Ontario
Agency for Health Protection and Promotion
Agence de protection et de promotion de la santé

Cholera: Information for Clinicians
December 1, 2010

Key Messages:

- Cholera should be suspected in travelers returning from endemic areas with symptoms of acute watery diarrhea with onset <5 days after return.
- Management of cholera includes aggressive rehydration and good hygiene. Adjunctive antibiotics are recommended for severe cases.
- Stool specimens must specifically request "cholera" and should be submitted in usual (Cary Blair) transport media for stool C&S.
- Report all suspect and confirmed cases of cholera to your public health department.

Background

On November 26, 2010, the Ministère de la Sante Publique et de la Population (MSPP) in Haiti reported 72,017 cases of cholera and 1,648 deaths since mid October 2010.[1] The outbreak has extended to all of the country's ten health departments and the capital city of Port-au-Prince. No cholera outbreaks have been reported in Haiti in the last century.

Vibrio cholerae, the causative agent of cholera, is a water- and food-borne organism that can cause acute watery diarrhea, vomiting, severe dehydration and death.[2] The Haitian outbreak strain of cholera is confirmed as *Vibrio cholerae* serogroup O1, serotype Ogawa, biotype El Tor.[3] All isolates of *Vibrio cholerae* from the Haiti outbreak that have been typed demonstrate a common pulsed field gel electrophoresis pattern.

There have been two cases of cholera imported from Haiti confirmed to date; one in Florida and the second in the Dominican Republic.[1, 4] The purpose of this document is to highlight the potential for cholera disease in returning travelers, to provide clinical guidance on diagnosis, management and infection control practices of cholera, and to present information for travelers to areas with cholera disease.

Epidemiology

In 2009, The World Health Organization reported a total of 221,226 cholera cases from 45 countries worldwide, including 4,946 deaths.[5] This is known to be an underestimate of cholera infections due to limitations in reporting, surveillance and diagnostic capacity in the most vulnerable countries affected.[6] Since the early 2000s the majority of cases have been reported from the African continent, with a lesser incidence reported in Asia. Endemic cholera has not been reported in North America or Europe since the middle of the 19th century.

Lack of access to clean water and sanitation are the primary risk factors for cholera disease. *Helicobacter pylori* infection and O blood group are associated with increased risk of severe disease.[2] In populations without immunity, cholera affects people of all ages. In cholera endemic regions, children less than 4 years old are at highest risk of cholera. The incubation period of cholera is usually 2-3 days, with a range of a few hours to 5 days.

Regions with known cholera activity in 2009 are listed World Health Organization Cholera annual report (http://www.who.int/wer/2010/wer8531.pdf). [5] The current cholera outbreak in Haiti began in October 2010. In Ontario, there has been one laboratory confirmed case per year from 2005-2009. No imported cases from Haiti have been identified in Ontario as of November 26th, 2010.

Clinical Presentation

Cholera infection can be either symptomatic or asymptomatic. Asymptomatic persons infected with cholera can shed *Vibrio cholerae* in stools for 7-14 days after infection. Those who will develop symptoms do so within 5 days of exposure: symptoms include watery diarrhea or "rice water" stools (up to 0.5-1 liter per hour), vomiting, and dehydration. Fever is rare (less than 5 %). Mild to moderate cases may be indistinguishable from other infectious forms of diarrhea. Severe cases of cholera may present with electrolyte abnormalities, hypotension, and renal failure.[2]

Microbiological Diagnosis of *Vibrio cholerae* in Ontario

Who to test	Individuals who have profuse watery diarrhea < 5 days after returning from a region with known cholera.
Specimen type	Stool
Specimen container	Stool culture containers with usual (Cary-Blair) transport media
Requisition requirements	Must specify "Cholera" or "*Vibrio cholerae"* on requisition
Laboratory submission	Submit specimen to local hospital/ private laboratory Stool specimens will be forwarded from these laboratories to the OAHPP Public Health Laboratories (PHL) for testing.
Urgent requests	Must be communicated directly to the OAHPP PHL at 416 526-5441, prior to submitting specimen.
Tests not available	Serology, rapid stool tests
Other considerations	Other bacterial, viral and parasitic causes of acute diarrhea should be considered. Testing should be performed as per routine practice.

Management of *Vibrio cholerae* infection

Medical evaluation	Travelers returning from regions with known cholera should present immediately to medical evaluation if they have onset of watery diarrhea <5 days after their return.
Fluid and electrolyte replacement	Mortality from cholera can be reduced from 10-50% to less than 1% with appropriate fluid and electrolyte replacement. **Fluid and electrolyte therapy is the cornerstone of cholera therapy, and will save lives if given rapidly and in adequate volume to replace and maintain losses.** For full details of appropriate fluid and electrolyte replacement therapy for cholera, including 1) using oral rehydration therapy in mild to moderate cases, and 2) intravenous replacement in severe dehydration preferentially with Ringer's lactate, please see the CDC guidelines, http://www.cdc.gov/haiticholera/clinicalmanagement/, accessed November 27, 2010.

Antimicrobials

Antimicrobial therapy is of secondary priority to ongoing fluid and electrolyte replacement, and is indicated for severe cholera disease only. Antibiotics should not be prescribed for asymptomatic cholera infections.

In severe cholera, antimicrobial treatment is associated with decreases in the following: 1) duration of diarrhea (from 4 to 2 days on average), 2) stool volume, 3) intravenous fluid requirements, and 4) clinical relapses.[8]

The initial strains of *Vibrio cholerae* identified in Haiti in October and November 2010 are susceptible to tetracycline (a proxy for doxycycline) and azithromycin, resistant to sulfisoxazole and nalidixic acid, and show reduced susceptibility to ciprofloxacin.[7]

Recommended empiric therapy for individuals for suspected severe cholera returning from Haiti as of November 27, 2010 is:

Patient population	**Recommended antimicrobials (First line)**
Non pregnant adults	Doxycycline 300 mg PO x 1 dose
Pregnant women	Azithromycin 1gm PO x 1 dose
Children (oral suspension recommended for children less than 12 months/ children unable to swallow pills)	Azithromycin: 20 mg/kg X 1 dose or Erythromycin: 12.5 mg/kg QID x 3 days

Adapted from http://www.cdc.gov/haiticholera/clinicalmanagement/pdf/clinicalmanagement.pdf accessed November 28, 2010.

Antimicrobial therapy must be chosen in accordance with individual clinical circumstances. [8]

Other medications

Antimotility agents, analgesics and antiemetics are not recommended in the treatment of cholera

Zinc supplementation has been associated with decreased duration and severity of diarrhea in children infected with cholera in a randomized controlled trial in Bangladesh.[9] If severe cholera is suspected, zinc supplementation with 10-30 mg per day for 5-7 days may be considered.

Infection control recommendations

Vibrio cholerae is spread primarily by contaminated water and food sources. Access to clean water and modern sanitation systems mitigate ongoing transmission of cholera infections in Ontario.

While it is very rare for cholera to spread directly from person to person, patients hospitalized with severe cholera should be cared for in isolation using contact precautions until the diarrhea has resolved.[10,11]
When possible, hospitalized individuals with diarrhea possibly due to cholera should not share toilet facilities with other patients.

Public health reporting

All suspected and confirmed cases of cholera must be reported to the local health unit under the Ontario Health Protection and promotion act.

Information for travelers to regions with cholera activity

Measures to reduce illness from *Vibrio cholerae* for travelers to endemic regions are detailed on Public Health Agency of Canada and the US CDC websites (http://www.phac-aspc.gc.ca/tmp-pmv/info/cholera-eng.php, http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/cholera.aspx, accessed Nov. 27, 2010). These recommendations include ensuring safe water and food, and frequent hand washing. Additional considerations include bringing a prescription antibiotic to take in case of travelers' diarrhea, water purification tablets, and oral rehydration salts.[3] Travel advisories for Canadians travelling abroad can be found on the Foreign Affairs and International Trade Canada website at http://www.voyage.gc.ca/index-eng.asp (Accessed November 29, 2010).

Cholera vaccination is recommended for travelers to endemic regions with a high risk of exposure such as humanitarian relief workers, and travelers visiting areas of high risk with limited access to clean water and food.[12] Two oral cholera vaccines targeted to *V. cholerae* O1 serogroup are available in Canada: 1) killed whole-cell *V. cholerae* O1 with purified recombinant B-subunit of cholera toxoid (WC/rBS) sold as Dukoral™ and 2) an attenuated live oral genetically modified *V. cholerae* O1 vaccine (CVD 103-HgR) sold as Mutacol®. Studies of WC/rBS have demonstrated overall efficacy of 64-90% against infection with *Vibrio cholerae* O1 El Tor. In adults, the WC/rBS vaccine (Dukoral™) requires 2 doses of vaccine administered 1-6 weeks apart, and in children aged 2 to 6 years 3 doses must be administered 1-6 weeks apart. Full immunity is not attained until 10-14 days after completing the vaccination series, and protection against cholera is estimated to be 6 months to 2 years. This vaccine is not protective against *V. cholerae* O139, and is not approved for children less than 2 years old.

If travelling to a cholera endemic area, consultation with a clinician experienced in travel medicine is advised.

References

1. Pan American Health Organization (PAHO). http://new.paho.org/disasters/index.php?option=com_content&task=view&id=1423&Itemid=1 , accessed November 26, 2010.
2. Sack DA, Sack RB, Nair GB, Siddique AK. Cholera. *Lancet.* 2004 Jan 17;363(9404):223-33.
3. CDC Outbreak notice: Cholera in Haiti. http://wwwnc.cdc.gov/travel/content/outbreak-notice/haiti-cholera.aspx, accessed November 27, 2010.
4. Goddard J. New York Times online Nov 17, 2010. http://www.nytimes.com/2010/11/18/us/18florida.html?scp=7&sq=haiti%20cholera&st=cse, accessed Nov 26, 2010.
5. World Health Organization Cholera annual report 2009. *Weekly Epidemiological Record*, 2010, 85(31):293-308. http://www.who.int/wer/2010/wer8531.pdf, accessed November 26, 2010.
6. Zuckerman JN, Rombo L, Fisch A. The true burden and risk of Cholera: implications for prevention and control. *Lancet Infect Dis.* 2007 Aug;7(8):521-30
7. Centers for Disease Control and Prevention. Update: Cholera Outbreak — Haiti, 2010. *MMWR Weekly*: Vol. 59, No. 45.November 19, 2010
8. Lindenbaum J, Greenough WB and Islam MR. Antibiotic therapy of cholera, *Bull World Health Organ* **36** (1967), pp. 871–883.
9. Roy SK, Hossain MJ, Khatun W, Chakraborty B, Chowdhury S, Begum A, Mah-e-Muneer S, Shafique S, Khanam M, Chowdhury R. Zinc supplementation in children with cholera in Bangladesh: Randomized controlled trial. *BMJ* 2008; 336:266-268.
10. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2010. Atlanta: U.S. Department of Health and Human Services, Public Health Service, 2009. Online Edition. http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/cholera.aspx, accessed Nov. 27, 2010.
11. Swaddiwudhipong W, Peanumlom P. A Case of Nosocomial Cholera during a Community Outbreak in a Thai-Myanmar Border Area. *J Med Assoc Thai* 2010; 93 (9): 1112-4.
12. Committee to Advise on Tropical Medicine and Travel. Statement on New Oral Cholera and Travellers' Diarrhea Vaccination. CCDR Volume 31 • ACS-7 1 July 2005. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/05vol31/asc-dcc-7/index-eng.php, accessed Nov 27, 2010.