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Cholera

Surveillance and Investigation Protocol

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Office of Epidemiology and Prevention Services
Division of Communicable Disease Epidemiology
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I. ABOUT THE DISEASE

A. Clinical Presentation

Cholera is an acute bacterial intestinal infection caused by toxigenic *Vibrio cholerae.* It commonly manifests as acute watery diarrhea with nausea and vomiting in an afebrile person. The pathogen remains in the gastrointestinal tract and does not invade the bloodstream. Infection is often mild or asymptomatic, but it can be severe. Severe cholera (*cholera gravis*) occurs in about 10% of cases and is characterized by profuse watery diarrhea (rice water stools).

Clinical findings include dry mucous membranes and loss of skin turgor, hypotension, tachycardia, and thirst. Muscle cramps occur as a result of electrolyte imbalance. Untreated cholera can cause rapid loss of body fluids, which can lead to severe dehydration, hypovolemic shock, and death within hours.

B. Etiologic Agent

Cholera is caused by the bacterium *Vibrio cholerae*, which produces a toxin that leads to severe diarrhea; the toxigenic *Vibrio cholerae* O-group 1 (O1) or O-group 139 (O139). Other serogroups of *V. cholerae*, with or without the cholera toxin gene (including the nontoxigenic strains of the O1 and O139 serogroups), can cause a cholera-like illness. Only toxigenic strains of serogroups O1 and O139 have caused widespread epidemics and are reportable.

V. cholerae O1 has 2 biotypes: classical and El Tor. Each biotype can be divided into distinct serotypes, Inaba Ogawa, and rarely, Hikojima. The symptoms of infection are indistinguishable, but more people infected with the El Tor biotype remain asymptomatic or have only a mild illness. Globally, most cholera cases are caused by O1 El Tor.

C. Reservoir

Cholera has 2 main reservoirs: humans and water. Water contaminated with feces from an infected person is the main source of cholera infection. The bacterium can be found in surface or well water. Contaminated public wells are frequent sources of large-scale cholera outbreaks. People living in crowded conditions without adequate sanitation are especially at risk. Primary infection in humans is incidentally acquired. *V cholerae* is rarely isolated from animals, and animals do not play a role in transmission of disease.

D. Incubation Period

The incubation period for cholera can range from a few hours to five days. Most commonly, the incubation period is between two and three days. The median incubation period for toxigenic cholera is estimated to be 1.4 days.

E. Mode of Transmission

Toxigenic *V. cholerae* O1 and O139 are free-living bacterial organisms found in fresh and brackish water, often in association with copepods or other zooplankton, shellfish, and aquatic plants. Cholera infections are acquired most often following consumption of untreated drinking water in which toxigenic *V. cholerae* naturally occurs or has been introduced from the feces of an infected person. Cholera can also be

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transmitted by eating raw or undercooked food, especially fish and shellfish. Other foods, including produce, are less commonly implicated.

To prevent cholera, drink only water that is safe to drink, eat only food that is thoroughly cooked and still hot, avoid undercooked or raw fish or shellfish, and avoid foods and beverages from street vendors.

F. Period of Communicability

Patients are infectious from the onset of symptoms until seven days after diarrhea has resolved. The carrier state may develop and persist for a few months. The convalescing carrier has the potential to transmit cholera as long as stools test positive for the bacterium, most likely until a few days after recovery from symptoms. Antibiotics effective against the infecting strains shorten the period of communicability.

II. DISEASE INVESTIGATION

A. Case Definition and Case Classification

Source: **Global Task Force on Cholera Control** and CDC

In areas where a cholera outbreak has NOT been declared:

Clinical Criteria

An illness characterized by diarrhea and/or vomiting; severity is variable.

Laboratory Criteria For Diagnosis

- Isolation of toxigenic (i.e., cholera toxin-producing) Vibrio cholerae O1 or O139 from stool or vomitus, OR
- Serologic evidence of recent infection

Case Classification

Confirmed

A clinically compatible illness that is laboratory confirmed.

Comments

Illnesses caused by strains of V. cholerae other than toxigenic V. cholerae O1 or O139 should not be reported as cases of cholera. The etiologic agent of a case of cholera should be reported as either V. cholerae O1 or V. cholerae O139. Only confirmed cases should be reported to National Notifiable Diseases Surveillance System (NNDSS) by state health departments.

CDC requests that all Vibrio isolates be forwarded to the Enteric Diseases Laboratory Branch (EDLB) for characterization. EDLB (specifically the Epidemic Investigations Laboratory) requests that state public health labs immediately forward all suspect V. cholerae isolates for serogrouping and cholera toxin testing as well as biotype and antimicrobial susceptibility testing.

In areas where a probable or confirmed cholera outbreak has been declared:

- A suspected case is any person presenting with acute watery diarrhea, or who died from acute watery diarrhea.
- A confirmed case is any person with *Vibrio cholerae* O1 or O139, as confirmed by culture (including seroagglutination) or PCR.

B. Reporting Timeframe to Public Health

Healthcare providers and laboratories are required to report cholera within 24 hours of notification to the local health department.

C. Outbreak Recognition

An outbreak is defined as two or more people experiencing similar illness after consumption of a common food or drink, or different food from a common place.

D. Healthcare Provider (HCP) Responsibilities

1. Be familiar with cholera clinical presentation. Consider cholera as a possible cause of watery diarrheal infection in patients who have recently traveled or consumed contaminated water or eaten raw or undercooked food.
2. If cholera is suspected, immediately initiate hydration and treatment. Do **not** wait for public health consultation or laboratory confirmation.
3. Depending on the clinical presentation, obtain clinical specimens (stool) from patients suspected with cholera and send for testing. For instructions on how to collect a specimen, see **II. E. Laboratory Responsibilities** below. Notify the laboratory if cholera infection is suspected as special techniques may be used to identify the organism. The infection may need to be confirmed by bacterial culture and the isolate (or clinical specimen) forwarded to the West Virginia Office of Laboratory Services (WV OLS) for molecular characterization. Contact WV OLS at telephone number (304) 558-3530 prior to shipment.
4. Obtain exposure history from patients suspected of having cholera.
    - For patients with travel history: Multidrug-resistant isolates are emerging, particularly in South Asia, with resistance to quinolones, trimethoprim-sulfamethoxazole, and tetracycline. Consider antimicrobial susceptibility testing to inform treatment choices.
5. Antibiotics can be lifesaving for patients with severe illnesses.
6. Notify the local health department of the patient's county of residence about a potential case of cholera.
7. Collect and share the following with the local health department: clinical, laboratory, exposure, and other relevant information.

E. Laboratory Responsibilities

A case of cholera is confirmed in the laboratory using culture-based or molecular methods such as PCR.

For specimen collection and transport, use the Cary Blair transport medium. See CDC's Collecting and Transporting Specimen for details.

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For laboratory methods to isolate, identify, and test the susceptibility of *Vibrio cholerae* to antimicrobial agents, see CDC's Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera.

Commercial and hospital laboratories should send *Vibrio* isolates to the WV OLS for submission to CDC's Enteric Diseases Laboratory Branch (EDLB). For information about sending specimens to OLS, see the WV OLS Specimen Collection Instructions and complete the WV OLS Specimen Collection Form.

For rapid diagnostic testing, the Crystal® VC Rapid Diagnostic Test (RDT) can provide an early warning for an outbreak of cholera but cannot confirm an individual case. Fecal specimens that test positive by RDT for *Vibrio cholerae* O1 or O139 should be sent to the laboratory for confirmation by a validated method.

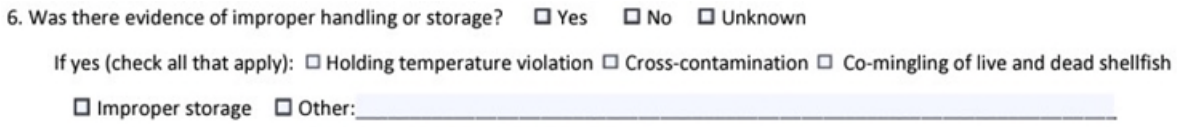
G. Local Health Responsibilities

1. Be familiar with the *Cholera Surveillance and Investigation Protocol*.
2. Educate healthcare providers about the reporting requirements. Cholera is reportable to a local health department within 24 hours of diagnosis.
3. Using the standard form for Cholera and Other *Vibrio* Illness Surveillance (COVIS), complete the CDC COVIS Form and enter the information into WVEDSS. Ensure that the information entered in WVEDSS is correct and complete. Attach the completed CDC COVIS Form to the Attachments section in the Supplemental Info tab in the WVEDSS investigation.
    a. Interviewing Tips
        i. If case consumed seafood from restaurant, look up the restaurant menu online and ask:
            1. What was the date and time of meal?
            2. Which meal was eaten: dinner, brunch, happy hour, etc.?
            3. Which menu did the case order from: dinner, special oyster menu, bar or happy hour menu?
            4. What is the exact name and description of the item (the online menu can help)?
            5. How much/how many did they eat?
            6. Do they have receipts, photos, etc.?
        ii. If case consumed seafood from a seafood stand or grocery store, look up the seafood stand or store online to see what they typically sell and ask:
            1. What type of seafood was purchased?
            2. The date and time of purchase
            3. The date and time of consumption
            4. How was the seafood handled between the time it was purchased and eaten?
            5. Do they have a receipt?
            6. If they purchased bivalve shellfish, do they still have the tag attached to the plastic net the shellfish was sold in?

7. If they purchased pre-shucked bivalve shellfish, do they still have the container (jar and lid) it was sold in?

iii. If case consumed recreationally harvested seafood: Gather details about who harvested the shellfish or other seafood, when and where it was harvested, storage conditions, and how the items were prepared (served raw, if cooked, how cooked, possibilities for cross-contamination in storage or preparation).
iv. If case traveled outside the United States: Obtain travel dates and locations visited and detailed restaurant exposure as above.
v. If case had skin exposure to brackish or saltwater: Obtain date and exact location of exposure (beach name, closest intersection, etc.).

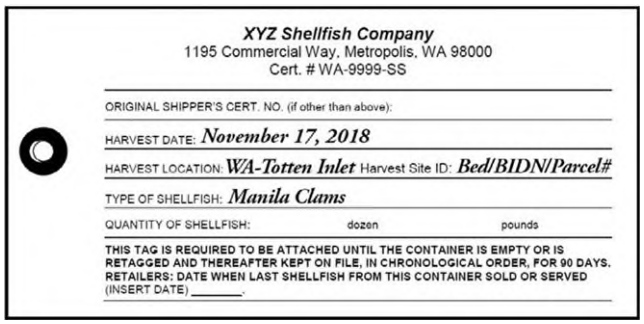
4. Educate the patient and household members about cholera prevention and control. See **III. C. Disease Prevention and Control Intervention** for details.
5. Inform the patient, household and close contacts to consult their healthcare provider if they are or know of anyone who is exposed (through consumption) and exhibits similar symptoms.
6. Notify the Division of Communicable Disease Epidemiology within 24 hours of detection of a case of cholera by calling the Epidemiologist on-call at (304) 558-5358 ext. 2.
7. In the event of an outbreak, immediately notify the WV Dept. of Health Epidemiologist on-call at (304) 558-5358 ext. 2.
8. Facilitate specimen collection and submission to WV OLS, tel. number: (304) 558-5358. Notify OLS if an isolate is being sent from a laboratory.
9. See **III. C. Disease Prevention and Control Intervention** (below) for prevention and control strategies.
10. An Environmental Health (EH) assessment should be conducted for every vibriosis case involving a restaurant, grocery/market, food truck, or other commercial establishment. If a facility in West Virginia is implicated, the county where the restaurant is located is responsible for the investigation which includes obtaining seafood tags and/or invoices for products. If the restaurant is out of state, please notify the Food and Waterborne Disease Epidemiologist right away, so that investigation can be passed on to the appropriate state.
    a. Determining if contributing factors at the retail establishment may have contributed to the proliferation or survival (in the case of cooked product) of Vibrio is an important component of the investigation. In the event that an illness is traced back to a particular shellfish growing area, regulatory action may not be taken unless contributing factors at the facility can be ruled out. Information regarding improper handling and storage should be completed on page 5 of the CDC COVIS form:


6. Was there evidence of improper handling or storage? ☐ Yes ☐ No ☐ Unknown
If yes (check all that apply): ☐ Holding temperature violation ☐ Cross-contamination ☐ Co-mingling of live and dead shellfish
☐ Improper storage ☐ Other:_____

    b. Overall, the environmental assessment should focus on:
        i. Confirming approved shellfish source (including collecting shellfish tags and invoices)
        ii. Identifying risks associated with receiving, storage, preparation, cooking, and temperature control
        iii. Investigating if cross-contamination potentially took place (if applicable)

iv. Ensuring the appropriate consumer advisory (if required)
v. Instituting control measures (as needed)

c. Shellstock tagging is required by the FDA through the National Shellfish Sanitation Program (NSSP). These tags are designed to allow traceback of shellfish associated with illness to the growing area and harvest date. Retailers are required to maintain tags onsite for 90 days after sale. Shellfish tags include information related to growing location, date of harvest, and shippers, distributors, etc. If tags are not available or if it is not possible to identify which shellfish tags belong with the shellfish served to the case-patient, EH investigators should collect shellfish invoices.



d. Once the environmental assessment has been completed, update the seafood investigation section of the CDC COVIS Report form using information gathered during the environmental health assessment and attach the shellfish tags.

For the purpose of case investigation, ***lost to follow-up*** **(LTF)** is defined as a disease investigation outcome reported by a local health department staff in WVEDSS after:

- All avenues (e.g. phone call, text messaging, visit, mailed letter, email, etc.) of obtaining patient information, on at least 3 separate occasions (different days and times) have been exhausted, **AND**
- Attempts to collect patient medical information from the healthcare provider on at least 3 separate occasions have been exhausted, **AND**
- Attempts to contact patient or obtain information has been clearly documented in WVEDSS *General Comments* section, **AND**
- Documentation has been completed within 30 days of the patient's laboratory report.

H. State Health Responsibilities

1. Provide technical assistance and training to local health departments and healthcare providers.
2. In addition to reporting through the National Notifiable Diseases Surveillance System (NNDSS), a COVIS Form needs to be completed. Ensure that LHDs know where to access the CDC COVIS Form.
3. One COVIS case report form should be submitted for each patient which includes all supportive and confirmatory laboratory evidence related to the patient.

4. Review and ascertain cases submitted in WVEDSS. Ensure information is correct and complete.
    - ***No Public Health Action*** is defined as incomplete disease investigation and no activity occurring at the local level for at least 60 days since the date of the patient's laboratory report. The state health department staff should document "no public health action" in WVEDSS *General Comments* section before administratively closing the investigation.
5. Summarize data at least annually and report back the findings and recommendations to stakeholders.

I. Occupational Health

Cholera is not typically transmitted person-to-person. However, practice of standard precautions is recommended.

III. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

Prevent additional cases of cholera through early recognition and investigation of cases so the common food source or drink is removed from commerce in a timely manner.

B. Disease Prevention Objectives

Reduce the incidence of cholera by educating the public, especially travelers about disease prevention, see recommendations below under **III. C. Disease Prevention and Control Intervention.**

C. Disease Prevention and Control Intervention

TREATMENT:

Rehydration is the cornerstone of cholera treatment. Administer oral rehydration solution and, when necessary, intravenous fluids and electrolytes. Timely administration in adequate volumes will reduce case-fatality ratios to <1%. Antibiotics will reduce fluid requirements and duration of illness and are indicated in conjunction with aggressive hydration for severe cases and for patients with moderate dehydration and ongoing fluid losses.

Whenever possible, antimicrobial susceptibility testing should inform treatment choices. In most countries, doxycycline is recommended as the first-line antibiotic treatment for children, adults, and pregnant people. Previously, tetracycline antibiotics (including doxycycline) were not recommended for children due to concern for dental discoloration, or pregnant people due to concern for teratogenic effects. A recent systematic review among young children and pregnant people receiving doxycycline did not demonstrate a safety risk.

Multidrug-resistant isolates are emerging, particularly in South Asia, with resistance to quinolones, trimethoprim-sulfamethoxazole, and tetracycline. The strain from Hispaniola is also multidrug resistant; as of 2013, however, tested isolates were still sensitive to doxycycline and tetracycline. Macrolides, including erythromycin and azithromycin, are alternative agents for multidrug-resistant isolates. Zinc

supplementation reduces the severity and duration of cholera and other diarrheal diseases in children living in resource-limited areas.

PREVENTION:

- Food & Water (see Food & Water Precautions).
  - Travelers should follow safe food and water precautions and frequently wash hands.
  - Wash hands before preparing food and drinks. When soap and water are not available, travelers should use an alcohol-based hand sanitizer containing ≥60% alcohol, then wash hands with soap and water as soon as possible. Hand sanitizer is not as effective as handwashing for removing germs.
  - Travelers should carefully select their food: avoid consuming salads, uncooked vegetables, raw unpeeled fruits, and unpasteurized fruit juices.
  - Rinse produce with clean and safe water.
  - Travelers should not bring perishable food from high-risk areas back to their home country without refrigeration.
- Antibiotic chemoprophylaxis is not recommended.
- Vaccine
  - No country or territory requires vaccination against cholera as a condition for entry. CVD 103-HgR, a live, attenuated, single-dose oral cholera vaccine (Vaxchora, PaxVax), is licensed in the United States. The vaccine was previously marketed under the names Orochol and Mutacol in other countries.

IV. DISEASE SURVEILLANCE

A. Public Health Significance

Cholera is a disease of significant public health concern. It is highly contagious and a potentially fatal diarrheal disease that can spread rapidly in areas with poor sanitation and limited access to clean water causing severe dehydration and death within hours if left untreated. The case-fatality ratio for untreated cholera can reach >50%, but with adequate and timely rehydration, the case-fatality ratio is <1%.

In the last five decades, resistance profile of *V. cholerae* has changed. Multi-drug resistant *V. cholerae* belonging to serogroup O139 was first described in 1996. Studies have shown that most of the clinical isolates of *V. cholerae* are resistant to almost all routinely used antibiotics. The antimicrobial resistance encoding functions are also being identified as in self-transmissible plasmids.

B. Disease Surveillance Objectives

1. Detect cases and track infections of cholera in West Virginia.
2. Identify the food, patient, and other risk factors.

C. Surveillance Indicators

1. The proportion of cases with complete demographic, clinical, and laboratory information.
   - Count of cases reported
   - Types of laboratory tests performed
2. Proportion of cases with complete exposure information.
3. Proportion of cases with complete travel history.
4. Proportion of cases reported in a timely manner.

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