

Date: November 16, 2010

To: State and Territorial Epidemiologists
State and Territorial Public Health Laboratory Directors

Through: Director, National Center for Emerging and Zoonotic Infectious Diseases

SUBJECT: Outbreak of cholera in Haiti and surveillance for imported cases

Epidemic cholera appeared in Haiti in October 2010. When water and sewage treatment is inadequate, as in post-earthquake Haiti, cholera can spread rapidly. Cholera incidence and prevalence is difficult to predict, even in areas where it is endemic, due to variability in environmental factors and individual immune responses. Cholera may continue to occur in Haiti for months or years, may spread to other countries, and, even if it wanes soon, may recur in coming years. Epidemic-associated *Vibrio cholerae* infections may occur in the United States as a result of persons traveling to affected areas. Because of the considerable traffic between Haiti and the United States, further introductions of toxigenic *V. cholerae* O1 may occur. However, widespread chlorination of drinking water and treatment of sewage make transmission of imported cholera unlikely in this country; imported cases of cholera are reported yearly in the United States, but secondary transmission has been negligible. Because you may receive inquiries concerning the current epidemic, we are providing the following background information.

Microbiology: Epidemic cholera is caused by *Vibrio cholerae* serogroup O1 and O139 strains that produce cholera toxin. Other serogroups of *V. cholerae* can also cause diarrhea and are more common than toxigenic *V. cholerae* O1 in the United States, but cause less severe illness and have no recognized epidemic potential. *V. cholerae* O1 can be further categorized into two major serotypes, Inaba and Ogawa, and two biotypes, classic and El Tor but classic biotype strains have disappeared. A third serotype, Hikojima, is very rare. The strain of *V. cholerae* O1 that is endemic to the U.S. Gulf Coast and responsible for most domestically acquired cholera infections is biotype El Tor, serotype Inaba; these infections are generally attributed to seafood consumption. The seventh cholera pandemic that dramatically affected Latin America during the 1990s was caused by *V. cholerae* O1 biotype El Tor strains, of both Ogawa and Inaba serotypes. To date, all isolates from Haiti that have been examined are indistinguishable, and are *V. cholerae* O1, serotype Ogawa, biotype El Tor. Pulsed-field gel electrophoresis (PFGE) analysis and other methods indicate that the Haiti outbreak strain is indistinguishable from other strains found in South Asia and elsewhere. The origin of the strain isolated in Haiti and the means by which it was introduced into Haiti are not known at this time.

Prevention: The risk of cholera to the American traveler in areas with endemic and epidemic disease has been extremely low. Nevertheless, careful attention to food and water sources is the most important preventive measure. This includes not drinking unboiled or untreated water, and not eating uncooked vegetables, food and beverages from street vendors, and raw fish and shellfish (including ceviche). The general rule is "boil it, cook it, peel it, or forget it." More detailed advice is at www.cdc.gov/cholera/general. The risk of importation of cholera via commercial foodstuffs has been extremely low; however, cholera has occurred in the United States from consumption of improperly stored seafood brought back in the luggage of travelers who visited endemic areas (CDC. Epidemiologic Notes and Reports Cholera – New York, 1991.

MMWR. 40[No. RR-30];516-518. 1991; available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00014926.htm>). CDC discourages travelers from bringing noncommercial, perishable “souvenir seafood” from Haiti to the United States.

At this time, no cholera vaccines are licensed or available in the United States and CDC does not recommend their use in travelers because their risk of contracting the disease is extremely low. Antibiotic use is also not recommended for prophylaxis against cholera or other diarrheal illnesses. Such use can harm travelers by allergic reactions, antibiotic-associated diarrhea, and increased susceptibility to some infections, and can also provide a false sense of security.

Clinical Suspicion: Cholera should be considered in any patient, especially an older child or adult, presenting with severe watery diarrhea and vomiting with severe dehydration. The illness is often accompanied by marked leg cramps because of electrolyte disturbances. The spectrum of *V. cholerae* O1 or O139 infection ranges from asymptomatic infection to mild diarrhea to life-threatening, dehydrating diarrhea. Clinical suspicion should be increased, and milder diarrheal illnesses more suspect, in persons returning from areas known to have epidemic cholera, or in persons with a recent history of ingestion of raw or undercooked shellfish. The incubation period of cholera is between 2 hours and 5 days. The infectious dose varies by the bacterial strain and the host immune response. A healthy North American requires a dose of 10^8 - 10^{11} cells. When stomach acid is reduced (e.g., by acid-reducing pills), the infectious dose is decreased by 50%.

Diagnosis: Culturing a fecal specimen on thiosulfate-citrate-bile salts-sucrose (TCBS) medium increases the likelihood of isolation of *Vibrio*. Culture on TCBS should be requested for any suspect cholera case. The characteristic yellow colonies can be picked, subcultured on nutrient agar, and agglutinated using polyvalent *V. cholerae* O1 antiserum. Polyvalent O1 and monovalent Inaba and Ogawa antisera are commercially available. All isolates of suspect *V. cholerae* should be referred to the Enteric Diseases Laboratory Branch (EDLB), Division of Foodborne, Waterborne and Environmental Diseases (DFWED), CDC, according to already existing strain submission guidelines for *V. cholerae* for serogrouping, determination of cholera toxin production, and further strain characterization. Please see the “Surveillance” section below for isolate forwarding instructions.

Treatment: The mainstay of treatment of cholera is replacement of fluid and electrolyte losses with rehydration therapy. All but the most severe cases can be managed largely or completely with adequate oral rehydration solution. Although the oral rehydration salt solution developed and distributed by UNICEF and the World Health Organization (WHO) is manufactured in the United States by Jianis Brothers, Kansas City, Missouri (telephone 816-421-2880), and can be purchased by bulk order from that company, most of this product is shipped overseas and it is often not easily available in this country*. Most oral glucose electrolyte solutions commercially available in this country, like Gatorade™ and Pedialyte™, contain insufficient sodium to achieve rapid volume replacement. Rehydration of the dehydrated patient requires an oral solution with at least 75 meq per liter of sodium, as well as 20 meq per liter of potassium and 10 meq per liter of base in addition to carbohydrate†. Rehydralyte™ is one commercially available solution that does provide adequate ratios of salts and sugars. Even patients with mild to moderate vomiting will absorb rehydration liquids taken in small sips. Intravenous therapy should be reserved for patients who are severely dehydrated, unable to take oral solutions, or who present in hypovolemic shock. Ringer’s lactate or other intravenous solutions with appropriate amounts of

bicarbonate and potassium as well as sodium and chloride should be used. An MMWR article published in 2003 discusses the current guidelines for oral rehydration in children. (CDC. Managing acute gastroenteritis among children. MMWR. 52[No. RR-16];1-16. 2003; available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5216a1.htm>)

Antimicrobial drugs are useful adjunctive therapy for severely ill patients, decreasing the duration and severity of diarrhea and diminishing the volume of fluid replacement needed. Isolates of the Haitian strain tested to date have been resistant to trimethoprim-sulfamethoxazole and nalidixic acid, and showed intermediate resistance to ampicillin. Options for treatment include doxycycline, azithromycin, tetracycline, ciprofloxacin, and erythromycin. Recommended doses are outlined on the CDC's "Defeating Cholera" webpage (<http://www.cdc.gov/haiticholera/clinicalmanagement/>) and are summarized in the attached worksheet entitled "Consider Cholera" (Appendix 1). CDC will continue to monitor circulating *V. cholerae* O1 strains in Haiti to determine if resistance to additional antimicrobial agents emerges.

Family members of suspected cholera patients should be questioned about their health status and advised to seek medical attention immediately if they develop watery diarrhea during the week following onset of illness in the index case. Chemoprophylaxis of family contacts is not recommended, as secondary transmission in the United States is rare. The family should receive instructions in proper hand-washing and in cleaning contaminated clothes and linens. Contaminated surfaces—particularly in food preparation, eating, and bathing areas—should be disinfected with a household disinfectant product or a dilute bleach mixture of one part bleach to nine parts water. The sanitary facilities in a cholera patient's home should be inspected to make sure that the patient's feces are disposed of via adequate sewage treatment system or septic tank. Patients and family members should not swim while ill with diarrhea or for 2 weeks after resolution of symptoms. (These recommendations are summarized in Appendix 2, "Infection Control Guide for Family Members of Patients with Suspect or Confirmed Cholera".)

Surveillance and Reporting: In accordance with the Council of State and Territorial Epidemiologists (CSTE) Executive Board's Interim Position Statement of November 10, 2010 (Appendix 3), cholera should be reported as an immediately notifiable disease. Cases are classified as temporary "immediate urgent" and should be reported to CDC within 24 hours of a state health department's becoming aware of the case. Immediate notification should occur through voice contact by the State/Territorial Epidemiologist (or delegate) with the CDC Emergency Operations Center (EOC) Duty Officer. The CDC EOC phone number is 770-488-7100 and is staffed 24/7. A CDC subject-matter expert will call back within 4 hours.

For surveillance purposes CSTE defines a confirmed case of cholera as a compatible illness with either 1) isolation of *V. cholerae* from stool or vomitus, demonstration that it is serogroup O1 or O139, and confirmation that the isolate produces cholera toxin, OR 2) demonstration of a significant rise in vibriocidal or antitoxin antibody titers between acute and convalescent sera or significant fall in vibriocidal antibodies in early and late convalescent-phase sera. It should be remembered that domestically acquired cases of *V. cholerae* O1 infection are reported each year from Gulf Coast seafood and recreational water exposure.

State Public Health Laboratories are requested to follow the established guidelines and regarding submission of isolates during the outbreak in Haiti (see Appendices 4 and 5: "Enteric Isolate

Submission to CDC” and “Submission of foodborne disease-associated bacterial isolates and specimens to the Enteric Disease Laboratory Branch (EDLB)”). Presumptive *Vibrio cholerae* isolates should be forwarded to EDLB as soon as they are isolated for confirmatory testing. The Enteric Diseases Epidemiology Branch (EDEB) recommends continued reporting of all *Vibrio* infections, including suspect *V. cholerae* O1 cases, to CDC through the Cholera and Other *Vibrio* Illness Surveillance (COVIS) system. The *Vibrio* surveillance form (CDC form 52.79) should be used to report illnesses to CDC and can be used as a data-gathering tool for investigating a suspect case. This form has fields for detailed reporting of places visited. Detailed information on travel history will help state and local health departments to investigate exposures and will assist CDC in formulating advice for travelers to Haiti. This surveillance form is available at:

http://www.cdc.gov/nationalsurveillance/PDFs/CDC5279_COVISvibriosis.pdf. The annual reports from this surveillance system are available at http://www.cdc.gov/nationalsurveillance/cholera_vibrio_surveillance.html.

If you have any questions concerning cholera and its diagnosis or management, please call or email the CDC’s Emergency Operations Center at 770-488-7100 (Fax 770-488-7107) or eocreport@cdc.gov.

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Appendices: 1) “Consider Cholera”; 2) Infection Control Guide for Family Members of Patients with Suspect or Confirmed Cholera; 3) CSTE Executive Board’s Interim Position Statement of November 10, 2010; 4) Enteric Isolate Submission to CDC; 5) Submission of foodborne disease-associated bacterial isolates and specimens to the Enteric Diseases Laboratory Branch

* WHO Formula Oral Rehydration Salts (ORS) † Electrolyte formulation according to WHO standards: can be ordered from:

Janis Brothers, 2533 Southwest Blvd
Kansas City, MO 64108-2395
Phone: (816) 421-2880
FAX: (816) 421-2883

	Standard ORS solution		Reduced Osmolarity ORS solutions	
	(mEq or mmol/l)	(mEq or mmol/l)	(mEq or mmol/l)	(mEq or mmol/l)
Glucose	111	111	75-90	75
Sodium	90	50	60-70	75
Chloride	80	40	60-70	65
Potassium	20	20	20	20
Citrate	10	30	10	10
Osmolarity	311	251	210-260	245

Appendix 1

CONSIDER CHOLERA

There is an outbreak of cholera in Haiti.

Physicians in the United States need to be on the lookout for possible cases.

What is cholera?

Cholera is an acute bacterial enteric disease with sudden onset of profuse watery diarrhea and vomiting. If severe, it can lead to severe dehydration, shock, acidosis, and death in hours.

When should I suspect cholera?

You should suspect cholera in any patient presenting with severe watery diarrhea and vomiting with severe dehydration, particularly after recent travel from Haiti. The patient may complain of painful cramping in the legs due to electrolyte disturbances. Clinical suspicion should be increased, and milder diarrheal illnesses are more suspect, in persons returning from Haiti, or in persons with a recent history of ingestion of raw seafood. The incubation period of cholera is between two hours and five days.

How do I diagnosis cholera?

The diagnosis is made by culturing the organism from the stool. Notify your lab that you are considering cholera so that they will culture on TCBS agar. However, you should not wait for a positive culture before starting aggressive treatment.

How do I treat cholera?

The severe cholera patient may have lost more than 10% of body weight and needs swift volume replacement. Cholera deaths can be prevented by the aggressive administration of fluids. This will correct the dehydration, shock, and acidosis. Antibiotic treatment is less important, but will decrease the duration of illness.

What fluids should I give?

This depends on the patient's condition. Patients with mild to moderate dehydration can be given an appropriate oral rehydration salt solution such as Rehydralyte™ or WHO Formula Oral Rehydration Salts (ORS). Only solutions that contain the proper balance of electrolytes should be given.

Patients with severe dehydration or those with intractable vomiting need intravenous therapy with Ringer's lactate solution. Intravenous fluid should be given quickly to restore the circulation, followed by oral fluids as soon as possible.

How much fluid should I give?

Fluid therapy needs to be individualized. Severely dehydrated adults may require several liters of fluid immediately to restore an adequate circulating volume. Base your therapy on the degree of dehydration. Remember that cholera patients will have significant on-going fluid losses that also need to be measured and replaced.

What antibiotic should I use?

Based on antimicrobial susceptibility testing on strains from the ongoing cholera outbreak in Haiti, the following antimicrobial regimens may be used to treat confirmed or suspected cases of cholera possible linked to this outbreak. Note that oral suspensions of most of these medications are available for young children.

Doxycycline

Adult (non-pregnant): 300 mg in a single dose

Child: 2-4 mg/kg in a single dose

Azithromycin

Adult: 1g in a single dose

Child: 20 mg/kg in a single dose

Tetracycline

Adult (non-pregnant): 500 mg, 4 times/day for 3 days

Child: 12.5 mg per kg, 4 times/day for 3 days

Ciprofloxacin

Adult (non-pregnant): 1g in a single dose OR 500 mg 2 times/day for 3 days

Child: 20mg/kg in a single dose

Erythromycin

Adult: 500 mg, 4 times/day for 3 days

Child: 12 mg/kg, 4 times/day for 3 days

Clinical management guidelines including antibiotic treatment are also posted on CDC's website at <http://www.cdc.gov/haiticholera/clinicalmanagement/>

What else should I do?

All suspected or confirmed cases of cholera should be reported to your county or state health department immediately. Do not swim while ill with diarrhea or for 2 weeks after resolution of symptoms.

Appendix 2

Infection Control Guide for Family Members of Patients with Suspect or Confirmed Cholera

- Drink and use safe water
- Cook food thoroughly
- Wash hands with soap and safe water after caring for the patients, and especially after handling fecal matter
- Remove and wash any bedding or clothing that may have had contact with diarrheal stool, preferably in a washing machine, in warm or hot water. Usual machine detergents are sufficient; bleach is not necessary.
- Use a flush toilet or approved septic system; double bag soiled materials when discarding in trash.
- Use any household disinfectant or a 1:10 dilution of bleach solution (1 part bleach to 9 parts water) to clean any area that may have contact with fecal matter, including the patient's bathroom, bedpan, as soon as possible after being soiled.
- When possible, use rubber gloves when cleaning any room or surface that may have had contact with the patient's fecal matter.
- Patients with cholera should not swim while ill with diarrhea or for 2 weeks after resolution of symptoms.
- If a household member develops acute, watery diarrhea, administer oral rehydration solution (ORS) and seek healthcare immediately
- While caring for persons who are ill with cholera, do not serve food or drink to persons who are not household members
- Visitors can be allowed if the ill person wants company; visitors should also observe hand hygiene recommendations