16-ID-05

Committee: Infectious Disease

Title: Public Health Reporting and National Notification for Vibriosis

I. Statement of the Problem

Culture-independent diagnostic testing (CIDT), defined as the detection of antigen or nucleic acid sequences of the pathogen, is rapidly being adopted by clinical laboratories. For the family *Vibrionaceae*, these are generally PCR-based testing methods which do not require a stool culture and thus do not yield an isolate. While concerted efforts are being made to ensure reflexive culture is performed at the clinical laboratory or the state or local public health laboratory, CIDT positive reports are not always culture-confirmed.

The CSTE case definition for vibriosis was modified in 2011 to expand the case definition to include former *Vibrio* species that had been reassigned to new genera. Current case classification is dependent on isolation of a species from the family *Vibrionaceae.* Further modification of this case definition is needed to address the following two concerns:

1. There is no classification for CIDT-positive reports for *Vibrio* that are not culture-confirmed. These reports are not being systematically captured in state-based surveillance and are not being reported to national surveillance. The number of *Vibrio* positive CIDT reports is growing, leading to substantial under-ascertainment of laboratory-diagnosed cases.
2. Case definitions for bacterial enteric pathogens are not consistent. In the 2014 CSTE position statement for *Campylobacter*, a CIDT positive report that is not culture-confirmed is classified as a probable case and is reported to national surveillance.

To prevent an increase in underreporting of vibriosis cases and to make case definitions for enteric bacterial pathogens more consistent, this position statement proposes to add a case classification for a case with a *Vibrio* positive CIDT result as a 'probable' vibriosis case.

II. Background and Justification

Background:

Vibriosis is an under-recognized and under-reported cause of human illness. Vibriosis is caused by infection with pathogenic species of the family *Vibrionaceae* (species other than toxigenic *Vibrio cholerae* O1 and O139, which cause cholera). These pathogens typically cause gastrointestinal illness with watery diarrhea that can range in severity from mild to severe. They may also cause bacteremia, wound infections, or other extra-intestinal infections. The most common mode of transmission is consumption of raw or undercooked seafood; raw oysters are the most frequent source. Transmission can also occur through contact with water, especially seawater. Persons with liver diseases, cirrhosis, iron storage disorders, immune suppression, malignancies, and alcoholism are at particularly high risk of serious infection. Surveillance is needed to better define the burden of disease, identify and control outbreaks, as well as define and evaluate prevention strategies.

Taxonomic improvements have resulted in some *Vibrio* species being reassigned to new genera. For example, *Vibrio hollisae* was reclassified to the new genus *Grimontia* as *G. hollisae,* and *Vibrio damsela* was transferred to the genus *Photobacterium* as *Photobacterium damselae* subsp. *damselae*. Both *Grimontia* and *Photobacterium* are in the family *Vibrionaceae*. A 2011 position statement broadened the case definition of vibriosis to include these new genera.

Vibrio cases are thought to be substantially under-diagnosed, even when an ill person seeks health care. Surveys of clinical microbiology laboratories conducted in FoodNet sites and among Gulf Coast states have indicated that fewer than half of laboratories surveyed routinely cultured all stool specimens for the family *Vibrionaceae*. Even fewer used media specific for detection of the family *Vibrionaceae*. FoodNet

estimates of domestically-acquired foodborne illness used a multiplier of 142 to account for underdiagnosis of *Vibrio parahaemolyticus* infections.

Vibrio species are included in several of the commercially available multiplex PCR panels, so it is possible that more laboratories will routinely test for *Vibrio* in stool specimens and more laboratory-diagnosed cases will be reported to public health. The sensitivity and specificity of these new tests is not yet known, in large part because these infections are rare. Further, as with other enteric bacterial pathogens, reflexive culture of specimens with positive CIDT results is not always performed at the clinical laboratory or the state or local public health laboratory. This increase in testing provides public health with an opportunity to learn more about the epidemiology of this family of organisms, but only if CIDT-positive as well as culture-confirmed cases are reported to public health.

Justification:
Surveillance data are essential for monitoring trends and detecting outbreaks. Methods for surveillance must keep pace with changing laboratory diagnostic methods.

- Use of CIDT to detect *Vibrio* has increased rapidly at clinical laboratories following FDA approval of several multiplex nucleic acid tests in 2014. As of March 3, 2016 FoodNet data indicate 22/301 (7%) of laboratories in the FoodNet catchment area are using CIDT. FoodNet has detected a large increase in the number of positive *Vibrio* CIDT reports during 2015 (9) compared with 2012-2014 (mean 3 per year).
- CIDT positive reports are not always culture-confirmed, either because the culture is negative at the clinical or public health laboratory, or because culture was not attempted.
- In 2015, 9 cases of vibriosis positive (+) by CIDT and not culture-confirmed were reported to FoodNet. These cases represent 4% of all reported vibriosis cases in the FoodNet catchment area.
- During 2015, FoodNet received reports of 9 *Vibrio* CIDT-positive results for which culture was also performed. Of those, 2 (22%) were confirmed by culture. There are many possible explanations for these negative cultures including how the specimen was preserved/transported, whether optimal culture media was used, the temperature at which the specimen was stored, and the time between specimen collection and culture. These details are not known for the 9 culture results reported here, but could have a substantial impact on isolate recovery rates.
- Unlike for other enteric bacterial pathogens, there is no current case classification for a *Vibrio* report that is positive with a CIDT and is not culture-confirmed. These cases are not reported to CDC for use in national surveillance, and because there is no case classification for them, some states cannot collect routine surveillance information about them and/or they are not reportable.
- The current (2014) case definition for campylobacteriosis classifies a CIDT positive result without culture confirmation (PCR or antigen-based testing) as a probable case. These are transmitted to CDC for use in national surveillance.
- Some state health departments have barriers to investigating suspected cases. For example, some have rules that require local jurisdictions to investigate confirmed and select probable cases but not suspected cases. Increasing numbers of positive CIDT results that are non-culture confirmed could affect outbreak detection and result in missed opportunities to implement control measures at the local level.
- As the use of CIDT increases, counting only culture-confirmed cases will grossly undercount the total number of laboratory-diagnosed vibriosis cases. Public health case definitions must keep pace or surveillance will suffer. Although the sensitivity and specificity of the Vibrio CIDTs are not yet known, it is important to capture laboratory-diagnosed cases so that the full range of laboratory-diagnosed illnesses are captured in surveillance.

This position statement proposes that positive CIDT results for *Vibrio* that are not culture-confirmed be reported as probable cases. Illnesses among persons who are epidemiologically linked to a confirmed, or probable case with supportive laboratory evidence, will be classified as probable cases.

III. Statement of the desired action(s) to be taken

1. Utilize standard sources (e.g. reporting*) for case ascertainment for vibriosis. Surveillance for vibriosis should use the following recommended sources of data to the extent of coverage presented in Table III.

Table III. Recommended sources of data and extent of coverage for ascertainment of cases of vibriosis.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Extracts from electronic medical records	X	
Telephone survey		
School-based survey		
Other _____		
2016 Template		

2. Utilize standardized criteria for case identification and classification (Sections VI and VII) for vibriosis and add vibriosis to the *Nationally Notifiable Condition List.*

☐2a. Immediately notifiable, extremely urgent (within 4 hours)
☐2b. Immediately notifiable, urgent (within 24 hours)
☒2c. Routinely notifiable

CSTE recommends that all States and Territories enact laws (statue or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

3. CDC should publish data on vibriosis as appropriate in *MMWR* and other venues (see Section IX).

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outlined above.

Terminology:
* Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local or state public health.
**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

4. State health departments should create a variable to distinguish CIDT-diagnosed probable *Vibrio* cases from probable cases that are epidemiologically linked to a culture-confirmed or CIDT-diagnosed case. This differentiation of probable cases will facilitate assessment of the impact of CIDT on surveillance.

5. Likewise, CDC should include a variable to distinguish CIDT-diagnosed probable cases from probable cases that are epidemiologically linked in the disease-specific Message Mapping Guide (MMG), to assess the impact of CIDT on surveillance.

6. State health departments should attempt to capture the type(s) of *Vibrio* testing performed for reported vibriosis cases. This could include surveys of laboratory testing practices, capture of LOINC and SNOMED codes from electronic laboratory reporting, or other methods.

7. When available, species identification and, if applicable, serotype designation (i.e., *Vibrio cholerae* non-O1, non-O139 or *Grimontia hollisae*) should be reported.

IV. Goals of Surveillance
To provide information on the temporal, geographic, and demographic occurrence of vibriosis to facilitate its prevention and control.

V. Methods for Surveillance:
Surveillance for vibriosis should use the recommended sources of data and the extent of coverage listed in Table III.

VI. Criteria for case identification

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Report any illness to public health authorities that meets any of the following criteria:

1. Any person with a species of the family *Vibrionaceae* isolated from a clinical specimen (other than toxigenic *Vibrio cholerae* O1 and O139, which are reportable as cholera).
2. Any person with a species of the family *Vibrionaceae* detected in a clinical specimen using culture-independent diagnostic tests (CIDT).
3. Any person with clinically-compatible illness who is epidemiologically linked (i.e., shared a seafood meal) to a case of vibriosis or a member of a risk group defined by public health authorities during an outbreak investigation.
4. A person whose healthcare record contains a diagnosis of vibriosis.
5. A person whose death certificate lists vibriosis as a contributing or underlying cause of death.

Other recommended reporting procedures

- All cases of vibriosis should be reported according to state regulations.
- Reporting should be on-going and routine.
- Frequency of reporting should follow the state health department's routine schedule.

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	**Reporting**	
Clinical Evidence		
Clinically compatible illness		N
Healthcare record contains diagnosis of vibriosis	S	
Death certificate lists vibriosis as a cause of death or a significant condition contributing to death	S	
Laboratory Findings		

Isolation of a species of the family *Vibrionaceae* from a clinical specimen	S	
Detection of the family *Vibrionaceae* in a clinical specimen using a CIDT	S	
Epidemiological Risk Factors		
Epidemiologically linked (consumed same seafood as) to a case of vibriosis		O
Member of a risk group as defined by public health authorities during an outbreak investigation		O

Notes:
S = This criterion alone is Sufficient to report a case.
N = All "N" criteria in the same column are Necessary to report a case.
O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.
* A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria.

C. Disease-specific data elements

Clinical Information

- Liver Disease
- Cirrhosis
- Alcoholism
- Immune Deficiency or Immune Suppression
- Hematologic disease
- Chronic Renal Disease
- Malignancy
- Wound
- Diabetes
- Peptic ulcer
- Gastric surgery
- Heart disease
- Renal Disease
- Any of the following in previous 30 days:
    - Antibiotics
    - Chemotherapy
    - Radiotherapy
    - Systemic steroids
    - Immunosuppressants
    - Antacid therapy, especially H2 blockers or Proton Pump Inhibitors

Epidemiological Risk Factors

- History of consuming raw or under-cooked seafood, including type of seafood consumed and restaurant and seafood traceback information
- Contact with seawater or brackish water
- Occupation

Laboratory Information

- Method(s) of laboratory testing (e.g., culture or CIDT [FDA-approved or not FDA-approved PCR or antigen-based test])
- Name of test and manufacturer, as available

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

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

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.

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.

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

Case Classification

Confirmed: a case that meets the confirmed laboratory criteria for diagnosis.

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.

Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance:

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.

Comment:
The use of CIDTs as stand-alone tests for the direct detection of *Vibrio* in stool is increasing. 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. State and local public health agencies should make efforts to encourage reflexive culturing by clinical laboratories that adopt culture-independent methods, should facilitate submission of isolates/clinical material to state public health laboratories, and should be prepared to perform reflexive culture when not

performed at the clinical laboratory as isolates are currently necessary for serogrouping and cholera toxin testing as well as biotype and antimicrobial susceptibility testing.

CDC requests that *Vibrio* isolates be forwarded to the Enteric Diseases Laboratory Branch (EDLB) per the isolate submission memo and table found at http://www.cdc.gov/ncezid/dfwed/edlb/additional.html. EDLB (specifically the Epidemic Investigations Laboratory) requests that state public health labs immediately forward all suspect *V. cholerae* isolates.

Genera in the family *Vibrionaceae* (not all have been recognized to cause human illness) currently include:
Aliivibrio
Allomonas
Catenococcus
Enterovibrio
Grimontia
Listonella
Photobacterium
Salinivibrio
Vibrio

In addition to reporting through the National Notifiable Diseases Surveillance System (NNDSS), CDC requests that states collect and report the information for cases on the standard form for Cholera and Other *Vibrio* Illness Surveillance (COVIS), available at: http://www.cdc.gov/nationalsurveillance/cholera_vibrio_surveillance.html. CDC intends to integrate the COVIS form into the National Electronic Diseases Surveillance System (NEDSS) in the future. Reporting sites should use the COVIS reporting form until the integration is successfully implemented.

B. Classification Tables

Table VII-B. Criteria for defining a case of vibriosis.

Criterion	Probable		Confirmed
Clinical Evidence			
Clinically compatible illness	N		
Laboratory evidence			
Detection of the family *Vibrionaceae* in a clinical specimen using a CIDT		N	
Isolation of the family *Vibrionaceae* from a clinical specimen			N
Epidemiologic evidence			
Epidemiologically linked to a case of vibriosis with laboratory evidence	O		
Member of a risk group as defined by the public health authorities during an outbreak investigation	O		
Criteria to distinguish a new case:			
Not counted as a new case if occurred within 30 days of a previously reported infection in same individual.		N	N
Report infection with separate species of *Vibrionaceae* as distinct cases.	N		

2016 Template

Notes:
N = All “N” criteria in the same column are Necessary to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below). If the

absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the Absence of criterion as a Necessary component.
O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case. (These "O" criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an "O" indicates that this criterion is only required for a specific disease/condition subtype.

VIII. Period of Surveillance
Surveillance should be ongoing.

IX. Data sharing/release and print criteria

States and territories should notify CDC of confirmed and probable cases of vibriosis.

- Data will be used to determine the burden of illness due to infection with a species of the family *Vibrionaceae* (other than toxigenic *V. cholerae* O1 and O139, which are reportable as cholera), assess the effectiveness of national control programs, and assess progress toward national goals in vibriosis control. Data may be used to compare cases across jurisdictions.
- Data will be compared with information from other foodborne disease surveillance systems.
- Electronic reports of vibriosis cases in NNDSS are summarized weekly in the MMWR Tables. Annual case data on vibriosis is summarized in the yearly Summary of Notifiable Diseases. State-specific compiled data will continue to be published in the weekly and annual MMWR. All cases are verified with the states before publication.
- Annual COVIS reports will continue to be published.
- The frequency of reports/feedback to the states and territories will be dependent on the current epidemiologic situation in the country. Frequency of cases, epidemiologic distribution, importation status transmission risk, and other factors will influence communications.

X. Revision History

Position Statement ID	Section of Document	Revision Description
11-ID-12	Statement of the desired action(s) to be taken	ADDED recommendation that states and CDC add a variable to distinguish between probable cases with laboratory evidence and probable epi-linked cases.
11-ID-12	Section VII-A – Laboratory criteria	ADDED Detection of the family *Vibrionaceae* in a clinical specimen using a CIDT will meet criteria for supportive laboratory evidence.
11-ID-12	Table VII-B – Probable laboratory evidence	ADDED Detection of the family *Vibrionaceae* in a clinical specimen using a CIDT will meet criteria for a probable case.

XI. References

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