

CHOLERA: general aspects

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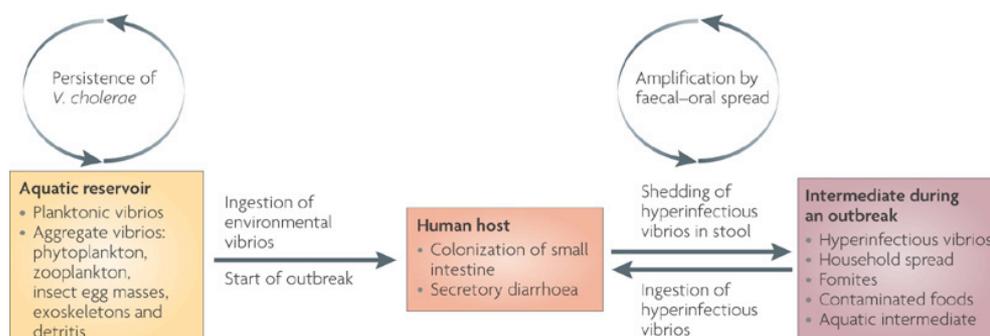
Definition

Cholera is a diarrhoeal disease caused by infection of the intestine with the bacterium *Vibrio cholera* (strains O1 and O139, producers of specific pathogenic toxin). In most cases, infection causes only mild diarrhoea or no symptoms at all. Among those infected, around 20% develop acute watery diarrhoea (very severe in 10-20%) and vomiting from 6 hours to 3 days after exposure to the bacterium. In these cases, the loss of a large amounts of fluids can rapidly lead to severe dehydration. In absence of a prompt and adequate treatment, death can occur within hours (especially in children) with a case fatality rate of 30-50%.



Transmission

The infection can be acquired by drinking water or eating food contaminated by the bacterium. Common sources of foodborne infection include raw or poorly cooked seafood, raw fruit and vegetables, and other foods contaminated during preparation or storage. Bacteria present in the faeces of an infected person are the main source of contamination; person-to-person transmission is extremely rare, probably because the necessary inoculum to cause the disease is high ($>10^5$ bacteria in most cases). The bacterium can also live in the environment in brackish rivers and coastal waters. The disease can thus spread rapidly in areas where water supplies, sanitation, food safety, and hygiene are inadequate; the greatest risk occurs in overpopulated communities and refugee settings characterized by poor sanitation and unsafe drinking water.



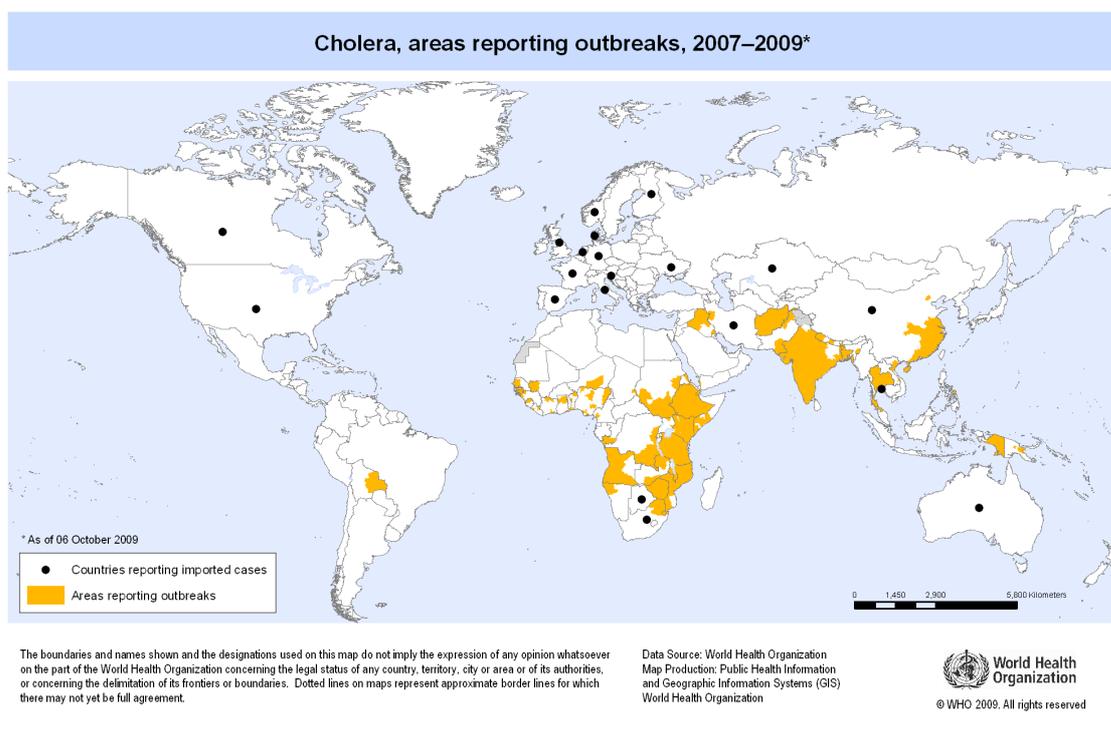
Epidemiology

Global situation

From 2004 to 2008, a cumulative total of 838 315 cholera cases was reported to WHO, compared with 676 651 cases between 2000 and 2004, representing a 24% increase in the number of cases reported for this most recent 5-year period.

In 2008, both the number of cholera cases and the number of countries reporting cholera cases to WHO increased compared with 2007. WHO registered a total of 190 130 cases including 5143 deaths, with a case-fatality rate (CFR) of 2.7% in 2008. This represents, compared to 2007, 7.6% and 27% increase in reported number of cases and deaths respectively. In 2007 and 2008 around 94% of the total cholera cases were registered in African countries. In 2008 massive outbreaks occurred in Zimbabwe and Guinea-Bissau, accounting for 41.5% of all cases from Africa or 39% of the global total.

Many cases of cholera cannot be easily identified and notified in most countries affected by cholera; for these reasons WHO consider that cholera is extremely underestimate. The actual global disease burden is estimated to be 3-5 million cases and 100 000-300 000 death per year



Treatment

Cholera is a treatable disease. The mainstay of treatment is rehydration and up to 80% of cholera cases can be treated successfully using only oral rehydration salts; in case of severe dehydration the patient must receive fluids intravenously. Prompt and appropriate medical

management of cases (simple and inexpensive) can significantly decrease mortality; when applied properly, case-fatality rate should be below 1%. In untreated cases the case fatality rate may reach 30-50%. These levels are often observed in crisis situations with overcrowding, limited access to health care and precarious environmental management.

Antibiotic treatment (usually Azithromycin 1 g per os once or Ciprofloxacin 1 g per os once) for individual cases decreases duration of disease, volume losses and duration of bacteria's excretion through faeces. For whole communities, however, preventive mass treatment with an antibiotic does not limit the spread of cholera and is thus not recommended. Antibiotics are a part of the treatment of severe cholera cases, but are not useful if used mild cases, and are contraindicated for prophylaxis. Anti-diarrhoeal medicines, such as loperamide, are not recommended and should be avoided.

Prevention

General advices

The provision of safe water and sanitation is a formidable challenge but remains the critical factor in reducing the impact of cholera outbreaks. Recommended control methods, including standardized case management, have proven effective in reducing the case-fatality rate. Comprehensive surveillance data are of paramount importance to guide the interventions and adapt them to each specific situation.

Cholera is an example of preventable disease. Everybody can protect him/herself adopting simple rules of hygiene and safe food preparation as for example:

- Drink only water that has been boiled or disinfected with chlorine, iodine or other suitable products. Products for disinfecting water are generally available in pharmacies. Beverages such as hot tea or coffee, wine, beer, carbonated water or soft drinks, and bottled or packaged fruit juices are usually safe to drink.
- Avoid ice, unless you are sure that it is made from safe water.
- Eat food that has been thoroughly cooked and is still hot when served. Cooked food that has been held at room temperature for several hours and served without being reheated can be an important source of infection.
- Avoid raw seafood and other raw foods. The exceptions are fruits and vegetables that you have peeled or shelled yourself.
- Boil unpasteurized milk before drinking it.
- Ice cream from unreliable sources is frequently contaminated and can cause illness. If in doubt, avoid it.
- Be sure that meals bought from street vendors are thoroughly cooked in your presence and do not contain any uncooked foods.

WHO Statements concerning cholera and related to international travel and trade

WHO has issued the following statements relating to international travel and trade to and from countries/areas experiencing outbreaks of cholera:

- WHO does not advise implementation of embargoes or similar restrictions on trade related to countries or affected by cholera outbreaks;
- WHO does not advise routine screening or quarantine of travelers coming from areas affected by cholera;
- WHO does not consider that requiring proof of vaccination for entry plays a useful role in preventing the international spread of cholera and, therefore, such a requirement is considered an unnecessary interference with international travel;
- WHO does not advise requiring prophylactic administration of antibiotics or proof of such administration for travelers coming from or going to a country affected by cholera.

Vaccine against cholera

Considering that available vaccines against cholera do not provide 100% protection, basic hygienic precautions should always be followed.

Actually two types of oral cholera vaccines are available:

1. Dukoral (WCrBS):

- Based on formalin and heat-killed whole cells (WC) of *V. cholerae* O1 plus recombinant cholera toxin B subunit (rBS).
- Licensed in >60 countries (not licensed for children aged <2 years), primarily as a vaccine for travelers to cholera-endemic areas
- Primary immunization consists of 2 oral doses given >7 days apart (but <6 weeks apart) for adults and children aged ≥ 6 years. Children aged 2–5 years should receive 3 doses >7 days apart (but <6 weeks apart). Intake of food and drink should be avoided for 1 hour before and after vaccination. Protection may be expected about 1 week after the last scheduled dose. A booster dose is recommended after 2 years for adults and children aged ≥ 6 years. For children aged 2–5 years a booster dose is recommended every 6 months.
- The efficacy is around 85% after 6 months and 60% after 2 years from vaccination
- In several studies this vaccine has been shown to cross-protect against diarrhea caused by Enterotoxigenic Escherichia Coli (ETEC).

(i) Shanchol and mORCVAX

- The two vaccines are identical, but they have been licensed with different name in India and Viet Nam respectively

- Primary immunization consists of 2 oral liquid doses 14 days apart for individuals aged ≥ 1 year. A booster dose is recommended after 2 years.
- The efficacy is around 66% after 2 years from vaccination and 50% after 3-5 years. These results are similar in adults and children aged > 1 year.
- These vaccines do not contain the bacterial toxin B subunit and will therefore not protect against ETEC (Enterotoxigenic Escherichia Coli).

The injectable vaccine prepared from phenol-inactivated strains of *V. cholera* is still manufactured in a few countries; the use of this vaccine is not recommended by WHO, mainly because of its limited efficacy and short duration of protection.