

Shiga-toxigenic *Escherichia coli* (including O157:H7) & HUS

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify outbreaks and potential sources or sites of ongoing transmission.
2. To assess the risk of the case transmitting infection to others, and to prevent such transmission.
3. To educate people about how to reduce their risk of infection.
4. To identify other cases.
5. To better characterize the epidemiology of this infection.

B. Laboratory And Physician Reporting Requirements

Laboratories and physicians are required to report within one working day of identification/diagnosis. Hemolytic uremic syndrome (HUS) is a clinical diagnosis; physicians must report cases regardless of identification of a specific etiologic agent.

C. Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but *not* suspect) cases to the OHD (see definitions below) as soon as possible, and no later than the end of the calendar week of initial physician/lab report. If your investigation is incomplete at the time of initial report, just fax in page 1 of the case investigation form with as much information as you have.
2. Begin follow-up investigation within one working day. Use the STEC/*Escherichia coli* O157 case investigation form, unless it is HUS without antecedent diarrhea (see box below). Send a copy of the completed form to the OHD as soon as possible, and no later than seven days after the initial report. Fax is better than mail.
3. Ensure that labs forward all patient isolates to the OSPHL for further characterization as required by law.

A Note about HUS Reporting

The requirement for HUS reporting is primarily a roundabout way of finding otherwise unreported STEC infections, and secondarily a way of learning about other potential causes of HUS. A case is defined as such by the attending physician—typically a nephrologist or gastroenterologist (see §2B). HUS reports can occur in one of three contexts.

1. Secondary to a confirmed O157 infection

Follow-up as for any other O157 case.

2. Secondary to a presumptive O157 infection (see definitions in §3B).

Consult immediately with Communicable Disease Section epidemiologists for current protocols in place to confirm an etiology for these cases; otherwise follow-up as for any other O157 case.

3. Not following any diarrheal illness and not epi-linked to any O157 cases.

Consult with Communicable Disease Section epidemiologists. Generally no specific follow-up is required for these cases by the LHD. Mark them “NOT O157-related.”

The following guidelines generally presume you are investigating STEC-related illness.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agents

Shiga-toxigenic *Escherichia coli*.

There are hundreds of different *E. coli* serotypes—which (collectively) are ubiquitous in the intestines of warm-blooded vertebrates. These Gram-negative bacteria are classified by their “O” (cell wall) and “H” (flagellar) antigens. [Note that it is a letter “oh”, not a zero.] Most *E. coli* serotypes are non-pathogenic. Those that cause human disease are sometimes grouped by pathogenic mechanisms: enterohemorrhagic, enteroinvasive, enteropathogenic, enterotoxigenic, and enteroadherent, although the terms can be misleading. Enterohemorrhagic *E. coli* (EHEC) are now more commonly referred to as Shiga-toxigenic *E. coli* (STEC) or sometimes Vero-toxigenic *E. coli* (VTEC). In Oregon and the rest of North America, but far the most common STEC is *E. coli* O157:H7. Less commonly, non-motile O157 organisms (O157:NM, aka O157:H-) or non-O157 STEC (e.g., O157:H16, O104:H21, O55) may cause similar illness.

The information in this chapter comes mostly from study of O157:H7 infections and outbreaks. It is possible that other STEC, which are rarely identified in the U.S., are somewhat or even quite different from O157. Note also that the epidemiology of the non-reportable, non-STEC organisms, (e.g., ETEC, EPEC) has nothing to do with O157 or other STEC. Forget about cows and bloody diarrhea in those contexts.

B. Description of Illness

Mild, non-bloody diarrheal illness and even asymptomatic infections are common, albeit rarely diagnosed outside outbreak settings. Most *diagnosed* cases report bloody stools, which typically begins 6-48 hours after the onset of non-bloody diarrhea. Diarrhea may be accompanied by abdominal cramps, often quite severe (and sometimes the chief complaint). Nausea and vomiting are also common. Fever is generally absent or low-grade, in contrast to, say, salmonellosis, shigellosis, or campylobacteriosis.

HUS. After 3-10 days, 5-15% of diagnosed patients may develop hemolytic uremic syndrome (HUS; a combination of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure). Early clinical signs of HUS may include decreased urine output, pallor, and lethargy. Patients with HUS have a variable degree of renal insufficiency that may necessitate dialysis (short- or long-term) or even transplant; there is a greatly increased risk of stroke and other complications. O157 infections are the principal cause of HUS in Oregon, particularly for children. Thrombotic thrombocytopenic purpura (TTP), another complication of O157 infection, is very similar to HUS, with prominent neurologic signs (seizures, confusion, etc.); TTP primarily affects adults. Although uncommon, O157-caused HUS or TTP can occur without antecedent diarrheal illness.

C. Reservoirs

Cattle are the best characterized reservoir species for O157. Some 50-80% of cattle herds—both beef and dairy—may be colonized, although on any given day very few animals may test positive. Within a herd, colonization of individual animals (and/or fecal shedding) is transient. Thus, negative results from herd screening are difficult to interpret. O157 does not cause any illness in bovines, and there is no way known to eradicate it from herds. Wild cervids (deer and elk) are another, and may also be long-term reservoir hosts. Sheep and goats are other potential sources of human infection. There have been a handful of isolations reported from other creatures, including dogs, horses, flies, and seagulls. Environmental reservoirs such as water troughs and cattle feed may be important in maintaining O157 in cattle herds.

The reservoirs for STEC other than O157 are not well characterized.

D. Sources and Routes of Transmission

Fecal-oral. Most human infections are probably foodborne. The infectious dose is very low—probably <100 organisms. O157 is excreted in the feces of colonized humans and other animals. Undercooked beef (especially hamburger), other foods cross-contaminated with same, and raw milk are among the most commonly identified sources of infection in common-source outbreaks, reflecting the fact that these foods are essentially always contaminated with cattle manure.

Venison is another potential source. Contaminated produce, including lettuce, alfalfa sprouts, and unpasteurized apple cider are other well-recognized sources. Person-to-person transmission is also common, either directly (especially in day care centers) or indirectly (as in contaminated drinking or recreational water). Infected food handlers are another possible source, although they are rarely identified. Airborne transmission (ingestion of dried manure?) was suggested to have contributed to the Lane County Fair outbreak in 2002.

E. Incubation Period

Variable; for O157 almost all within 1-10 days (most commonly 2-6 days).

F. Period of Communicability

The organism is shed in stool for at least the initial period of diarrhea, and variably thereafter. Children typically shed O157 for 2-4 weeks after onset—adults a bit less—but excretion for up to four months has been reported. Long-term carriage has been reported in cattle, but has not been documented in humans. Antibiotic treatment is not known to affect duration of excretion.

G. Treatment

No specific therapy for O157 has been identified that mitigates or shortens illness. Rehydration may be indicated when vomiting and/or diarrhea is severe. *In vitro* tests of antibiotic susceptibility do not correlate with *in vivo* efficacy, and at this time most experts recommend *no* antibiotic therapy. Although (unfortunately) commonly given, sulfa drugs (e.g. Septra® [TMP-SMZ]) are probably contraindicated; some early data suggested that they may *increase* the risk of developing HUS. Other studies suggest they are probably harmless, but none suggest that they do any good. Anti-motility drugs (e.g. Lomotil®) may also increase the risk of complications. At this writing we discourage antibiotics.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

O157 infections are probably about as common as shigellosis in Oregon, and may be the most common bacterial cause of bloody diarrhea. The diagnosis is often missed, however, in part because O157 is *not* detectable by routine stool culture; special media or antigen detection kits must be used.

Most labs culture stools and either use latex agglutination kits to identify the specific O157 antigens or at a minimum, use biochemical test results to identify sorbitol-“negative” (i.e., non-fermenting) colonies on special media (typically sorbitol-MacConkey agar, aka SMAC). Roughly half of the sporadic sorbitol-negative isolates sent to the OSPHL for confirmation turn out to be O157. At least one large lab (Quest) doesn’t culture these specimens at all; rather, they use a commercial kit to identify the presence of Shiga toxin. This is good because it is about the only way we would learn about non-O157 STEC, but bad because they don’t follow up their screening tests with culture for the positives, making it impossible to confirm and obviously giving us nothing to subtype. It is important to get specimens from these patients to the OSPHL for culture. Often there is leftover stool at the lab, but otherwise try to get a proper specimen from the patient. We send all non-O157 STEC to CDC for further identification (which may take several months).

Almost all patients with HUS develop antibodies to the O antigen of the bacteria. For culture-negative patients with HUS, arrange for a serum sample that can be tested for O157 antibodies at CDC. Two to six weeks after onset is the best time to draw.

A. Confirmed Case Definitions

For O157, *E. coli* O157 cultured from stool. For other STEC, positive toxin assay. For HUS, physician diagnosis with signs of thrombocytopenia, anemia, and renal failure.

B. Presumptive Case Definitions

- Compatible illness in someone epidemiologically linked to a confirmed case, *or*
- absent evidence of another cause, persons with HUS and antecedent diarrheal illness.

C. Suspect Case Definition (not reportable to OHD)

Bloody diarrhea with abdominal pain, fever absent or $<38\frac{1}{2}^{\circ}\text{C}$, and no other identifiable cause.

D. Public Health Laboratories Services

The OSPHL provides isolate confirmation as well as stool culturing for *E. coli* O157 (see their *Guide to Services*). A swab with stool on it, completely submerged in a Cary-Blair tube, is ideal. Recovery rates are higher if the Cary-Blair is cold at inoculation and is kept refrigerated or on ice until it reaches the lab, but ambient temperature handling is ok if refrigeration is not feasible. Culture for O157 must be *specifically* requested. For isolate identification, submit a pure isolate of the organism growing on an agar slant of some growth-supporting media (e.g., blood, nutrient agar). All specimens must be properly packaged in double containers with absorbent material around them. Use the Bacteriology/Parasitology form (#75).

Food samples can be tested for O157 if ok'ed by ACDP epidemiologists. Food samples should be refrigerated. O157 isolates are subtyped by micro-restriction fingerprinting or pulsed-field gel electrophoresis (PFGE) and other molecular techniques; matches (particularly by PFGE) are consistent with but do not prove a connection, whereas isolates that don't match (by any method) presumptively come from different sources. Serologic tests for antibody levels are available in special circumstances; consult with the Communicable Disease Section for more details.

4. ROUTINE CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent information. The case investigation form will help structure your interview(s). Make sure you are using a current form (from the OHD web site). If you suspect an outbreak, see §6.

A. Identify Source of Infection

Seek information about possible exposures 1–7 days before onset of symptoms. (Longer incubations are possible but not worth pursuing as a matter of routine).

1. Name, diagnosis, and phone number or address of any acquaintance or household member with a diarrheal illness. (Anyone meeting the presumptive case definition should be reported and investigated in the same manner as a confirmed case.)
2. Handling or eating ground beef. Ask about consumption of undercooked hamburger (pink or red), but because of the possibility of cross-contamination, any ground beef consumption is potentially suspect. Get details about *any* ground beef consumed (stores where purchased, dates of purchase, type of meat [e.g., lean or extra-lean hamburger], and how handled/cooked). Of course, any raw beef is potentially a source of kitchen contamination, but intact cuts of meat sold at retail are unlikely to cause multi-household outbreaks.
3. Consumption of unpasteurized milk. Identify the brands and/or sources, and find out when this milk consumption began. If a commercial raw milk source is named, notify the Communicable Disease Section immediately.
4. Name, date, and location of any restaurant meals.
5. Date, location, and sponsor of any public gathering where the case ate a meal.
6. Dried meats (particularly home prepared) are another possible source, as is anything related to deer or elk hunting (either consumption, slaughtering, or being around same).
7. Recreational water exposures: swimming, playing, or other exposure to lakes, streams, or pools where water may have been swallowed. Don't forget those little backyard wading pools—inflatable cesspools, really.
8. Contact with livestock, especially cattle.
9. Contact with diapered children with diarrhea, or children in day care.
10. Occupational exposures: evaluate the potential for exposure to human or animal excreta.
11. Travel outside the local area. If part of a group, find out who was in the group, the coordinator, etc.

B. Identify Potentially Exposed Persons

1. Contacts - Not important except for persons who have changed diapers of infected children.
2. Other ill persons - Household and other close contacts of confirmed or presumptive cases should be evaluated; symptomatic contacts should be cultured. Household members with more-or-less concurrent disease are presumptive cases, and should be reported as such on separate forms.

C. Environmental Evaluation

None, unless a commercial food service facility, day care center, or public water supply appears to be implicated as the source of infection. See §6.

5. CONTROLLING FURTHER SPREAD

A. Education

Advise individuals on measures to avoid further or future exposures.

1. Avoid eating raw or undercooked meat or poultry, especially hamburger. Hamburger should be cooked to an internal temperature of *at least* 70½C (160½F). While not foolproof, cooking until there is no red or pink remaining and meat juices no longer are red tinged is better than nothing; best is to use a thermometer.
2. Avoid cross-contamination with meat or other potentially contaminated foods.
3. Wash hands after caring for diapered children and after using the toilet;
4. Wash hands after handling pets, fowl, other animals, raw meat, and raw poultry, and always before food preparation.
5. Eschew unpasteurized milk and related dairy products. (For diehards, the Extension Service at Oregon State University publishes a bulletin on home pasteurization of small quantities of milk).
6. Avoid drinking or swallowing untreated surface water. Untreated water should be boiled or otherwise disinfected before consumption.

B. Isolation and Work or Day Care Restrictions

1. Hospitalized patients.

Standard precautions are adequate to protect employees and other patients.

2. Work Restrictions.

Persons should not work as food handlers, school or day care workers, or health care workers so long as they have diarrhea. In general, cases with Shiga-toxigenic *E. coli* (STEC) infection, including O157, require two negative approved fecal specimens collected at least 24 hours apart before returning to work. Restrictions can be waived or modified at the discretion of the local health department. Individuals may continue to be infectious for several weeks, however (see §5B3f), and should be cautioned accordingly.

3. Case is a Day-Care Worker or Attendee.
 - a. Interview the operator and inspect attendance records to identify other possible cases among staff or attendees in the past two weeks.
 - b. Review food handling and hand washing techniques with the operator and staff.
 - c. Collect stool specimens or rectal swabs from any other attendees or staff with a history of diarrheal illness within the past two weeks.
 - d. Cases (including those who are asymptomatic) should be excluded from day care facilities until they have two negative stool cultures collected at least 24 hours apart.
 - e. If more than one case or suspected case is identified among attendees or workers at a day care facility, a thorough inspection of the facility is indicated. Contact the Communicable Disease Section to discuss screening of asymptomatic children.
 - f. The facility operator should be instructed to call the LHD immediately if new cases of diarrhea occur. The day care center should be called or visited once each week for two weeks after onset of the last case to verify that surveillance and appropriate hygienic measures are being carried out.

C. Follow-up of Cases

Stool cultures to document that fecal shedding of the organism has stopped are not routinely indicated, except for the purpose of lifting work/school/DCC restrictions. The importance of proper hygiene must be stressed, however, as excretion of the organism may persist in many cases.

D. Protection of Contacts

The importance of good hand washing should be stressed. There are no formal restrictions or requirements for contacts of cases.

E. Environmental Measures

Advice on improving food handling or day care environments may be indicated.

6. INVESTIGATION OF POSSIBLE OUTBREAKS

Many outbreaks have been described since O157 was first identified as a pathogen in 1982, and they are sometimes quite serious. Media attention can become intense. At even a hint of a common-source outbreak, consult with the Communicable Disease Section immediately. Active case finding will be an important part of any investigation.

A. Outbreaks Linked to Restaurants or Public Gatherings

Likely sources include undercooked meat, cross-contaminated food, or possibly food contaminated by an infected food handler. Any investigation should focus on implicating specific food items and evaluating their method of preparation. Ask about recent illness among food handlers.

B. Cases linked to Raw Milk Consumption or a Public Water Supply

Environmental evaluation of the dairy or water supply will be a necessary part of any further investigation. Dairy investigations will be conducted in cooperation with the employees of the Food Safety Division, Oregon Department of Agriculture ➡