



## Cholera

### Introduction

Cholera is an acute diarrhoeal disease caused by the gram negative bacillus *Vibrio cholerae* serogroup O1 or O139. Although more than 100 serogroups exist, only two are capable of causing epidemic cholera: *V. cholerae* O1 of which there are two biotypes (Classical and El Tor) and *V. cholerae* O139, which emerged in the Bay of Bengal in 1992. Cholera is known to cause worldwide pandemics. *V. cholerae* O1, biotype El Tor accounts for most cases in the current, seventh pandemic.

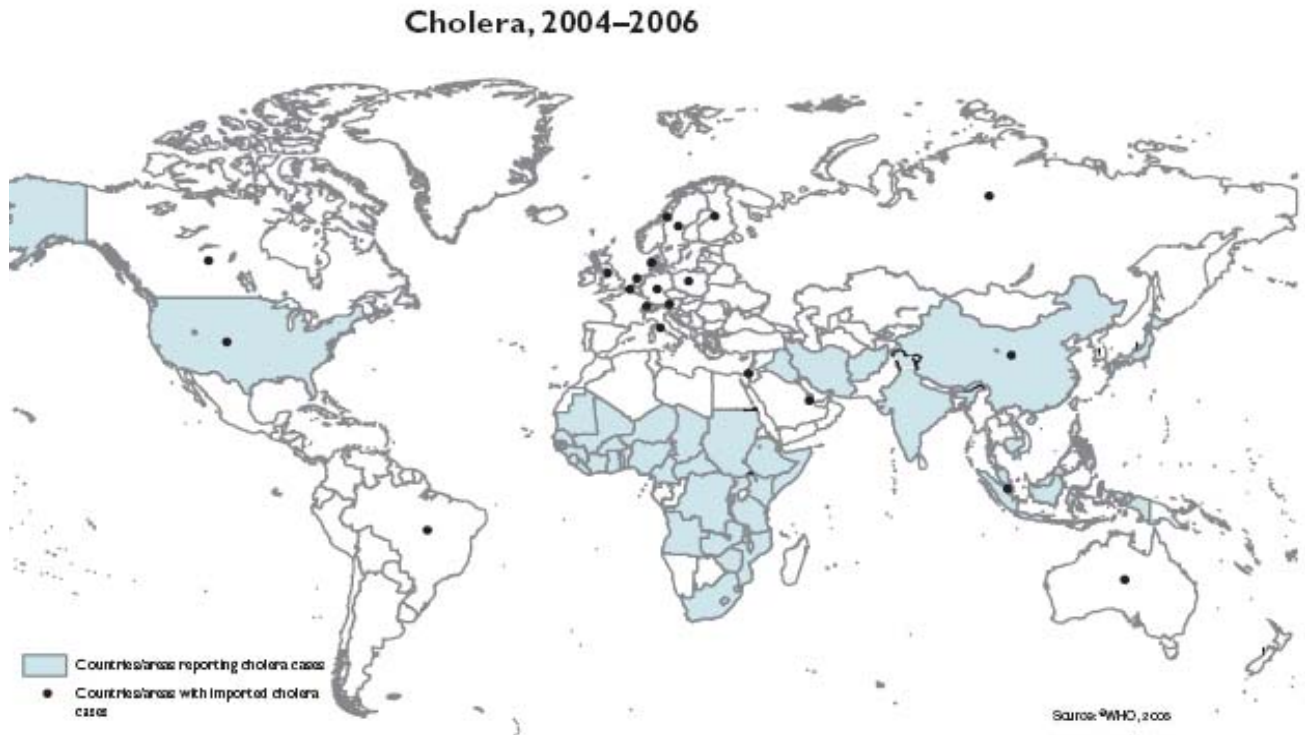
*V. cholerae* is endemic in many low income countries, particularly in areas of inadequate sanitation and food hygiene practices. Man is the only known host of cholera.

### Epidemiology

#### Global epidemiology of cholera

Cholera is a disease that occurs in low income regions of the world where sanitation and food and water hygiene are inadequate. In areas without clean water or sewage disposal (as may occur after natural disasters or in displaced populations in war zones), cholera can spread quickly. The World Health Organization (WHO) describes cholera as a global threat to public health and one of the key indicators of social development, stating that with the increased reporting of cholera in 2006, almost every developing country is facing either an outbreak or the threat of an epidemic [1]. Regions of the world where cholera is currently prevalent are Africa, Asia and parts of the Middle East [1]. Imported cases occasionally occur in richer countries in travellers returning from endemic areas [1, 2].

Figure 1. Map of Global Epidemiology of Cholera (courtesy of the World Health Organization)



Most cholera is caused by *Vibrio cholerae* serogroup O1, biotype Classical or El Tor. These biotypes are further divided into serotypes; Inaba, Ogawa and (rarely) Hikojima. Cholera usually occurs in large epidemics or pandemics. In the 19<sup>th</sup> century pandemics frequently originated from the Ganges delta in India, and up to the mid 20<sup>th</sup> century, were largely confined to Asia (except for a large epidemic in Egypt in 1947). The current, seventh pandemic caused by *V. cholerae* O1 El Tor originated in Indonesia in 1961 and spread rapidly through most of Asia [3]. In 1970, this biotype was introduced into West Africa, and it is now endemic in many African countries. In 1991, it was introduced into Peru where it had been absent for nearly 100 years, and from there spread throughout many countries of Latin America. In recent years, however, cholera in Latin America has been controlled. Another serogroup, *V. cholerae* O139, was discovered as the cause of cholera epidemics in India and Bangladesh in 1992 and has since spread to other countries in South East Asia. Apart from a few imported cases, this serogroup is not known to have occurred outside Asia [3].

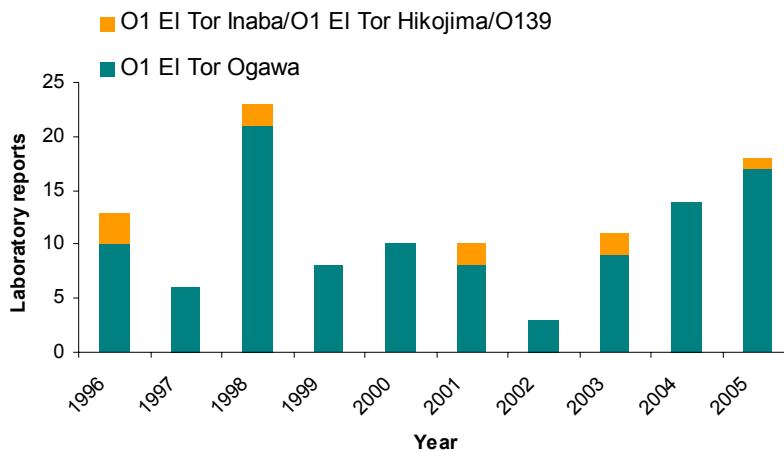
In 2006, 236,896 cases of cholera, including 6,311 deaths, were officially reported to WHO. This represents an overall increase of 79% compared with 2005 and reaches the levels of the late 1990s [1]. The actual number of global cases is likely to be much higher with under reporting and the limitations of surveillance systems contributing to fewer

reported cases [4]. Ninety-nine per cent of verified cases in 2006 were reported from Africa, with major outbreaks occurring in Angola, the Democratic Republic of Congo, Ethiopia and Sudan [1].

### Cholera in travellers from England and Wales

Cholera is rarely reported in UK travellers. Between 1996 and 2005, there were an average of 12 laboratory confirmed cases of *Vibrio cholerae* O1 in England and Wales [range three to 23]; the majority of which were due to biotype El Tor, serotype Ogawa (Figure). In 2005, there were 18 reports, the highest number reported since 1998; one of those cases was confirmed as serogroup O139. All reports were associated with recent travel abroad.

Figure 2. Laboratory reports<sup>1</sup> of *Vibrio cholerae*: England and Wales, 1996 - 2005.



The Indian sub-continent is the most common region of acquisition of cholera reported in England and Wales. Countries of travel for cholera cases reported in England and Wales in 2004 and 2005 are listed in the table below:

<sup>1</sup> Laboratory reports were supplied by the Laboratory of Enteric Pathogens of the Centre for Infections, Health Protection Agency.



Countries of travel for cases of cholera confirmed in England and Wales: 2004 and 2005

Country	2004	2005
India	5	3
Pakistan	3	9
Bangladesh	1	2
Mozambique	1	-
Cameroon	1	-
Mexico	-	1
China	-	1*
Brazil	1	-
No country stated	2	2
<b>Total</b>	<b>14</b>	<b>18</b>

\**V. cholerae* 0139

### Risk for travellers

The overall risk of cholera for travellers is extremely low and is in the order of 0.2 cases per 100,000 travellers [5-7]. For long-term travellers in areas of outbreaks the rate may be as high as 500 cases per 100,000 persons [8], and when routine screening for *V. cholerae* is done in returned travellers with diarrhoea who have returned from endemic areas, the rate may approach five cases per 100,000 [7]. Activities that can predispose to infection include drinking untreated water or eating poorly cooked seafood in endemic areas. Travellers living in unsanitary conditions, for example relief workers in disaster or refugee areas, are also at risk.

### Transmission

Cholera is transmitted via the faecal-oral route, most commonly by consumption of contaminated water and, to a lesser degree, food; direct person-to-person transmission is rare.

A high infecting dose (as many as  $10^{11}$  organisms) is required to cause illness in healthy individuals.

### Signs and symptoms

The usual incubation period is 2 to 5 days, although it can be as short as several hours [3, 9]. Severe cholera is characterised by a sudden onset of profuse, watery diarrhoea accompanied by nausea and vomiting. If left untreated this can rapidly lead to serious dehydration, electrolyte imbalance and circulatory collapse. Over 50% of the most severe cases die within a few hours; with prompt, effective treatment, mortality is less than 1% [9, 10].



Cholera may be asymptomatic or mild in healthy individuals, with diarrhoea as the only symptom.

## Treatment

Rapid fluid replacement with a balanced solution of sugar, electrolytes and water (oral rehydration salts) should be started urgently [3, 9]. This may be done orally, but severely dehydrated cases may require intravenous administration. Cases may also be treated with antibiotics, usually a tetracycline if the organism is sensitive, in order to improve symptoms and decrease the intestinal excretion of the organism. Patients who are promptly treated should respond rapidly and recover.

## Prevention

For the majority of travellers advice on [food and water hygiene](#) precautions is the most appropriate prevention strategy.

An oral cholera vaccine is available in the UK. Trials of this vaccine against cholera (serotype O1) indicate that it will protect up to 86% of people living in cholera endemic areas for four to six months [2]. Lower levels of protection continue for three years. Protection wanes more rapidly in young children.

The vaccine is not indicated for most travellers. It can be offered to humanitarian aid and relief workers and travellers with remote itineraries in areas of cholera outbreaks who have limited access to safe water and medical care.

It has been proposed that the vaccine can be used to protect against the syndrome of travellers' diarrhoea. While there is partial protection against one agent of travellers' diarrhoea, *Escherichia coli* that produce heat labile enterotoxin, the vaccine will not protect against the many other causes of travellers' diarrhoea [2].

## Cholera vaccine information

### Availability of vaccine

There is one cholera vaccine licensed for use in the UK, Dukoral™, which is made by SBL Vaccines (Sweden), was launched in the UK in May 2004. It is currently distributed in the UK by MASTA. The vaccine protects against infection caused by *Vibrio cholerae* serogroup O1. It is an inactivated vaccine, is thiomersal free and does not contain live organisms so therefore cannot cause cholera [10]. Each dose contains a total of  $1 \times 10^{11}$  bacteria of *Vibrio cholerae* with recombinant cholera toxin B [11]:

- O1 Inaba classical biotype (heat inactivated)
- O1 Inaba El Tor biotype (formalin inactivated)



- 01 Ogawa classical biotype (heat activated)
- 01 Ogawa classical biotype (formalin activated)
- recombinant cholera toxin B subunit (rCTB) 1 mg (produced in *V. cholerae* 01 Inaba, classical biotype)

#### Indications for use of vaccine

The vaccine can be considered for travellers visiting areas with epidemic cholera of the 01 strain, specifically [2, 10]:

- Aid workers assisting in disaster relief or refugee camps.
- travellers with remote itineraries in areas with cholera outbreaks and with limited access to medical care

The vaccine may also provide some protection against diarrhoea caused by *Escherichia coli* producing a heat-labile enterotoxin. However, it is unlicensed for this use, there is only limited data on its efficacy in travellers, and it is not generally recommended for this indication [2, 10]. For specific information on [travellers' diarrhoea](#) see the separate information sheet.

#### Vaccine schedules

Age	Primary course	Reinforcing doses
Adults and children from 6 years and older	2 doses with an interval of at least one week between them. If more than six weeks have elapsed between doses, the primary course should be restarted.	Single dose after two years. If more than 2 years have elapsed since initial course, the entire course should be repeated.
Age 2 to 6 years	3 doses with an interval of at least one week between doses. If more than six weeks have elapsed between doses, the primary course should be restarted.	Single dose after six months. As with adults and children over 6 years, if more than 2 years have elapsed, the whole course should be repeated.

#### Administration

Dukoral™ is an oral vaccine. The preparation consists of a 3ml suspension of vaccine and a separate packet of effervescent granules. For adults, the granules are first dissolved into approximately 150ml of water, and then the vaccine is added. The solution is stirred well and should be drunk within two hours of preparation [11].



For children aged two to six years, half the solution containing the effervescent granules is poured away and the vaccine suspension is added to the remaining approximate 75mls.

#### Interrupted courses

The Summary of Product Characteristics (SPC) advises that if more than six weeks have elapsed between doses during the primary vaccination course, the course should be begun again.

The SPC also suggests that if more than two years have elapsed between the completion of the primary course and administration of a reinforcing dose, the primary course should be repeated [11].

#### Contraindications

- Hypersensitivity to active substances or excipients of the vaccine.
- Current acute gastrointestinal illness or febrile illness.

#### Adverse events

In clinical trials, adverse events were uncommon; those most frequently reported were gastrointestinal. These included abdominal pain, diarrhoea, abdominal cramps and general discomfort [10, 11].

#### References

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### **Reading List**

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