Cholera: Information for Clinicians
December 1, 2010

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. 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. The Haitian outbreak strain of cholera is confirmed as Vibrio cholerae serogroup O1, serotype Ogawa, biotype El Tor. All isolates of Vibrio cholerae from the Haiti outbreak that have been typed demonstrate a common pulsed field gel electrophoresis pattern.

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.

There have been two cases of cholera imported from Haiti confirmed to date; one in Florida and the second in the Dominican Republic. 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. 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. 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. 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). 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**

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

**Management of *Vibrio cholerae* infection**

<table>
<thead>
<tr>
<th>Medical evaluation</th>
<th>Travelers returning from regions with known cholera should present immediately to medical evaluation if they have onset of watery diarrhea &lt;5 days after their return.</th>
</tr>
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<tbody>
<tr>
<td>Fluid and electrolyte replacement</td>
<td>Mortality from cholera can be reduced from 10-50% to less than 1% with appropriate fluid and electrolyte replacement. <strong>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.</strong></td>
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<tr>
<td></td>
<td>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, <a href="http://www.cdc.gov/haiticholera/clinicalmanagement/">http://www.cdc.gov/haiticholera/clinicalmanagement/</a>, accessed November 27, 2010.</td>
</tr>
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</table>
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:

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


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


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

This document was developed by the Ontario Agency for Health Protection and Promotion (OAHPP). OAHPP provides scientific and technical advice to Ontario’s government, public health organizations and health care providers. OAHPP’s work is guided by the best available evidence. This best practice document has been peer reviewed and reflects the consensus of experts advising OAHPP.

This document is intended to assist physicians in clinical decision-making by describing a range of generally acceptable approaches for diagnosis and management. This document should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment regarding care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient. OAHPP is not responsible for the results of the use by anyone of this document.

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