levels should also be checked in view of the high association of water and electrolyte imbalance. Hypokalemia may be a significant electrolyte problem and is important both because of the risk of cardiac complications and in the choice of intravenous and oral rehydration.

Treatment

Most cases of cholera in Australian travellers are mild and, in fact, many are missed. Rehydration is often all that is necessary; however, antibiotics may be used in more severe cases to reduce the length and severity of illness. Antibiotic treatment may include doxycycline or, for pregnant women and children under 8 years, amoxicillin.⁸ Travellers already taking doxycycline for malaria prophylaxis may unwittingly be treating mild cholera.

Prevention

The WHO and NHMRC do not advocate cholera vaccination for most travellers. This is partly because of the low risk of disease, but also because careful attention to avoidance of potentially contaminated food and water is much more important, and the vaccine may give travellers a false sense of security.¹⁴ We advise travellers to follow the dictum 'boil, bottle or peel' and provide verbal and written details about avoiding gastrointestinal disease in general.⁹ However, vaccination should be considered for travellers (for example, health care and refugee workers) in the following high risk situations:

- where there is poor water supply and sanitation
- in areas of low socioeconomic status
- where there are crowded living conditions
- if the traveller has hypochlorhydria
- in highly endemic rural areas.^{4,10}

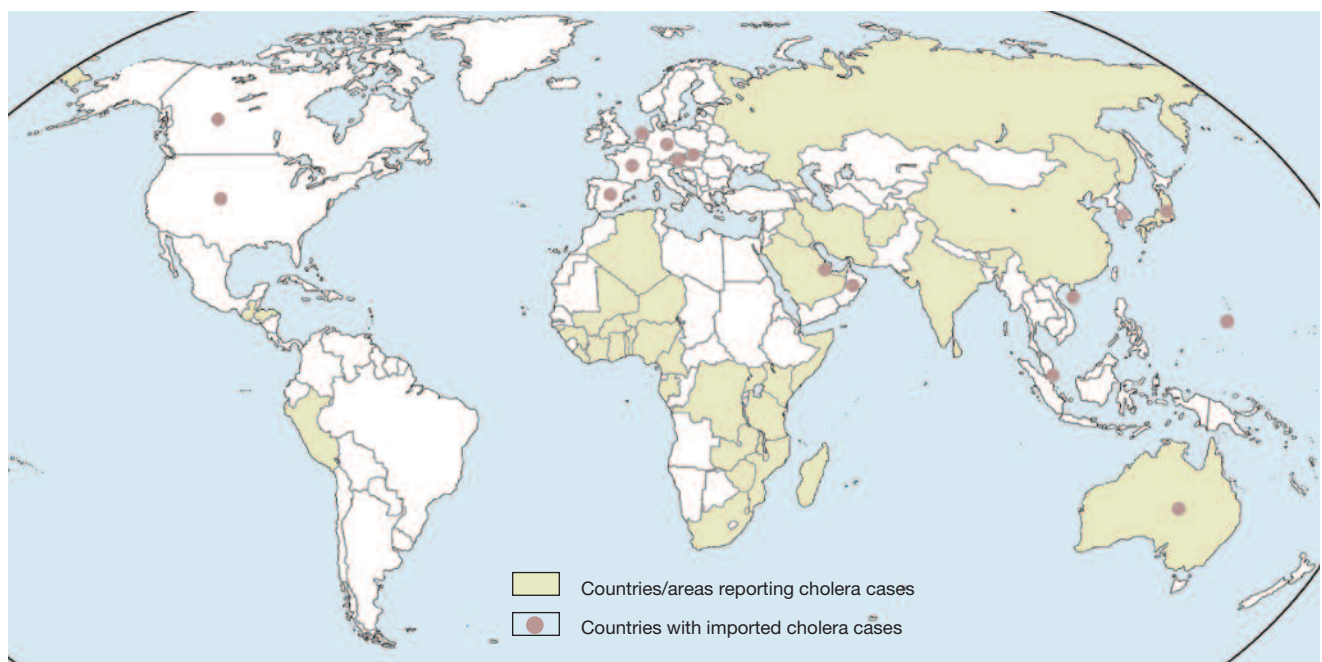


Figure 2. Countries reporting cholera cases and countries with imported cholera cases, 2002-2003 according to the WHO. Adapted with permission from: WHO. International travel and health, 2004. http://www.who.int/ith/chapter05_m01_cholera.html

Vaccination

Although several cholera vaccines have been available in Australia, the injectable cholera vaccine was taken off the Australian market some years ago, primarily due to its lack of efficacy as well as its poor side effect profile. In addition, the recombinant live oral *V. cholerae* CVD-HgR vaccine (Orochol) was withdrawn due to apparent problems with storage shelf-life and efficacy.

This leaves one vaccine, which despite being available overseas for over a decade, has only recently become available in Australia. Dukoral is an oral, killed recombinant B subunit/whole cell vaccine (rBS/WC), effective against both *V. cholerae* and enterotoxigenic *Escherichia coli* (ETEC). For cholera, the protective efficacy of the vaccine is 85% at six months and 60% at two years. Efficacy against ETEC ranges from 60 to 73% at three months.

The nontoxic B subunit-binding portion of the cholera toxin in the vaccine induces protective antitoxic IgA immunity. Because this is antigenically similar to the B subunit of the heat labile enterotoxin of *E. coli*, protection has been demonstrated against ETEC. The heat and formalin killed whole cell component of the vaccine induces mucosal IgA immunity against *V. cholerae* O1 Classical and El Tor biotypes.

The manufacturer's recommendations are to give three doses of the vaccine to children aged between 2 and 6 years, and two doses to adults and children over the age of 6 years. Doses need to be given one to six weeks apart, at least one hour before or after food or drink, and with the last dose at least two weeks before departure. In Australia the vaccine is approved only for the cholera component; however, it may still be used 'off-label' for the prevention of ETEC in at-risk travellers. It is the only cholera vaccine recommended by the WHO for prophylactic use in epidemic situations. The vaccine has an excellent safety and side effect profile, and can be administered concurrently with most other vaccines and in pregnancy (category B2) and lactation.

Summary

Cholera, although not common, is a potentially serious disease. It is a low risk for most travellers; however, this risk may be underestimated. Food hygiene and vaccination should not be neglected in terms of offering travellers protective advice options, especially emergency relief and health workers in refugee situations.¹ **MT**

A list of references is available on request to the editorial office.

DECLARATION OF INTEREST: Dr Cohen is Medical Director, Travel Clinics Australia.

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