SHIGA TOXIN-PRODUCING ESCHERICHIA COLI (STEC) AND HEMOLYTIC UREMIC SYNDROME (HUS)

I. DESCRIPTION AND EPIDEMIOLOGY

A. Overview

Escherichia coli are gram-negative bacteria that are commonly found in animal and human intestinal flora. *E. coli* are categorized into serotypes by antigens in their cell wall (somatic O antigen) and in their flagella (H antigen). Most *E. coli* serotypes are not pathogenic to humans. Of the *E. coli* that cause disease, Shiga toxin-producing *E. coli* (STEC), also known as enterohemorrhagic *E. coli* (EHEC) or verotoxin-producing *E. coli* (VTEC), can cause especially severe illness. STEC produce Shiga toxin 1 and/or Shiga toxin 2, potent toxins responsible for many of the pathogenic effects of STEC infection. The most widely recognized serogroup among STEC is O157; however, numerous other STEC serogroups which are often grouped together as non-O157 may cause illness similar to O157. The six most common non-O157 serogroups in the U.S. are O26, O45, O103, O111, O145, and O121. STEC infections are associated with gastrointestinal disease characterized by abdominal cramps, diarrhea, and hemorrhagic colitis, and can be complicated by hemolytic uremic syndrome (HUS).

B. STEC and HUS in California

The California Department of Public Health (CDPH) Infectious Diseases Branch (IDB) monitors cases and epidemiologic trends of STEC infections and post-diarrheal HUS in California and assists in the investigation of outbreaks and clusters. Between 2011 and 2019, laboratory-confirmed cases of STEC infections reported annually in California ranged from 489 to 2680; the majority were sporadic infections rather than outbreak-related cases. The proportion of non-O157 STEC infections has steadily increased since non-O157 STEC reporting became mandatory in 2006, and now accounts for approximately 65% of all STEC infections reported in California. Fewer than 100 cases of HUS are reported per year in California; most are associated with STEC O157 infections. California STEC outbreaks in recent years have been associated with contaminated foods including undercooked ground beef, raw milk, pre-packaged salads, romaine lettuce, and other leafy greens, commercially packaged cookie dough, and Gouda cheese, and environmental exposures such as petting zoos and recreational water.

C. Symptoms

After ingestion, STEC colonize the intestine then release Shiga toxins which act locally or systemically to cause disease. Symptoms typically begin with abdominal cramps and non-bloody diarrhea, which frequently progress to bloody diarrhea. Nausea and vomiting may also be reported but fever is generally low-grade or absent. Infection may also be mild or asymptomatic. The duration of uncomplicated gastroenteritis due to STEC infection is generally 4 to 10 days.

The most severe clinical manifestation of STEC infection is HUS, defined as a combination of hemolytic anemia, renal failure, and often a low platelet count. HUS complicates 2-15% of STEC O157 infections; children under 5 years of age are at highest risk. Another post-diarrheal complication of STEC is thrombotic thrombocytopenic purpura (TTP) which has a similar clinical presentation as HUS but usually also includes fever and neurologic symptoms, such as altered mental status. HUS and TTP are more likely to be associated with STEC O157 than with STEC non-O157 infections.

D. Transmission

STEC is most often transmitted through the ingestion of undercooked food derived from infected animals or food contaminated by feces of an infected animal or person. Cattle may be asymptomatic but colonized with STEC and serve as the main reservoir for STEC. STEC has also been isolated from other animals, including deer, sheep, pigs, and goats. STEC has been documented to survive in the environment for months.

Raw and improperly cooked or handled foods of animal origin such as beef and dairy products are the most common sources of STEC infection, but transmission has also occurred through the consumption of contaminated produce and ready-to-eat foods such as pre-packaged lettuce and nuts. Other potential modes of transmission include waterborne transmission by ingesting contaminated water, for example through drinking untreated well water or by swimming in a lake or under-chlorinated pool; direct contact with farm animals such as in petting zoos or at fairs; and person-to-person fecal-oral transmission, especially when diarrhea is present and hands are not washed adequately.

The infectious dose of STEC O157 is low; less than 100 organisms can cause infection. The risk of transmission exists for the duration of fecal excretion of organisms. Duration of shedding for adults is typically one week but may be longer in children. Prolonged asymptomatic carriage is unusual.

E. Incubation Period

The incubation period is typically 3 to 4 days but ranges from 1 to 10 days.

F. Clinical Management

The patient's primary care physician or infectious disease specialist is responsible for clinical management decisions. Because some studies have found an association between the use of antimicrobials and the development of HUS, most experts, including the U.S. Centers for Disease Control and Prevention (CDC), do not recommend the routine use of antibiotics for treatment.

II. COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS (CSTE) SURVEILLANCE CASE DEFINITIONS

A. Shiga Toxin-Producing Escherichia coli 2018 Case Definition

The <u>2018 CSTE case definition for STEC</u> can be found on the <u>CDC Surveillance Case</u> <u>Definitions for Current and Historical Conditions website</u>.

(https://wwwn.cdc.gov/nndss/conditions/shiga-toxin-producing-escherichia-coli/case-definition/2018/)

CSTE STEC Position Statement

(https://c.ymcdn.com/sites/www.cste.org/resource/resmgr/2017PS/2017PSFinal/1 7-ID-10.pdf)

Clinical Criteria

An infection of variable severity characterized by diarrhea (often bloody) and/or abdominal cramps. Illness may be complicated by HUS (note that some clinicians still use the term TTP for adults with post-diarrheal HUS).

Laboratory Criteria for Diagnosis

Confirmatory laboratory evidence

- Isolation of *E. coli* O157:H7 from a clinical specimen **OR**
- Isolation of *E. coli* from a clinical specimen with detection of Shiga toxin or Shiga toxin genes.

Supportive laboratory evidence

- Isolation of *E. coli* O157 from a clinical specimen without confirmation of H antigen, detection of Shiga toxin, or detection of Shiga toxin genes, **OR**
- Identification of an elevated antibody titer against a known Shiga toxin-producing serogroup of *E. coli*, **OR**
- Detection of Shiga toxin or Shiga toxin genes in a clinical specimen using a culture-independent diagnostic test (CIDT) and no known isolation of *Shigella* from a clinical specimen, **OR**
- Detection of *E. coli* O157 or STEC/Enterohemorrhagic *E. coli* (EHEC) in a clinical specimen using a CIDT.

Epidemiologic Linkage

- A clinically compatible illness in a person that is epidemiologically linked to a confirmed or probable case with laboratory evidence, **OR**
- A clinically compatible illness in a person that is a member of a risk group as defined by public health authorities during an outbreak.

Criteria to Distinguish a New Case from an Existing Case

A new case should be created when a positive laboratory result is received more than 180 days after the most recent positive laboratory result associated with a previously reported case in the same individual. (See formula referenced in Appendix B of the 2017 CSTE Position Statement [17-ID-10] for details on time period calculation, hierarchy of dates and interpretation), **OR**

When two or more different serogroups/serotypes are identified in one or more specimens from the same individual, each serogroup/serotype should be reported as a separate case.

Case Classification

Suspected

- Identification of an elevated antibody titer against a known Shiga toxin-producing serogroup of *E. coli* in a person with no known clinical compatibility, **OR**
- Detection of Shiga toxin or Shiga toxin genes in a clinical specimen using a CIDT and no known isolation of Shigella from a clinical specimen in a person with no known clinical compatibility, **OR**
- Detection of *E. coli* O157 or STEC/EHEC in a clinical specimen using a CIDT in a person with no known clinical compatibility, **OR**
- A person with a diagnosis of post-diarrheal HUS/TTP (see HUS case definition).

Probable

- A person with isolation of *E. coli* O157 from a clinical specimen without confirmation of H antigen, detection of Shiga toxin or detection of Shiga toxin genes, **OR**
- A clinically compatible illness in a person with identification of an elevated antibody titer against a known Shiga toxin-producing serogroup of *E. coli*, **OR**
- A clinically compatible illness in a person with detection of Shiga toxin or Shiga toxin genes in a clinical specimen using a CIDT and no known isolation of *Shigella* from a clinical specimen, **OR**
- A clinically compatible illness in a person with detection of *E. coli* O157 or STEC/EHEC from a clinical specimen using a CIDT, **OR**
- A clinically compatible illness in a person that is epidemiologically linked to a confirmed or probable case with laboratory evidence, **OR**
- A clinically compatible illness in a person that is a member of a risk group as defined by public health authorities during an outbreak.

Confirmed

• A person that meets the confirmatory laboratory criteria for diagnosis.

Comments

Asymptomatic infections and infections at sites other than the gastrointestinal tract in people (1) meeting the confirmatory laboratory criteria for diagnosis or (2) with isolation of *E. coli* O157 from a clinical specimen without confirmation of H antigen, detection of Shiga toxin, or detection of Shiga toxin genes, are considered STEC cases and should be reported.

Although infections with Shiga toxin-producing organisms in the United States are primarily caused by STEC, in recent years an increasing number are due to infections by Shiga toxin-producing *Shigella*. Persons with (1) detection of Shiga toxin or Shiga toxin genes using a CIDT and (2) isolation of *Shigella* spp. from a clinical specimen should not be reported as an STEC case.

Due to the variable sensitivities and specificities of CIDT methods and the potential for degradation of Shiga toxin in a specimen during transit, discordant results may occur between clinical and public health laboratories. Persons with (1) detection of Shiga toxin or Shiga toxin genes using a CIDT and (2) the absence of isolation of *Shigella* from a clinical specimen, should be classified as a suspect or probable case, regardless of whether detection of Shiga toxin or Shiga toxin genes is confirmed by a public health laboratory.

B. Hemolytic Uremic Syndrome, Post-Diarrheal (HUS) 1996 Case Definition

The <u>1996 CSTE case definition for HUS, Post-Diarrheal</u> may be found on the <u>CDC</u> <u>Surveillance Case Definitions website</u>.

(https://wwwn.cdc.gov/nndss/conditions/hemolytic-uremic-syndrome-post-diarrheal/case-definition/1996/)

CSTE HUS Position Statement

(http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/09-ID- 37.pdf)

Clinical Description

HUS is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. TTP also is characterized by these features but can include central nervous system (CNS) involvement and fever and may have a more gradual onset. Most cases of HUS (but few cases of TTP) occur after an acute gastrointestinal illness (usually diarrheal).

Laboratory Criteria for Diagnosis

The following are both present at some time during the illness:

- Anemia (acute onset) with microangiopathic changes (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear, **AND**
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., greater than or equal to 1.0 mg/dL in a child aged less than 13 years or greater than or equal to 1.5 mg/dL in a person aged greater than or equal to 13 years, or greater than or equal to 50% increase over baseline)

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not less than 150,000/mm³, other diagnoses should be considered.

Case Classification

Probable

- An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding 3 weeks, **OR**
- An acute illness diagnosed as HUS or TTP that a) has onset within 3 weeks after onset of an acute or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed.

Confirmed

An acute illness diagnosed as HUS or TTP that both meets the laboratory criteria and began within 3 weeks after onset of an episode of acute or bloody diarrhea.

Comments

Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as post-diarrheal TTP also should meet the criteria for HUS. These cases are reported as post-diarrheal HUS. Most diarrheaassociated HUS is caused by STEC, most commonly *E. coli* O157. If a patient meets the case definition for both STEC and HUS, the case should be reported for each of the conditions.

III. CASE SURVEILLANCE, INVESTIGATION, AND REPORTING

A. Purpose of Surveillance, Investigation, and Reporting

- To identify STEC outbreaks, recognize food and non-food vehicles, and interrupt potential sources of ongoing transmission
- To detect new and emerging STEC serotypes and monitor epidemiologic trends
- To better understand the epidemiology of STEC infections and post-diarrheal HUS in California in order to develop targeted interventions to decrease rates of illness
- To educate people about how to reduce their risk of STEC infection

B. Local Health Department (LHD) General Case Investigation Recommendations

• Begin case investigation as soon as Shiga toxin-positive stool, STEC O157, STEC non-O157, or HUS is reported from a clinical laboratory or health care provider. Clinical laboratories and health care providers are required to report

STEC infections by electronic transmission (including FAX), telephone, or mail within one working day of identification. Culture confirmation is not necessary to initiate the investigation. Note that non-STEC *E. coli* that are part of many gastrointestinal CIDT panels are not reportable (IV. D. Special Considerations).

- The sooner a patient is interviewed, the better the recall of food and other exposures. While most STEC infections are sporadic, approximately 20 percent of cases in California that have undergone strain typing have been part of a recognized cluster. Most multi-jurisdictional clusters are identified through whole genome sequencing (WGS); pulsed-field gel electrophoresis (PFGE) was discontinued as of July 2019. Because of inherent delays in the current system, an isolate is often identified as part of a cluster several weeks after the presumed exposure has occurred. In order to improve the likelihood of determining the vehicle of an outbreak, it is helpful to try to get as much information as possible in the initial patient interview, and to document any activities which may help prompt recall later (such as a party or other significant event, or daily food diary in the week prior to illness onset).
- Interview patients using the appropriate CalREDIE forms or the CDPH Shiga Toxin-Producing Escherichia coli (STEC) and/or Hemolytic Uremic Syndrome (HUS) Case Report Form (CRF, CDPH 8555) (see III. C. LHD Reporting). Inform patient about the possibility of follow-up calls for additional information, especially if the patient is later identified to be part of a cluster or outbreak.
- 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 case or outbreak investigation, call the CDPH IDB Disease Investigations Section (DIS) at 510-620-3434.
- Ensure that the STEC isolate or Shiga toxin-positive specimen is saved and forwarded to the local public health laboratory (PHL) or to the CDPH Microbial Diseases Laboratory (MDL) for serogrouping and molecular subtyping (see III. D. MDL Resources). This includes Shiga toxin-positive broths if testing by the clinical or local PHL does not identify a pathogen, or if further testing was not performed.

C. LHD Reporting

LHD Reporting Overview

STEC O157 infections and post-diarrheal HUS have been reportable conditions in California since 1996. In 2006-7, infections due to STEC non-O157 and Shiga toxin-positive stool (without culture confirmation) were added to the Title 17 California list of reportable diseases, sections 2500 and 2505.

CDPH STEC and HUS reporting categories, which reflect the CSTE surveillance case classifications, include the following:

- Shiga toxin-producing *E. coli* (STEC) with HUS
- Shiga toxin-producing *E. coli* (STEC) without HUS
- Hemolytic uremic syndrome (HUS) without evidence of STEC

Both CDC's Annual Tables of Infectious Diseases and Conditions

(https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp) and California's final case count for the Yearly Summary Reports include only confirmed and probable cases of "Shiga toxin-producing *E. coli*" and "hemolytic uremic syndrome post-diarrheal". As the case classifications for these conditions are complex, it is important that the LHD investigator completes all of the fields needed to appropriately classify and close a case. These fields must be completed, whether entering the information into a CalREDIE record or a STEC Case Report Form (CDPH 8555).

Please refer to **Appendix 1**. STEC Diagram for CDPH Case Classification and Reporting.

Important Considerations:

- As of January 2020, the CDPH public-facing website has been updated to remove documents that are not compliant with the new requirements of Section 508 of the Rehabilitation Act of 1973. Therefore, some documents intended primarily for LHDs and not the general public, such as case report forms, have been moved to the CalREDIE *Document Repository* under the CDPH tab of the ribbon in the CalREDIE application. This includes a fillable PDF version of the STEC CRF (CDPH 8555).
- As long as there is clinically compatible illness, any person with a CIDT-positive only result (not culture-confirmed) should be reported as a **probable** STEC case. This is true regardless of the type of test (i.e., polymerase chain reaction [PCR] or enzyme immunoassay [EIA]) or performing laboratory (i.e., clinical laboratory or PHL). This is true even when PHL testing is negative if the clinical laboratory testing indicated a CIDT-positive result.
- As of January 1, 2014 (see Section V, Applicable State Statutes), California Code of Regulations (Title 17, section 2505[m]) added Shiga toxin-positive broths as well as STEC 0157 and non-0157 isolates to the list of specimens and isolates that must be saved and submitted by the clinical laboratory to a PHL.
- If the specimen was sent to MDL, the final test results are returned to the submitting laboratory, not necessarily the PHL of the patient's residence. Please follow up with the submitting laboratory to verify final results if not received. Please allow 4-6 weeks from the date of collection for MDL serogrouping results.
- If the clinical laboratory did not forward the specimen/isolate to a PHL or MDL, notify the clinical lab that they are required to forward CIDT-positive specimens or STEC isolates to a PHL per Title 17 state regulations.
- CDPH tracks and analyzes STEC O157 and STEC non-O157 separately. This is due to differences in demographics and possibly exposures among persons infected with STEC O157 compared with STEC non-O157. Therefore, it is

important to enter in the final serogroup identification.

• A person with both STEC infection and HUS is counted as two cases (i.e., a case of STEC and a case of HUS) for the purposes of case counting.

Fields Necessary to Correctly Classify an STEC Case:

The following fields are most important for case classification and should be filled out in the CaIREDIE STEC record or the CDPH STEC CRF:

Clinical Section

- Symptoms: Clinically compatible illness is defined as diarrhea, bloody diarrhea, and/or abdominal cramps, and is necessary when classifying a patient as a probable case when only CIDT results are available.
- The presence or absence of HUS (since the presence of HUS is counted separately). For patients with HUS, please answer each classification criteria (anemia, anemia with microangiopathic changes, and renal injury).

Laboratory Section

- Presence of Shiga toxin, or STEC, EHEC, or *E. coli* O157-positive on a CIDT panel
- For *E. coli* O157, the presence of Shiga toxin or H7 antigen is necessary to confirm as a case. This can usually be done at the clinical laboratory.
- For STEC non-O157, indicate the final serogroup identification. For most STEC non-O157, this identification is done at a local PHL or MDL. The six most common non-O157 serogroups are O26, O45, O103, O111, O145, and O121. If none of these serogroups were identified, the serogroup is considered to be "O-undetermined" or "O-UND".
- Note that if a laboratory reports "*E. coli* not O26, O103, O111, O145, O121 or O157", or "O-undetermined", this means that a STEC was isolated (i.e., is not a negative culture) but could not be identified by MDL or a PHL.
- If culture was negative, or not done, please indicate accordingly.

Please refer to **Appendix 2**. *Guide to Important CalREDIE Fields*, which highlights required fields necessary in order to classify a case.

Detailed Instructions for CalREDIE-participating Jurisdictions (see Appendix 1 and 2)

 Begin the case investigation and enter the patient information into CalREDIE upon notification of the case by a clinical laboratory or health care provider. All three STEC-related conditions are disease options in CalREDIE; please select the correct "Disease Being Reported". The body of the case report form (i.e., the Clinical, Laboratory, Epidemiologic, and Case Investigation tabs) is the same for all three conditions.

- <u>Clinical Info</u> tab: Complete the signs and symptoms fields, including HUS fields. For patients who were hospitalized, particularly for HUS, please upload the patient discharge summary into the electronic filing cabinet (EFC) if available.
- Laboratory Info tab:
 - Complete the following fields in "Section B: CDPH Microbial Diseases Laboratory (MDL) or Other Reference Public Health Laboratory (PHL) Results":
 - Was isolate or broth forwarded to a local public health lab?
 - Was isolate or broth forwarded to MDL?
 - Shiga toxin test result (indicate Shiga toxin type if known)
 - Culture result (Please do not leave this field blank!)
 - Indicate final culture result/serogroup confirmation: confirm with your PHL, reference PHL, or MDL for the results if necessary.
 - Specify serogroup if STEC is isolated; this includes **O157** and **non-O157**.
 - If you select non-O157, you will get a drop-down menu which will allow you to select one of the six most common non-O157 serogroups (O26, O45, O103, O111, O145, and O121.). If none of these serogroups were identified, the serogroup is considered to be "O-undetermined", or "O-UND". (See III.D. Laboratory Considerations/MDL Resources).
 - If the culture was negative, or not done, please indicate.
 - Uploading laboratory results to the electronic filing cabinet, especially PHL/MDL results, is encouraged.
 - Clearance specimen results do not need to be entered into CalREDIE; only the details of the first positive result and PHL/MDL confirmation need to be entered.
- <u>Case Investigation</u> tab:
 - Do not enter "Closed by LHD" in the process status until the final results from the PHL or MDL have been entered.
 - For "STEC with HUS" the resolution status on the Case Investigation tab should be based on the <u>STEC case definition</u> (not the HUS case definition).
 - For "Hemolytic uremic syndrome (HUS) without evidence of STEC" the resolution status on the Case Investigation tab should be based on the <u>HUS</u> case definition (since STEC was not detected).
- CalREDIE incidents of "Shiga toxin-producing E. coli (STEC) without HUS" no longer

require review and closure by an IDB STEC subject matter expert (SME); incidents with the LHD process status of "Closed by LHD" will be counted for national reporting based on the LHD resolution status.

• The STEC SMEs will continue to review and close CalREDIE incidents for "Shiga toxin-producing *E. coli* (STEC) **with** HUS" and "Hemolytic uremic syndrome (HUS) without evidence of STEC" after closure by LHDs; these incidents will continue to be counted for national reporting after the process status of "Closed by State". The STEC SME will set the HUS case resolution status for "STEC with HUS", as each record counts as two separate cases (a case of STEC and a case of HUS).

<u>Instructions for LHDs not participating in CalREDIE</u> (referred to as extended data exchange jurisdictions or EDEJs)

- For EDEJs, confidential morbidity report (CMR) and case report data must be provided to CDPH, including the information requested in the CDPH STEC CRF (CDPH 8555, revised 12/17). The use of the STEC CRF allows for the standardized collection of potential exposures for rapid comparison when clusters and outbreaks are identified.
- EDEJs may contact IDB for the STEC CRF (CDPH 8555) if needed.
- Fill out the STEC CRF as completely as possible, especially for the fields needed for proper case classification, as specified above under "Instructions for CalREDIE-participating Jurisdictions".
- EDEJs should continue to send all completed STEC and HUS case report forms to CDPH in order to maintain statewide surveillance.
- When submitting the STEC CRF to the state, including the final PHL or MDL laboratory report is highly encouraged, as this assists the STEC SME to properly categorize the Resolution Status. Clearance specimen results are not necessary.
- Please make an effort to transmit completed STEC CRFs to the CDPH IDB Surveillance and Statistics Section throughout the year as it allows the STEC SME to finalize records throughout the year instead of a large volume at the yearend closeout.

Reporting Outbreaks and Clusters

Report suspected STEC outbreaks, including point-source outbreaks and WGS clusters within your jurisdiction, immediately 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.
- *EDEJs*: For foodborne outbreaks, complete and submit the Foodborne Disease Outbreak Report form (CDPH 8567).

D. Laboratory Considerations/ MDL Resources

Laboratory Testing Overview

Most STEC O157 isolates can be identified accurately in the clinical laboratory because of their ability to grow in selective media. However, most clinical laboratories do not use selective media for the isolation of STEC non-O157; therefore, a PHL or MDL must perform the STEC non-O157 serogroup identification.

Clinical laboratories are increasingly adopting CIDT, which is the detection of antigen or nucleic acid sequences of the pathogen without culture isolation. Use of CIDT to detect Shiga toxin or Shiga toxin genes has increased rapidly at clinical laboratories following U.S. Food and Drug Administration (FDA) approval of several multiplex nucleic acid tests. These tests may indicate the presence of Shiga toxin or Shiga toxin genes, or the presence of STEC, EHEC, or *E. coli* O157. While CIDT allows for timely public health response, isolation of the pathogen is needed for serogrouping and molecular characterization, which are both essential for public health action.

Title 17, California Code of Regulations requires clinical laboratories to submit STEC isolates and Shiga toxin-positive specimens or enrichment broths to a PHL as soon as possible for confirmation, isolation, and additional characterization. The local PHL will do additional testing which includes Shiga toxin testing, identification of serogroup (STEC O157 and STEC non-O157), and strain typing, depending on capacity.

CDPH MDL Resources

- Shiga toxin-producing Escherichia coli (STEC) testing: MDL receives Shiga toxinpositive stools, enrichment broths, and STEC isolates. MDL will culture the stools and broths and screen isolates for the presence of Shiga toxin, including verifying the Shiga toxin type (1 or 2). Isolates confirmed as Shiga toxin positive will be serogrouped. If STEC is not isolated from stools or broths, it will be reported out as "No Shiga toxin-producing Escherichia coli isolated." Because of the advent of CIDT, MDL no longer performs Shiga toxin testing directly from clinical stool specimens.
- Serogrouping: If a STEC is identified, MDL will attempt to serogroup the O antigen. In the United States, six non-O157 serogroups (O26, O45, O103, O111, O121, and O145) account for the majority of reported non-O157 STEC infections. MDL has the capacity to test for the presence of five of these serogroups (O26, O103, O111, O121, and O145) as well as O157. Enteric identification of isolates that do not fall into these serogroups will be reported to the LHD as "Escherichia coli not O26, O103, O111, O121, O121, O145, O157". This designation is also referred to as STEC O-undetermined. MDL does not test STEC isolates for the flagellar H antigen.
- Whole Genome Sequencing (WGS): MDL will conduct WGS on all STEC O157 isolate submissions. WGS of STEC non-O157 isolates is done per request by local, state, and/or federal partners to aid in outbreak investigations. A growing number of local PHLs also have WGS capacity. The genetic sequences are

entered into a national surveillance database for foodborne pathogens, called PulseNet, and compared to other isolate sequences in the database using coregenome multilocus sequence typing (cgMLST). If a cluster of isolates with closely related sequences are detected, MDL will notify a DIS epidemiologist, and the DIS epidemiologist will notify the communicable disease control staff of the patient's jurisdiction of residence. Requests to MDL for WGS of STEC non-O157 and data analysis are evaluated on a case-by-case basis. PFGE was discontinued as of July 2019.

 MDL mails a final printed report with Shiga toxin and serogroup test results to the PHL that submitted the specimen, not necessarily the patient's jurisdiction of residence. It is the responsibility of the local PHL to notify the communicable disease control staff of the test results and ensure that the results are reported to the LHD of the patient's residence. Of note, at this time, certain clinical laboratories send specimens directly to MDL. MDL will provide results to the clinical laboratory and to the Health Officer of the county of the patient's residence. The clinical laboratories should also notify the LHD of the patient's residence about the test results. It is the responsibility of the LHD to follow up with the appropriate laboratory for the final serogroup result and enter this information into the CalREDIE report or CRF.

IV. CASE MANAGEMENT AND PUBLIC HEALTH CONTROL MEASURES

A. Management of Cases

All patients with STEC infection should be educated regarding disease transmission and appropriate infection control measures. In addition, patients should be instructed to monitor for signs and symptoms of HUS in the weeks following the onset of diarrhea.

Title 17 exclusion criteria for foodhandlers, childcare or eldercare workers, and health care workers do not apply specifically to STEC infections. However, there is language in the California Health and Safety Code Section 113949.1 which specifies particular actions for employees of food facilities with STEC infections. Details may be found in the Applicable State Statutes (Section V).

The California Association of Communicable Disease Controllers (CACDC) has proposed the following recommendations for the management of STEC patients, which are not bound by state regulations (and therefore left to the discretion of the Local Health Officer).

• For persons in sensitive occupations and for children 5 years and younger in a group setting (e.g., day care): Restrict/exclude until 2 consecutive stool specimens, taken at least 24 hours apart, and collected at least 48 hours after cessation of antibiotics, are negative.

For additional information, see the <u>Enteric Disease Matrix</u> (password protected). (https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/CACDC-

Enteric-Disease-Matrix-2016-2017.pdf)

Of note, STEC can be shed in stool for several weeks after the resolution of symptoms. In particular, young children shed for a greater duration although chronic carriage is unusual. Nonetheless, the infectious dose, especially for STEC O157, tends to be quite low, and therefore, asymptomatic shedders are capable of infecting others.

B. Management of Contacts

There are no specific applicable codes guiding the management of contacts. The CACDC has proposed the following recommendations for the management of symptomatic contacts to confirmed STEC case-patients. These recommendations are not bound by state statute and therefore left to the discretion of the Local Health Officer. See CACDC Enteric Disease Matrix for details. No restriction is recommended for asymptomatic contacts.

• For a person in a sensitive occupation or for a child 5 years and younger in a group setting who is a symptomatic contact to a confirmed or probable case: Restrict/exclude until 2 consecutive stool specimens, taken at least 24 hours apart, and at least 48 hours after cessation of antibiotics, are negative.

C. Infection Control Measures

Environmental inspection is indicated if a commercial food service facility, childcare center, or public drinking water supply is suspected as the source of infection.

Hospitalized patients should be cared for using standard precautions. Contact precautions should be used for diapered or incontinent persons for the duration of the illness to control institutional outbreaks.

The STEC patient should be educated regarding effective hand washing, particularly after using the toilet, changing diapers, and before preparing or eating food. The importance of proper hygiene must be stressed, as excretion of the organism may persist for several weeks.

D. Special Considerations

Available CIDT panels for gastrointestinal illness frequently detect more than one type of *E. coli*. Although several strains of *E. coli* are thought to cause human illness, most are not reportable to CDPH. At this time, only STEC is reportable; STEC is at times also identified as enterohemorrhagic *E. coli* (EHEC) or verotoxin-producing *E. coli* (VTEC). Other *E. coli* on the CIDT panel may include enterotoxigenic *E. coli* (ETEC), Enteropathogenic *E. coli* (EPEC) and Enteroaggregative *E. coli* (EAEC). These are <u>not</u> reportable to CDPH, except in the setting of an outbreak.

Shigella spp. is genetically similar to enteroinvasive *E. coli* (EIEC) and is sometimes identified on the CIDT panel as *Shigella*/EIEC. This should be reported as a case of shigellosis.

Shiga toxin-producing Shigella has been documented in California since 2014. Cases

reported to the LHD with positive results for both Shiga toxin and *Shigella* may be investigated as suspected cases of Shiga toxin-producing *Shigella*, though false-positive test results and coinfection with STEC and *Shigella* should also be considered. See the shigellosis chapter of <u>CDPH IDB Guidance for Managing Select Communicable</u> <u>Diseases</u> for additional details

(https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/IDBGuidanceforManagingSelect CommunicableDiseases.aspx).

I. APPLICABLE STATE STATUTES AND REGULATIONS

A. <u>California Code of Regulations, Title 17, Public Health, Sections 2500, 2502,</u> and 2505:

http://ccr.oal.ca.gov/linkedslice/default.asp?SP=CCR-1000&Action=Welcome

<u>2500 (h)(i)</u>: Health care providers are required to report Shiga toxin detected in feces, Hemolytic Uremic Syndrome, and Shiga toxin-producing *Escherichia coli* to the local health officer where the patient resides by electronic transmission, telephone, or mail within one working day of identification.

<u>2502</u>: The Local Health Officer is required to report Shiga toxin detected in feces, Hemolytic Uremic Syndrome, and Shiga toxin-producing *Escherichia coli* to the state Department of Public Health at least on a weekly basis.

<u>2505 (m)</u>: Laboratories must submit Shiga toxin-positive fecal broths and Shiga toxinproducing *Escherichia coli* (STEC) isolates, including O157 and non-O157 strains, as soon as possible to the local or state public health laboratory. Further, if there is a laboratory test result indicating infection with STEC, then the laboratory must attempt to obtain a bacterial culture isolate for submission to the public health laboratory. The laboratory shall take steps necessary to obtain an isolate, including requesting that additional specimens be collected and sending specimens to a laboratory able to carry out bacterial culture as soon as possible.

See also <u>Conditions for Which Clinical Laboratories Shall Submit an Isolate or a Specimen</u> to the Local Public Health Laboratory

(https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Conditionsf orWhichaClinicalLabShallSubmitaCulture.pdf)

B. California Health and Safety Code §113949.1:

http://leginfo.legislature.ca.gov/faces/codes_displaySection.xhtml

"It is the intent of the Legislature to reduce the likelihood of foodborne disease transmission by preventing any food employee who is suffering from symptoms associated with an acute gastrointestinal illness, or known to be infected with a communicable disease that is transmissible through food, from engaging in the handling of food until the food employee is determined to be free of that illness or disease, or incapable of transmitting the illness or disease through food as specified in this article." <u>Section 113949.1(a)</u> "When a local health officer is notified of an illness that can be transmitted by food in a food facility or by an employee of a food facility, the local health officer shall inform the local enforcement agency. The local health officer or the local enforcement agency, or both, shall notify the person in charge of the food facility and shall investigate conditions and may, after the investigation, take appropriate action, and for reasonable cause, require any or all of the following measures to be taken....."

<u>Section 113949.1(b)</u> "For purposes of this section, "illness" means a condition caused by any of the following infectious agents... Enterohemorrhagic or Shiga toxin producing *Escherichia coli.*"

<u>Section 113949.2</u>. "The owner who has a food safety certificate issued pursuant to Section 113947.1 or the food employee who has this food safety certificate shall instruct all food employees regarding the relationship between personal hygiene and food safety, including the association of hand contact, personal habits and behaviors, and food employee health to foodborne illness. The owner or food safety certified employee shall require food employees to report the following to the person in charge: (a) If a food employee is diagnosed with an illness due to one of the following... Enterohemorrhagic or Shiga toxin producing *Escherichia coli.*"

VI. ADDITIONAL RESOURCES

A. Food Safety

Detailed food handling recommendations and details about USDA product testing and other information may be found on the <u>USDA *E. coli* O157:H7 and Other STEC website</u>: (http://www.fsis.usda.gov/wps/portal/fsis/topics/food-safety-education/get-answers/food-safety-fact-sheets/foodborne-illness-and-disease/escherichia-coli- o157h7/ct_index)

B. General Information/ Patient Education

- <u>CDPH Shiga Toxin-Producing E. coli webpage</u>: https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Shiga-toxin-producing-Escherichia-coli.aspx
- <u>CDC E. coli webpage</u>: https://www.cdc.gov/ecoli/
- <u>CDC videos on food safety</u>: https://www.cdc.gov/ncezid/dfwed/medscape/foodsafety.html

C. References

- Heymann, DL Ed. *Control of Communicable Diseases Manual, 20th Edition.* Washington, DC, American Public Health Association, 2014
- <u>CIFOR (Council to Improve Foodborne Outbreak Response) Guidelines</u>: http://cifor.us/products/guidelines
- Pennington, H. *Escherichia coli* O157. *Lancet* 2010; 376:1428-1435

 Red Book Online. <u>Section 3: Summaries of Infectious Diseases; Escherichia coli</u> <u>Diarrhea</u>:

https://redbook.solutions.aap.org/chapter.aspx?sectionId=189640088&bookId=2205& resultClick=1

VII. UPDATES

- March 2021: Updated III. Case Surveillance, Investigation, and Reporting to reflect that STEC without HUS incidents no longer require review and closure by the IDB STEC SME.
- February 2020: Updated the laboratory section to reflect the exclusive use of WGS; corrected links; clarified steps necessary before LHD closure of a STEC incident; minor formatting and content updates. Updated V. Applicable State Statutes and Regulations to reflect 2500 (h), which changes reporting urgency to within one working day from immediate reporting.
- July 2018: Revised to reflect changes in CSTE case definition and CDPH reporting categories
- Original version finalized and completed on January 12, 2015.

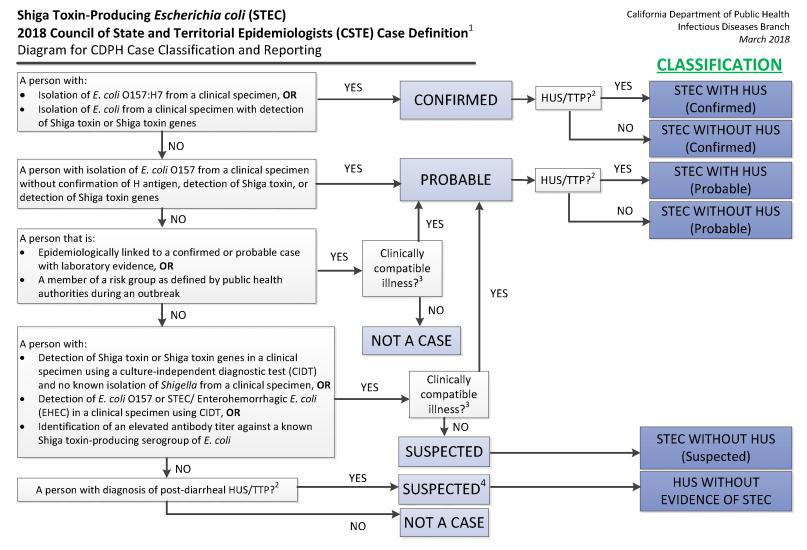
VIII. Summary of LHD Action Steps: STEC and HUS

Action Specific Store					
Action	Specific Steps				
Begin case investigation	 Review information in the <u>CDPH IDB Guidance and STEC</u> webpage as needed. 				
as soon as STEC or HUS is reported	Obtain and review clinical documentation, medical records, and lab reports as applicable.				
	Contact patient for interview.				
 Confirm case definition 	• See <u>2018 CSTE STEC case definition</u> and <u>1996 HUS case definition</u> for case classification guidelines.				
	 Refer to Appendix 1: STEC Diagram for CDPH Case Classification and Reporting for additional guidance. 				
Attempt to identify source	Use the STEC and/or HUS case report form in CalREDIE or the CDPH STEC CRF (CDPH 8555) to guide your interview.				
of exposure	 Include as many details that may later trigger memory, such as parties or special events, and inform patient that they may be contacted again. 				
	 If patient appears to be part of an outbreak, follow your protocol for foodborne outbreak investigations; this should include notifying CDPH about the outbreak. Report suspected STEC outbreaks within your jurisdiction to CDPH within 24 hours of identification. 				
 Implement control measures 	 Determine if the patient is in a sensitive occupation or situation (e.g., foodhandler, health care worker, day care attendee); administer appropriate infection control recommendations. 				
 Confirm status of STEC isolate 	 Shiga toxin-positive broths and STEC isolates must be saved and forwarded to a PHL for confirmation as per <u>Title 17, Section 2505</u> <u>regulations</u>. 				
or Stx + broth	 Ensure that the appropriate specimen has been sent to a local PHL or MDL for serogrouping and molecular subtyping. 				
□ Report to CDPH;	Confirm that the following information has been completed in the CaIREDIE incident or the STEC CRF:				
Confirmed and probable STEC cases	 Whether the patient had symptoms consistent with STEC infection (diarrhea, bloody diarrhea, and/or abdominal cramps) 				
must be	Whether or not the patient had HUS.				
reported	• Whether or not the isolate was forwarded to a PHL or to MDL.				
	• Refer to Appendix 2. Guide to Important CaIREDIE Fields				

Action	Specific Steps			
 Ensure proper documentation 	 Stx status (positive or negative), including Stx type (1 and/or 2), if available. 			
	 Culture results: Specify serogroup details (e.g., O157, O111, O26, or O undetermined). If culture was negative or not done, indicate accordingly. Do not leave this field blank! 			
	 Select the appropriate "Disease Being Reported" based on this information. 			
	 Complete above steps prior to closing the case by LHD or submitting to CDPH. 			

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

Appendix 1. STEC Diagram for CDPH Case Classification and Reporting



Note: Isolation or detection by any laboratory should be used for case classification, even when clinical and public health laboratory results are discordant

¹For STEC CSTE case definition, see https://wwwn.cdc.gov/nndss/conditions/shiga-toxin-producing-escherichia-coli/case-definition/2018/

²For CSTE case definition of post-diarrheal HUS, see https://wwwn.cdc.gov/nndss/conditions/hemolytic-uremic-syndrome-post-diarrheal/case-definition/1996/

³Clinically compatible illness includes one or more of the following: diarrhea (three or more loose stools within 24 hours), bloody diarrhea, abdominal cramps, hemolytic uremic syndrome (HUS)

⁴Case is considered Suspected STEC but should be reported to CDPH as "HUS without evidence of STEC"

Appendix 2. Guide to Important CalREDIE fields

Critical fields are circled.

PATIENT TAB

- 1) Please verify the disease being reported. There are three STEC associated fields:
 - Shiga toxin-producing E. coli (STEC) with HUS
 - Shiga toxin-producing E. coli (STEC) without HUS
 - Hemolytic uremic syndrome (HUS) without evidence of STEC

Patient	Clinical Info.	Laboratory Info.	Epidemiologic Info	PHEP Surveillance	Case Investigation
* Disease Being Rep	orted Shiga toxin-pro	ducing E. coli (STEC) w	ithout HUS		

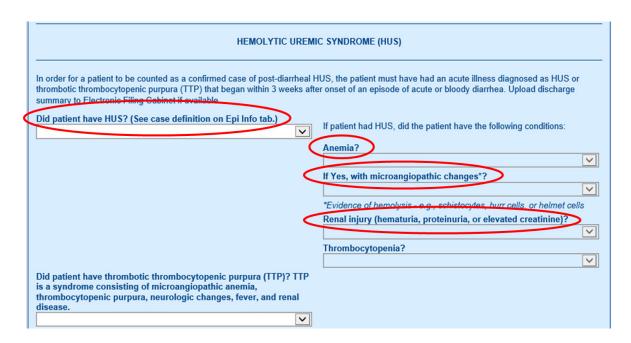
CLINICAL INFO TAB

 Clinically compatible symptoms (diarrhea, bloody diarrhea, and/or abdominal cramps) are necessary when classifying a probable case with CIDT positive results but not culture confirmed. Please check that onset date is before or on the date of diarrhea onset.

Symptomatic?		Duration of acute symptoms (days)
Onset date		Onset time (HH:MM AM/PM)
Diarrhea		
		If Yes, specify below: Max. number of stools in 24-hr period
		Onset date of diarrhea
Bloody diarrhea		
Fever	\checkmark	If Yes, highest temperature (specify F/C)
Vomiting		
Abdominal cramps		
Other		If Other, specify

 Indicate if the patient had HUS. HUS has a <u>defined case definition</u>, which includes anemia with microangiopathic changes (https://wwwn.cdc.gov/nndss/conditions/hemolytic-uremic-syndromepost-diarrheal/case-definition/1996/).

The HUS fields were updated in March 2021. Please indicate if the patient had anemia. If yes, then indicate if there were microangiopathic changes, which refers to the demonstration of destruction of red blood cells, and is characterized by evidence of hemolysis, which includes anemia and production of fragmented erythrocytes (schistocytes, burr cells, helmet cells) which is seen on the peripheral blood smear. The questions on anemia and renal injury confirm that the case definition has been met for a confirmed (if anemia with microangiopathic changes is present); or probable (if anemia is present, but unknown if with microangiopathic changes). Thrombocytopenia is a common finding, but not necessary to confirm a case. The diagnosis of HUS should also be included in the hospital discharge records. Please include any hospital records in the electronic filing cabinet (EFC).



4) Indicate if patient was hospitalized, especially for patients with HUS. Include the discharge diagnoses and upload the discharge summary into the EFC if available.

Did patient visit emergency room for illness?	•	Was patient hospitalized?
	~	
		If Yes, how many total hospital nights?
f there were any ER or hospital stays related to	this illness, specify details	below.
_		
HOSPITALIZATION – DETAILS		
D-001		
lospital name		Street address
City		State
City		State
		State Telephone
Žip code		Telephone
lip code		Telephone Discharge / transfer date
City Zip code Admit date Medical record number		Telephone

LABORATORY INFO TAB

5) SECTION A: Clinical Laboratory Results: If the clinical laboratory results were not submitted through electronic laboratory reporting (ELR), fill out the Clinical Laboratory results. The results in this Section A refers to <u>clinical</u> laboratory results, not PHL results.

Ċ	the bottom of the Epidemiologic Info tab. Note: Per Title 17, Shiga toxin positive brot (PHL) or CDPH Microbial Discusse Laborat	ths as well as STE	ication of case classification, please refer to the CASE DEFINITION section at <u>EC 0157 and non-0157 isolates must be forwarded to a public health laboratory</u> firmation. JLTS - Culture and Culture Independent Diagnostic Testing
	Specimen type Stool Other		If Other, specify
	Shiga toxin test result	Unknown	If Stx positive, specify type of toxin(s)
<	Type of Shiga toxin test Name of Shiga toxin assay (for CEIP use of Other CIDT identification for STEC? Yes No	Unknown	Some clinical labs identify the serogroup or organism (e.g., EC O157, EHEC, STEC) on their CIDT panel, if so, indicate result.
	If Yes, specify below: If CIDT postive, specify result(s) E. coli 0157 Enterohemorrhagie Other Unknown Type of other CIDT PCR Other	STEC	If Other, specify
	Name of other CIDT (for CEIP use only)		If Other, specify
	Clinical laboratory STEC culture complete?	Unknown	If culture completed, specify result(s) If Other, specify

6) SECTION B: CDPH MDL or other PHL Results: After filling out Section A, clinical laboratory information, scroll down to Section B (CDPH MDL or Other Reference PHL Results). The form will be returned to the LHD if this is left blank. This section refers to the public health laboratory, either at the local level or MDL, that made the final identification (i.e., Stx positive or negative, STEC 0157, STEC non-0157, culture negative)

HEALTH LABORATORY (PHL) RESULTS	SES LABORATORY (MDL) OR OTHER REFERENCE PUBLIC
Was isolate or broth forwarded to a local public health Yes No Unknown Was isolate or broth forwarded to MDL? With a few exceptions, serogroup confirmation for STEC non-O157 is done by MDL. Most isolates are therefore	laboratory. Please follow up with the clinical laboratory to determine if this was done. If specimen was not forwarded, the clinical lab is in violation of state regulations.
forwarded to MDL for serogrouping and strain typing.	
Shiga toxin test result Stipostive Stx negative Unkno If Stx positive, specify type of toxin(s) or toxin genes	
Type of Shiga toxin test	If Other, specify
Laboratory name MDL PHL Name of Shiga toxin assay (for CEIP use only)	If PHL, specify name If Other, specify

7) If Shiga toxin is negative, many PHLs will not forward the specimen to MDL. If that is the case, the Shiga toxin results, should be marked as negative, and culture result should be noted as "not done". If a culture was attempted by the PHL/MDL, and it was negative, indicate "negative" on the culture result. Please allow 4-6 weeks from collection date to final results. For specimens sent to MDL, the results will be sent to the health officer of the local public health laboratory that submitted the isolate/specimen. Do not close the record until Section B is completed.

Stool culture results from final PHL/MDL					
Culture result If E. coli 0157, specify flagellar (H) a					
If STEC non-O157, specify se If STEC non-O157 and H anti	drop- down menu. Upload the final PHL results into the				
Laboratory	Telephone number				

CASE INVESTIGATION TAB

8) For "STEC with HUS" the resolution status on the Case Investigation tab should be based on the STEC case definition (not the HUS case definition).

	Statuses		
	* Process Status		
	Closed by LHD	~	
	Set to the Next Status		
	Set to: Not a Case		
	Reported by:		
	Web Report		
	✓ Lab Report		
	Imported Status	-	without HUS" the resolution status on the Case In tab should be based on the <u>STEC case definition.</u>
<	Resolution Status Investigation (not the HU		with HUS" the resolution status on the Case n tab should be based on the <u>STEC case definition</u> S case definition).
	Not A Case	STEC" the i	resolution status on the Case Investigation tab should the <u>HUS case definition</u> (since STEC was not
		See Append	dix 1 for classification guidelines.