

Cholera



Case Definition

Confirmed Case: Isolation of cholera-toxin-producing *Vibrio cholerae* serotype O1 or serotype O139 from a person with gastrointestinal illness.

Reporting Requirements

- All positive specimens are reportable by laboratory.
- All cases are reportable by attending health care professional.

Clinical Presentation/Natural History

An acute bacterial enteric disease characterized in its severe form with sudden onset, profuse painless watery stools, occasional vomiting and, in untreated cases, rapid dehydration, acidosis, circulatory collapse, hypoglycemia in children and renal failure. Asymptomatic infection is much more frequent than clinical illness, especially with organisms of the El Tor biotype. Mild cases with diarrhea only are common, particularly among children. In severe untreated cases, death may occur within a few hours, and the case-fatality rate may exceed 50%; with proper treatment, the rate is less than 1%.

Etiology

Vibrio cholerae serogroup O1 includes two biotypes — classical and El Tor — each including organisms of Inaba, Ogawa and (rarely) Hikojima serotypes. The clinical pictures are similar because a similar enterotoxin is elaborated by these organisms. In any single epidemic, one particular type tends to be dominant; currently the El Tor biotype is predominant, except in Bangladesh, where the classical biotype has reappeared.

V. mimicus is a closely related species that can cause diarrhea; some strains elaborate an enterotoxin indistinguishable from that produced by *V. cholerae* O1 and O139.

Vibrios that are biochemically indistinguishable, but do not agglutinate in *V. cholerae* serogroup O1 antiserum (non-O1 strains, formerly known as nonagglutinable vibrios [NAGs] or noncholera vibrios [NCVs]), are now included in the species *V. cholerae*. Some strains elaborate the enterotoxin but most do not. Prior to 1992, non-O1 strains were recognized to cause sporadic cases and rare outbreaks of diarrheal disease, but not to be associated with large epidemics.

However, in late 1992, large-scale epidemics of severe dehydrating diarrhea, typical of cholera, were reported in India and Bangladesh. The causative organism was a new serogroup of *V. cholerae* O139, which elaborates the same cholera toxin but differs from O1 strains in lipopolysaccharide (LPS) structure and in producing capsular antigen. The clinical and epidemiologic picture of illness caused by this organism is typical of cholera and cases should be reported as cholera. The reporting of nontoxinogenic *V. cholerae* O1 or of non-O1 *V. cholerae* infections, other than O139, as cholera is inaccurate and leads to confusion.

Epidemiology

Reservoir and Source: Humans; recent observations in the United States, Bangladesh and Australia clearly demonstrated that environmental reservoirs exist, apparently in association with copepods or other zooplankton in brackish water or estuaries.

Transmission: Through ingestion of food or water contaminated directly or indirectly with feces or vomitus of infected persons. El Tor organisms can persist in water for long periods. In the United States, most sporadic cases of infection follow the ingestion of raw or inadequately cooked seafood. Outbreaks or epidemics attributed to raw or undercooked seafood from polluted waters have occurred on Guam and Kiribati, and in Portugal, Italy and Ecuador. The Louisiana and Texas cases

have been traced to eating shellfish from coastal and estuarine waters where the natural reservoir of *V. cholerae*, serotype Inaba, is presumed to exist. These cases were not related to sewage contamination of water. Clinical cholera in endemic areas is usually confined to the lowest socioeconomic groups.

Occurrence:

General: During the 19th century, pandemic cholera spread repeatedly from the Gangetic delta of India to most of the world. During the first half of the 20th century, the disease was confined largely to Asia, except for a severe epidemic in Egypt in 1947.

Since 1961, *V. cholerae* of the El Tor biotype has spread from Indonesia through most of Asia into eastern Europe and Africa, and from North Africa to the Iberian Peninsula and into Italy in 1973. In 1977 and 1978, there were small outbreaks in Japan and, for the first time in this pandemic, cholera occurred in the South Pacific. Disease has continued; in 1993, 16 countries in Africa, 25 in Asia, 21 in the Americas and three in Europe reported locally acquired cases. In 1993, a total of 376,845 cases and 6,781 deaths were reported from 78 countries. Eighty-six sporadic imported cases have occurred among returning travellers or immigrants to 21 countries in Europe, Canada, the United States and Australia. The *V. cholerae* O139 serogroup was isolated in seven countries in Asia — Bangladesh, China, India, Malaysia, Nepal, Pakistan and Sri Lanka. In 1994, cholera broke out among the Rwandan refugees in Zaire in July and appeared in Albania in September.

Except for two laboratory-acquired cases, there was no known indigenous cholera in the Western Hemisphere between 1911 and 1973, when a case due to *V. cholerae* El Tor Inaba occurred in Texas with no known source. In 1978, there were sporadic *V. cholerae* O1 El Tor Inaba infections in Louisiana, with eight cases and three asymptomatic infections; and in

1981, an outbreak due to the identical *V. cholerae* strain occurred involving 17 persons on a Texas floating oil rig. Cases have continued to occur sporadically during the summer and fall months. In 1992, there were 103 cases reported; 19 in 1993; and 31 in 1994. Most cases have been imported, with few indigenous cases. In January 1991, epidemic El Tor biotype *V. cholerae* O1 appeared in Perú, leading to an extensive epidemic which spread relentlessly to neighboring countries. In 1992, over 460,000 cases were reported, by 68 countries, to the World Health Organization (WHO). In 1993, over 50% of the total cases reported globally were from the Western Hemisphere. In 1994, over 300,000 cholera cases were reported to WHO by 66 countries. By 1994, a total of more than 950,000 cases of cholera had been reported in 21 countries in the Western Hemisphere.

Manitoba: There have been no documented cases of cholera since available records were maintained (1981).

Incubation Period: From a few hours to five days, usually two to three days.

Susceptibility and Resistance: Variable; gastric achlorhydria increases risk of illness, and breast-fed infants are protected. Cholera gravis, due to the El Tor biotype and O139 vibrio, occurs significantly more often among persons with blood group O. Infection results in a rise in agglutinating, vibriocidal and antitoxic antibodies, and increased resistance to re-infection that lasts longest against the homologous biotype. Field studies show that an initial clinical infection by *V. cholerae* O1 of the classical biotype confers protection against either classical or El Tor biotypes. In contrast, an initial clinical infection caused by biotype El Tor results in only a modest level of long-term protection that is limited to El Tor infections. In endemic areas, most people acquire antibodies by early adulthood. However, infection with O1 serogroup affords no protection against O139 infection and vice versa.

Period of Communicability: Presumably for the duration of the stool-positive stage, usually only a few days after recovery. However, occasionally the carrier state may persist for several months. Antibiotics known to be effective against the infecting strains (e.g., tetracycline presently against the O139 strain) shorten the period of communicability. Very rarely, chronic biliary infection, lasting for years, has been observed in adults, associated with intermittent shedding of vibrios in the stool.

Diagnosis

Diagnosis is confirmed by isolating *Vibrio cholerae* of the serogroup O1 or O139 from feces sent promptly to the laboratory. For clinical purposes, a quick presumptive diagnosis can be made by darkfield or phase microscopic visualization of the vibrios moving like “shooting stars,” inhibited by preservative-free, serotype-specific antiserum. For epidemiologic purposes, a presumptive diagnosis can be based on the demonstration of a significant rise in titre of antitoxic and vibriocidal antibodies. In non-endemic areas, isolated organisms from initial suspected cases should be confirmed by appropriate biochemical and serologic reactions and by testing the organisms for toxin production. In epidemics, once laboratory confirmation and antibiotic sensitivity have been established, not all cases need laboratory confirmation.

Key Investigations

- Source of infection (travel history).
- Contact history.
- Chemoprophylaxis history.
- Immunization history.

Control

Management of Cases:

Treatment:

- Prompt fluid therapy with volumes of electrolyte solution adequate to correct dehydration, acidosis and hypokalemia is the keystone of cholera therapy.

- Most patients with mild or moderate fluid loss can be treated entirely with oral rehydration using solutions that contain glucose 20 g/L (or sucrose 40 g/L or cooked rice powder 50 g/L); NaCl (3.5 g/L); KCl (1.5 g/L); and trisodium citrate dihydrate (2.9 g/L) or NaHCO₃ (2.5 g/L).
- Mild and moderate volume depletion should be corrected with oral solutions by replacing, over four to six hours, a volume matching the estimated fluid loss (approximately 5% of body weight for mild and 7% for moderate dehydration). Continuing losses are replaced by giving, over four hours, a volume of oral solution 1.5 times the stool volume lost in the previous four hours.
- Persons in shock should be given rapid IV rehydration with a balanced multi-electrolyte solution containing approximately 130 mEq/L of Na⁺; 25-48 mEq/L of bicarbonate, acetate or lactate ions; and 10-15 mEq/L of K⁺. Useful solutions include Ringer's lactate or WHO “diarrhea treatment solution” (4 g NaCl, 1 g KCl, 6.5 g sodium acetate and 8 g glucose/L), and “Dacca solution” (5 g NaCl, 4 g NaHCO₃ and 1 g KCl/L), which can be prepared locally in an emergency.
- Initial fluid replacement should be 30 ml/kg in the first hour for infants and in the first 30 minutes for persons over one year of age, after which the patient should be reassessed. After circulatory collapse has been effectively reversed, most patients can be switched to oral rehydration to complete the 10% initial fluid deficit replacement and to match continuing fluid loss.
- Tetracycline and other antimicrobial agents shorten the duration of the diarrhea and reduce the volume of rehydration solutions required, as well as

shortening the duration of vibrio excretion. Adults are given 500 mg four times a day, and children 12.5 mg/kg four times daily, for three days. When tetracycline-resistant strains of *V. cholerae* are prevalent, alternative antimicrobial regimens include TMP-SMX (320 mg trimethoprim and 1600 mg sulfamethoxazole twice daily for adults and 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole daily in two divided doses for children, for three days); furazolidone (100 mg four times daily for adults and 1.25 mg/kg four times daily for children, for three days); or erythromycin (250 mg four times daily for adults and 10 mg/kg three times daily for children, for three days). *V. cholerae* O139 strains are resistant to TMP-SMX.

- Since individual strains of *V. cholerae* O1 or O139 may be resistant to any of these antimicrobials, knowledge of the sensitivity of local strains to these agents, if available, should be used to guide the choice of the antimicrobial therapy.

Public Health Measures:

- Hospitalization with routine and contact precautions is desirable for severely ill patients.
- Food handlers, day care and health care workers should not return to work until three stools, taken at intervals of 24 hours and at least 48 hours after the cessation of antibiotics, are shown to be culture negative.

Management of Contacts:

- Public health nurses will identify contacts and coordinate collection of stool specimens if necessary.

- Persons who shared food and drink with a cholera patient should be asked to report any diarrheal symptoms for five days from their last exposure.
- If there is a high probability of transmission based on food preparation history and usual hygiene, household members should be given chemoprophylaxis; in adults with tetracycline (500 mg four times daily) or doxycycline (a single daily dose of 300 mg) for three days. Children may also be given tetracycline (50 mg/kg/day in four divided doses) or doxycycline (a single dose of 6 mg/kg) for three days; with such short courses of tetracyclines, staining of teeth is not a problem.
- Alternative prophylactic agents, useful where *V. cholerae* O1 strains are resistant to tetracycline, include furazolidone (Furoxone) (100 mg four times daily for adults and 1.25 mg/kg four times daily for children) or TMP-SMX (320 mg TMP and 1600 mg SMX twice daily for adults and 8 mg/kg TMP and 40 mg/kg SMX daily in two divided doses for children).
- TMP-SMX is not useful for *V. cholerae* O139 infections as these strains are resistant to this antimicrobial.
- Symptomatic contacts should have stool cultures arranged. Screening of asymptomatic contacts with stool cultures should be undertaken in:
 - household members and persons potentially involved in common source exposure if the source of infection is not obvious (e.g., recent history of travel in the index case);
 - household contacts who are food handlers, day care workers or health care workers, even when the exposure source for the index case is known.
- Immunization of contacts is not indicated.

Management of Outbreaks:

- Investigate source of infection and take appropriate measures to prevent further transmission.

Preventive Measures:

- Advise travellers to countries where cholera is endemic about appropriate cautions to take

when selecting food. A live, oral cholera vaccine will provide between 65-97% protection for selected travellers against O1 serogroup infections but will not protect against those caused by O139.

- For further vaccine information consult the Canadian Immunization Guide.