NON-CHOLERA VIBRIO INFECTIONS

I. DESCRIPTION AND EPIDEMIOLOGY

A. Overview

_Vibrio_ species are gram-negative bacteria that occur naturally in marine or brackish water environments. Infection with pathogenic _Vibrio_ spp. causes two distinct clinical syndromes: cholera and vibriosis. Cholera is caused only by toxigenic (i.e., toxin producing) _V. cholerae_ serogroup O1 or O139 and will be discussed separately in the Cholera chapter. This chapter focuses on vibriosis, which are infections caused by non-cholera _Vibrio_ spp.

Non-cholera _Vibrio_ spp. most frequently cause gastrointestinal illness, but may also cause infections ranging from wound infections to severe systemic disease. The most clinically relevant non-cholera _Vibrio_ species are _V. parahaemolyticus_ and _V. vulnificus_. However, illness has been associated with other organisms in the family Vibrionaceae, including _V. alginolyticus_, _V. cholerae_ non-O1 and non-O139, _V. fluvialis_, and _Grimontia hollisae_ (previously _V. hollisae_). _V. parahaemolyticus_ is the leading cause of seafood-associated gastroenteritis in the U.S. and is the most common non-cholera _Vibrio_ species to cause infection; however, _V. vulnificus_ causes the vast majority of non-cholera _Vibrio_ infection-related deaths.

B. Non-Cholera Vibriosis in California

Approximately 150 to 250 laboratory-confirmed cases of non-cholera vibriosis occur each year in California. Most cases are sporadic, though clusters associated with raw oyster consumption from certain harvest or growing areas have occurred.

C. Symptoms

The symptoms of infection depend on the species and route of infection (ingestion vs. direct contact). Infections caused by _V. parahaemolyticus_ most commonly present as gastroenteritis with watery diarrhea, abdominal cramps, nausea, vomiting, fever, and headache. Symptoms are generally self-limited, lasting 1 to 7 days. _V. parahaemolyticus_ can rarely cause a wound infection.

_V. vulnificus_ infections can range from mild to life-threatening. Primary septicemia occurs through ingestion of the organism and is fatal approximately 50% of the time. The clinical course of _V. vulnificus_ sepsis is frequently fulminant with rapid progression to death. Sepsis is often accompanied by distinctive bullous skin lesions filled with hemorrhagic fluid. _V. vulnificus_ can also cause a severe infection when open wounds are exposed to water where _V. vulnificus_ is present. These wound infections may be
complicated by necrotizing fasciitis or sepsis. Persons who are at high risk for severe \textit{V. vulnificus} disease and death are those with chronic liver disease, alcoholism, diabetes, hemochromatosis, or another immunocompromising condition.

\textit{V. alginolyticus} can cause either a wound or ear infection. \textit{V. cholerae} (non-toxigenic serogroups) can cause gastroenteritis or wound infections.

\section*{D. Transmission}

Transmission occurs most commonly through ingestion of undercooked or raw shellfish, particularly unprocessed raw oysters. Transmission may also occur through breaks in the skin when handling contaminated seafood or via wound exposure to contaminated seawater, such as swimming. Direct person-to-person transmission does not normally occur. Because \textit{Vibrio} spp. thrive in warm water temperatures, infections occur more often during the summer months.

\section*{E. Incubation Period}

The incubation period for \textit{V. parahaemolyticus} is usually 12 to 24 hours, but can range from 4 to 96 hours. For \textit{V. vulnificus}, the incubation period is usually 12 to 72 hours.

\section*{F. Clinical Management}

Clinical management decisions should be made by the patient’s primary care physician or infectious diseases specialist. High clinical suspicion and early initiation of treatment for invasive \textit{Vibrio} infections is important, because they may progress rapidly to death.

\section*{II. COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS (CSTE) SURVEILLANCE CASE DEFINITION}

\subsection*{A. Vibriosis (any species of the family \textit{Vibrionaceae}, other than toxigenic \textit{Vibrio cholerae} O1 or O139) (2017)}

Vibriosis has been a nationally notifiable condition since 2007. Please see the CSTE case definition (https://wwwn.cdc.gov/nndss/conditions/vibriosis/case-definition/2017/)

CSTE Position Statement
\texttt{16-ID-05}

\textbf{Clinical Criteria}
An infection of variable severity characterized by watery diarrhea, primary septicemia, or wound infection. Asymptomatic infections may occur, and the organism may cause extra-intestinal infection.
Laboratory Criteria for Diagnosis

**Confirmatory laboratory evidence:**
Isolation of a species of the family *Vibrionaceae* (other than toxigenic *Vibrio cholerae* O1 or O139, which are reportable as cholera) from a clinical specimen.

**Supportive laboratory evidence:**
Detection of a species of the family *Vibrionaceae* (other than toxigenic *Vibrio cholerae* O1 or O139, which are reportable as cholera) from a clinical specimen using a culture-independent diagnostic test (CIDT).

**Epidemiologic Linkage**
A clinically compatible case that is epidemiologically linked to a case that meets the supportive or confirmatory laboratory criteria for diagnosis.

**Criteria to Distinguish a New Case from an Existing Case**
- A case should not be counted as a new case if laboratory results were reported within 30 days of a previously reported infection in the same individual.
- When two or more different species of the family *Vibrionaceae* are identified in one or more specimens from the same individual, each should be reported as a separate case.

**Case Classification**

**Confirmed**
A case that meets the laboratory criteria for diagnosis. Note that species identification and, if applicable, serotype designation (i.e., *Vibrio cholerae* non-O1, non-O139 or *Grimontia hollisae*) should be reported.

**Probable**
A case that meets the supportive laboratory criteria for diagnosis, or a clinically compatible case that is epidemiologically linked to a case that meets the supportive or confirmatory laboratory criteria for diagnosis.

### III. CASE SURVEILLANCE, INVESTIGATION, AND REPORTING

**A. Purpose of Surveillance, Investigation, and Reporting**

- To understand the epidemiology of non-cholera vibriosis in California and to develop targeted interventions to decrease rates of illness
- To identify non-cholera *Vibrio* outbreaks, recognize food vehicles, and interrupt potential sources of ongoing transmission
- To detect new and emerging *Vibrio* species or serotypes, and monitor epidemiologic trends
- To educate people about how to reduce their risk of non-cholera *Vibrio* infection
B. Local Health Jurisdiction (LHJ) General Case Investigation Recommendations

- Begin investigation as soon as vibriosis is reported from a healthcare provider or clinical laboratory. These are reportable to public health within one working day of identification.

- Case-patients should be interviewed using the CDPH Cholera and Other Vibrio Illness Case Report Form (see below). Please obtain information about seafood eaten and water exposures in the 7 days prior to symptom onset. If seafood was consumed, obtain details on the date and location the seafood was purchased (such as a market or restaurant) and method of preparation. Of particular interest are shellfish exposures, especially raw oyster consumption. Effort should be made to determine the specific type of shellfish consumed, including variety (Pacific, Kumamoto, etc.).

- If seafood is suspected as the source of infection, local environmental health should investigate the source of the seafood and obtain available shellfish tags if oysters, clams, mussels, or scallops were consumed. Local environmental health should complete the Section 5 of the CDC COVIS form (see below) that documents the source of seafood that was ingested. Local environmental health should also notify the CDPH Food and Drug Branch seafood specialist.

- If the seafood exposure occurred in a California jurisdiction outside of the patient’s residence, the LHJ staff can directly notify the local California jurisdiction where the exposure occurred. If the seafood exposure occurred outside of California, please notify the Disease Investigations Section (DIS) at 510-620-3434 to coordinate the environmental health investigation.

- Determine if the patient is in a sensitive occupation and administer appropriate infection control recommendations.

- If the patient has a wound or ear infection due to a Vibrio species such as V. alginolyticus, it is not necessary to ask about a history of seafood ingestion, but be sure to inquire about water exposures, such as swimming.

- If the patient appears to be part of a point-source outbreak, follow your protocol for foodborne outbreak investigations. This should include notifying CDPH about the outbreak.

- If you require assistance with your investigation, call DIS at 510-620-3434.
C. LHJ Reporting

LHJ Reporting Overview

Non-cholera vibriosis became nationally notifiable in January 2007. Confirmed and probable vibriosis cases should be reported to CDPH. The CDPH Cholera and Other Vibrio Illness Case Report Form should be used to interview all patients, and is available in CalREDIE on the CDPH forms site (see below). This form collects data including demographic characteristics, signs and symptoms, medical history, treatment details, lab information, food and water exposures, and travel history. Of note, all *Vibrio* spp., including *cholerae* and non-*cholerae* species, are reported on the CDPH Cholera and Other Vibrio Illness Case Report form. However, cholera as a disease entity refers only to toxigenic *V. cholerae* serogroup O1 or O139. All other *V. cholerae* infections should be reported as a non-cholera vibriosis.

Please note that the CDC also has a reporting form called the Cholera and Other Vibrio Illness Surveillance Report Form (CDC COVIS, CDC OMB 0920-0728) that is divided into five separate sections. It is not necessary for the LHJ to complete the entire CDC COVIS form, as the CDPH Cholera and Other Vibrio Illness Case Report Form captures most of the pertinent data. We request that only Section 5 (the Seafood Investigation Section) of the CDC COVIS be completed and submitted. This Section 5 of the CDC COVIS form captures details regarding the source of seafood ingested during the incubation period that may be used for traceback purposes. Section 5 of the CDC COVIS should be completed for all vibriosis cases that ingested seafood during the 7 days before illness onset. This form is usually completed by local environmental health staff. Please note that Section 5 of the CDC COVIS is not in CalREDIE and must be completed as a hard copy and uploaded into the CalREDIE filing cabinet. Jurisdictions not participating in CalREDIE should send the hard copy case report form to CDPH (see Instructions for CalREDIE Non-participating jurisdictions below).

All non-cholera *Vibrio* reports are reviewed by the DIS *Vibrio* Subject Matter Expert (SME). *Vibrio* cases are not confirmed and closed by the state until reviewed by the SME. All confirmed and probable cases closed by the state SME are included in CDC’s year-end national case count.

Instructions for CalREDIE-participating jurisdictions (Non-Cholera *Vibrio* Infections):

- Enter the patient information into CalREDIE upon notification of the case by the clinical laboratory or healthcare provider. Select “Vibrio Infections (Non-Cholera)” as “Disease Being Reported”.

- In the Laboratory Information tab, please enter species information (*parahaemolyticus*, *vulnificus*, etc.), specimen type (stool, wound, etc.), and type of test (PCR, culture, etc.). If the isolate is *V. cholerae*, please indicate serotype (if known) and verify that it is not O1 or O139.
• Note: if toxigenic *V. cholerae* is confirmed or suspected, notify DIS immediately at (510) 620-3434. Please have the clinical laboratory forward the isolate or specimen to a public health laboratory for confirmation.

• If seafood exposure occurred, notify local environmental health to investigate and complete Section 5 of the CDC COVIS (https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/CDCOMB0920-0728.pdf). Scan the cover page and the completed Section 5 of the CDC COVIS (Seafood Investigation Section) and upload into the CalREDIE Electronic Filing Cabinet. Include copies of available shellfish tags, invoices, and/or labels.

• Note: Please document the status of environmental health investigations and shellfish tag collection in the Epidemiologic Info tab “Seafood Exposure/Environmental Health Investigation” section.

• Local Environmental Health investigators should also submit the completed Section 5 of the CDC COVIS and shellfish tags, invoices, and/or labels directly to the CDPH Food and Drug Branch Seafood Specialist by fax at (916) 636-6498 or email at SeafoodReporting@cdph.ca.gov.

• The CalREDIE report will NOT be reviewed by SME and “Closed by State” unless the process status is “Closed by LHD”, regardless of the resolution status. The “Closed by LHD” process status is the trigger for the SME to review the incident report.

Instructions for CalREDIE NON-participating jurisdictions:

• For jurisdictions currently not participating in CalREDIE, CMR and case report data must still be reported:

  • CMR (https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdp h110a.pdf)

  • Case Report Form (https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdp h8587.pdf)

• In the Laboratory Information Section, please enter species information (*parahaemolyticus*, *vulnificus*, etc.), specimen type (stool, wound, etc.), and type of test (PCR, culture, etc.). If the isolate is *V. cholerae*, please indicate serotype (if known) and verify that it is not toxigenic.

• Note: if toxigenic *V. cholerae* is confirmed or suspected, notify DIS immediately at (510) 620-3434. Please have the clinical laboratory forward the isolate or specimen to a public health laboratory for confirmation.

• If the case appears to be seafood-associated, please notify local environmental health to investigate and complete Section 5 of the CDC COVIS
Please also notify the Vibrio SME and CDPH Food and Drug Branch (FDB) Seafood Specialist by emailing the Vibriosis Preliminary Report Sheet. This alerts the FDB Seafood Specialist to follow up with the Local Environmental Health investigator and begin traceback to specific shellfish beds and growing regions. Early action ensures that potential regulatory action is not delayed. Please include the following information:

- First three letters of the patient’s last name
- Date of illness onset
- Type of seafood consumed/ date of consumption
- Location of purchase
- Name/ contact information of the LHJ environmental health specialist

- Once the case report form is completed, submit to the CDPH IDB Surveillance & Statistics Section by mail (address on form) through your communicable disease reporting staff. When Section 5 of the CDC COVIS has been completed by Environmental Health, submit the cover page, Section 5, and a duplicate copy of the corresponding case report form to CDPH IDB Surveillance and Statistics Section. Include available shellfish tags, invoices, and/or labels.

- Local Environmental Health investigators should also submit Section 5 of the CDC COVIS and shellfish tags, invoices, and/or labels directly to the CDPH FDB Seafood Specialist by fax at 916-636-6498 or email at SeafoodReporting@cdph.ca.gov.

Reporting Outbreaks and Clusters
Suspected outbreaks should be reported within 24 hours to CDPH.

- CalREDIE-participating jurisdictions: Create a new outbreak in CalREDIE. From the dropdown list for “Disease”, select the appropriate disease category such as “GI, Foodborne”, “GI, Waterborne”, “GI, Other/Unknown”, etc.

- Non-participating jurisdictions: For foodborne outbreaks, complete and submit the Foodborne Disease Outbreak Report form (CDPH 8567, [https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdph8567.pdf](https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdph8567.pdf)).

D. Laboratory Considerations/ Microbial Diseases Laboratory (MDL) and Food and Drug Laboratory (FDL) Resources

Laboratory Testing Overview

The diagnosis of vibriosis is typically made by the isolation of *Vibrio spp.* from stool, blood, or wound culture. However, a selective medium, usually thiosulfate-citrate-bile salts-sucrose (TCBS) must be used in order to isolate *Vibrio*. These tests are not done
routinely, and must be specifically ordered by the health care provider. Any suspected V. *cholerae* isolate should be forwarded to a public health laboratory for serogrouping and cholera toxin testing.

The use of culture-independent diagnostic tests (CIDTs) as stand-alone tests for the direct detection of *Vibrio* in stool is increasing. CIDTs include PCR-amplified, antigen-based and/or multi-analyte panel tests that are often ordered based on a clinical syndrome rather than a specific suspected pathogen. Specific performance characteristics such as sensitivity, specificity, and positive predictive value of these assays likely depend on the manufacturer and are currently unknown. It is therefore useful to collect information on the type(s) of testing performed for reported vibriosis cases. When a specimen is positive using a CIDT it is also helpful to collect information on all culture results for the specimen, even if those results are negative. Culture confirmation of CIDT positive specimens is ideal, although it might not be practical in all instances. Local public health agencies should make efforts to encourage reflexive culturing by clinical laboratories that adopt culture-independent methods.

As of January 2017, CSTE is defining *Vibrio* detected through CIDT as a probable case, which will be counted towards the year-end case count for vibriosis by CDC and by CDPH. CIDT-positive patients should be investigated by the local health jurisdiction as any other probable or confirmed vibriosis case.

**CDPH MDL Resources**

It is not required for clinical isolates of *Vibrio* spp. to be sent to MDL for confirmation. However, MDL has the capacity to identify *Vibrio* at the species level. MDL can also identify the serogroup of *V. cholerae* isolates and can test *V. cholerae* isolates for the presence of the cholera toxin gene.

- **Pulsed-field gel electrophoresis (PFGE):** PFGE is not routinely performed on *Vibrio* isolates, but may be requested in special circumstances, such as when illnesses appear to be related to a specific oyster bed or growing region.

- **Whole Genome Sequencing (WGS):** MDL will conduct WGS testing on selected *Vibrio* isolates submitted to MDL and upon request by local, state, and/or federal partners.

- **Shellfish Testing:** If shellfish are suspected to be the source of a cluster, shellfish testing is available. Contact DIS at 510-620-3434 and ask to speak with the *Vibrio* SME if interested in shellfish testing.
CDPH FDL Resources

FDL can test shellfish for *V. cholerae* and *V. parahaemolyticus* and can conduct PFGE and WGS testing on environmental isolates. Contact DIS at 510-620-3434 and ask to speak with the *Vibrio* SME if interested in shellfish testing.

IV. CASE MANAGEMENT AND PUBLIC HEALTH CONTROL MEASURES

A. Management of Cases

There are no specific codes guiding the management of patients with non-cholera vibriosis. The California Association of Communicable Diseases Controllers (CACDC) has proposed guidelines which are not bound by state statute (and therefore, is left to the discretion of the Health Officer).

- For a symptomatic case in a sensitive occupation or setting: Restrict/exclude until 48 hours after resolution of signs and symptoms. Clearance specimens not required.
- For an asymptomatic case or previously symptomatic but now recovered case: No restriction is needed.
- For a child 5 years and younger in a group setting who is symptomatic: Restrict/exclude until 48 hours after resolution of signs and symptoms. Clearance specimens not required.
- For a child 5 years and younger in a group setting who is NOT symptomatic or was previously symptomatic but now recovered: No restriction is necessary.

B. Management of Contacts

There are no specific codes guiding the management of contacts of non-cholera vibriosis. The CACDC has proposed guidelines which are not bound by state statute (and therefore, is left to the discretion of the Health Officer).

- For a symptomatic contact: Restrict/exclude until 48 hours after resolution of signs and symptoms.
- For an asymptomatic contact: No restriction is necessary.

C. Infection Control Measures

Cases must be educated regarding appropriate hand hygiene after using the toilet, changing diapers, and before preparing or eating food.

Hospitalized patients should be cared for using standard precautions. For patients who are diapered or incontinent, use contact precautions for the duration of the illness or to control institutional outbreaks.

D. Special Considerations
Most non-cholera vibriosis infections can be prevented by eating seafood that has been cooked thoroughly, particularly oysters. It is especially important for persons with conditions that predispose to invasive *Vibrio* infections that they avoid eating raw, unprocessed oysters.

For more information on safe seafood, see the FDA website (https://www.fda.gov/Food/FoodborneIllnessContaminants/BuyStoreServeSafeFood/default.htm)

To prevent wound infections, avoid exposing wounds to seawater, especially in summer months or along coastal regions in the southeastern U.S.

V. APPLICABLE STATE STATUTES

There are no applicable state statutes regulating the management of patients with vibriosis. However, in response to the risk of serious vibriosis associated with Gulf of Mexico oyster consumption, California adopted a regulation in 1991 to decrease these illnesses. Restaurants and other food establishments that sold or served raw Gulf Coast oysters were required to provide a written warning about the potential risk of consuming raw oysters. In 1997, this regulation was updated to require the written warning be provided both in English and in Spanish; as well as to require that these warnings were more prominently displayed.

Because serious illnesses continued, particularly due to *V. vulnificus*, an emergency regulation was enacted in 2003 to restrict the sale in California of raw oysters harvested from the Gulf of Mexico from April 1 through October 31 each year unless the oysters were treated with a scientifically validated process to reduce *V. vulnificus* to nondetectable levels.

The text of these regulations can be found here:


VI. ADDITIONAL RESOURCES

A. General Information/Patient Education

- CDPH Vibriosis (Non-Cholera) webpage (https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Vibriosis.aspx)
• CDC Vibrio webpage (https://www.cdc.gov/vibrio/index.html)

B. Shellfish Safety

• CDPH Food and Drug Branch Seafood and Shellfish Safety Program: Seafood processors are regulated by California statutes and federal regulations for Good Manufacturing Practices and Seafood Hazard Analysis Critical Control Point (HACCP). Shellfish dealers are also required to meet the requirements of the National Shellfish Sanitation Program. (https://www.cdphe.ca.gov/Programs/CEH/DFDCS/Pages/FDBPrograms/FoodSafetyProgram/SeafoodAndShellfishSafety.aspx)

• The FDA (https://www.fda.gov/food/guidanceregulation/federalstatefoodprograms/ucm2006754.htm)

• CDPH Environmental Management Branch, Marine Biotoxin Monitoring Program: The purpose of the preharvest shellfish activities is to establish sanitary requirements for shellfish growing waters and to regulate the commercial growing and harvesting of shellfish to assure that shellfish are safe for human consumption. (https://www.cdphe.ca.gov/Programs/CEH/DRSEM/Pages/EMB/Shellfish/Marine-Biotoxin-Monitoring-Program.aspx)

C. References


VII. UPDATES

• Original version finalized and completed on August 10, 2015.

• August 30, 2017: Updated to incorporate the 2017 CSTE case definition, change the FDB fax number for submitting COVIS section 5 forms, and update referenced web links.

• Updated version finalized and completed on August 30, 2017.

• June 19, 2018: Updated to change the FDB fax number and add email address.
## VIII. SUMMARY OF ACTION STEPS: NON-CHOLERA VIBRIO INFECTIONS

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<th>Action</th>
<th>Specific Steps</th>
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| ☐ Begin case investigation as soon as vibriosis is reported from a clinical laboratory or healthcare provider. | - Obtain and review clinical documentation, medical records, and lab reports as applicable.  
- Specify species and if isolate is *V. cholerae*, confirm that it is not O1 or O139.  
- Contact patient for interview. |
| ☐ Confirm case definition | - To count as a **confirmed** case of non-cholera vibriosis, only isolation of *Vibrio* spp. from a clinical specimen is necessary.  
- A **probable** case is a case with specimens that are CIDT positive for *Vibrio* without culture confirmation (i.e., culture negative or not done) OR a clinically compatible case that is epidemiologically linked to a confirmed or probable case. (Note: a negative culture result does not negate the CIDT result.) |
| ☐ Attempt to identify source of exposure | - Use the CDPH Cholera and Other *Vibrio* Illness case report form in CalREDIE or posted online to guide your interview.  
- Include as many details as possible that may trigger memory, including any receipts or records that may help identify location of seafood or water exposure.  
- If the patient appears to be part of a point-source outbreak, follow your protocol for foodborne outbreak investigations. This should include notifying CDPH about the outbreak. Suspected outbreaks should be reported within 24 hours to CDPH. |
| ☐ Submit Section 5 of CDC COVIS form (Seafood Investigation Section) | - If the case appears to be associated with seafood, work with your environmental health to complete Section 5 of CDC COVIS form.  
- CalREDIE jurisdictions: please complete Section 5 of CDC COVIS, scan, and upload into the Electronic Filing Cabinet for the corresponding CalREDIE Vibrio incident. Upload any available shellfish tags, invoices, and/or labels. |
- Non-CalREDIE jurisdictions: Once the case report form is completed, submit to the CDPH Surveillance and Statistics Section (SSS) through your communicable disease reporting staff. When Section 5 of CDC COVIS form is completed by Environmental Health, submit the cover page, the completed section, and a duplicate copy of the corresponding CDPH case report form, to the CDPH SSS. Include any available shellfish tags, invoices, and/or labels.

- Local environmental health investigators should send the completed Section 5 of CDC COVIS and shellfish tags, invoices, and/or labels to Food and Drug Branch Seafood Specialist via fax at 916-636-6498 or email at SeafoodReporting@cdph.ca.gov.

If you require assistance with your investigation, call IDB Disease Investigations Section at 510-620-3434.