

# Hemolytic Uremic Syndrome (HUS) and Thrombotic Thrombocytopenic Purpura (TTP)

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## Responsibilities:

**Hospital:** Report by IDSS, facsimile, mail or phone,

**Lab:** Report by IDSS, facsimile, mail or phone, send isolate to SHL - (319) 335-4500

**Physician:** Report by facsimile, mail or phone

**Local Public Health Agency (LPHA):** Report by IDSS, facsimile, mail or phone.

**Follow-up required**

**Iowa Department of Public Health**

**Disease Reporting Hotline: (800) 362-2736**

**Secure Fax: (515) 281-5698**

## 1) THE DISEASE AND ITS EPIDEMIOLOGY

### A. Agent

Hemolytic uremic syndrome (HUS) is a syndrome of anemia, renal failure and low platelet count, for which there are several causes. Among children, the most common cause of HUS is infection with a Shiga toxin-producing organism, most commonly *Escherichia coli* O157:H7 or some other strain of enterohemorrhagic *E. coli* (EHEC). *Shigella dysenteriae* also produces Shiga toxin and HUS can also occur after infection with this organism.

Thrombotic thrombocytopenic purpura (TTP) is a disorder characterized by lesions in various organs that contain platelet clots, low platelet counts, and hemolytic anemia [due to breakdown of red blood cells (RBC)]. Tissue hypoxia resulting from these clots may cause organ damage, most frequently affecting the nervous system or kidney.

### B. Clinical Description

HUS is an acute illness involving the renal system and blood clotting mechanisms. For HUS caused by infection with a Shiga toxin-producing organism, the syndrome will usually manifest itself within weeks after the onset of a diarrheal illness, which often includes bloody diarrhea. Worldwide approximately 2–7% of cases of enterohemorrhagic *E. coli* (EHEC), such as *E. coli* O157:H7, develop HUS.

Thrombotic thrombocytopenic purpura (TTP) is another potential consequence of infection with a Shiga toxin-producing organism. TTP symptoms include hemolytic anemia and signs of intravascular hemolysis, low platelet count, diffuse and nonfocal neurologic findings, decreased renal function, and fever.

HUS is most commonly seen in children, whereas TTP is more commonly seen in adults.

Both syndromes can be fatal. Most cases of HUS, but few cases of TTP, follow an acute gastrointestinal illness (usually diarrhea). Only HUS or TTP that follows an acute diarrheal illness should be reported.

### C. Reservoirs

While cattle appear to be the most significant reservoir for *E. coli* O157:H7 and other EHEC strains, other animals, such as deer, are also known to carry these bacteria. In contrast, humans are the only known reservoir for *Shigella dysenteriae*.

#### **D. Modes of Transmission**

See the chapters on *E. coli* -pathogenic and *Shigella* for modes of transmission for each organism.

#### **E. Incubation Period**

Onset of HUS or TTP usually occurs within 3 weeks of the onset of diarrhea. Diarrhea may have resolved and the case may appear to be improving when the onset of HUS or TTP occurs. (For the incubation periods of the specific bacteria, refer to the chapters on *E. coli* -pathogenic and *Shigella*.)

#### **F. Period of Communicability or Infectious Period**

People with HUS or TTP rarely are infectious due to shedding *E. coli* or *Shigella* in their stool. (Refer to the chapters on each of these organisms for information on their infectious periods.) These illnesses usually do not appear until after the shedding period is over. Thus, at this time, stool specimens are negative.

#### **G. Epidemiology**

HUS is seen worldwide and may occur in 2% - 7% of *E. coli* EHEC infections of children under 10 years of age. A bacterial pathogen is often not laboratory confirmed in cases of HUS, and therefore, the proportion of cases of HUS due to specific bacterial infections is difficult to ascertain. Cases of HUS have been attributed to several non-O157:H7 *E. coli* serotypes (e.g., other EHEC strains). Treatment with TMP-SMX, fluoroquinolones and other antibiotics may increase the risk of HUS and other complications.

Post diarrheal TTP is seen less frequently than HUS.

#### **H. Bioterrorism Potential**

None.

## **2) DISEASE REPORTING AND CASE INVESTIGATION**

#### **A. Purpose of Surveillance and Reporting**

- HUS has been clearly demonstrated to be an important sequela of infection with *E. coli* EHEC strains. Because HUS cases generally come to medical attention, surveillance for HUS can serve as a marker for *E. coli* EHEC activity in the community and may lead to the identification of outbreaks at the state or local level. HUS is also an important event for assessing morbidity caused by *E. coli* EHEC strains.
- TTP may also occur after infection caused by *E. coli* EHEC, therefore risk factors for the disease must be assessed as in HUS.
- To identify whether the case may be a source of infection for other persons (e.g., a diapered child, child care attendee or food handler) and, if so, to prevent further transmission.
- To identify transmission sources of public health concern (e.g., a restaurant or a commercially contaminated food product) and to stop transmission from such sources.

#### **B. Laboratory and Healthcare Provider Reporting Requirements**

Iowa Administrative Code 641-1.3(139) stipulates that the laboratory and the healthcare provider report any case of HUS or TTP related to *E. coli* O157:H7 or enterohemorrhagic *E. coli* (non-O157). The reporting number for IDPH Center for Acute Disease Epidemiology (CADE) is (800) 362-2736. After completing the investigation and gathering the information to complete the investigation form, enter information into IDSS, or FAX the report form with supporting laboratory documentation to (515) 281-5698 or mail (in an envelope marked "Confidential") to the IDPH/CADE, mailing address:

IDPH, CADE  
Lucas State Office Building, 5<sup>th</sup> Floor  
321 E. 12<sup>th</sup> St.  
Des Moines, IA 50319-0075

### **Laboratory Testing Services Available**

After communicating with IDPH, contact the University of Iowa State Hygienic Laboratory (SHL) bacteriology for further instructions at (319) 335-4500.

## **C. Local Public Health Agency Reporting and Follow-Up Responsibilities**

### **1. Case Investigation**

- a. It is the LPHA responsibility to complete a *HUS Disease Case Investigation form* by interviewing the case and others who may be able to provide pertinent information. The Iowa Disease Surveillance System (IDSS) is the preferred method of recording case information.
- b. Use the following guidelines to assist you in completing the investigation:
  - 1) Accurately record the demographic information, date of symptom onset, symptoms, and medical information.
  - 2) When asking about exposure history (food, travel, activities, etc.), use the incubation period of 21 days.
  - 3) If possible, record any restaurants at which the case ate, including food item(s) and date consumed. If it is suspected that the case became infected through undercooked food, especially ground meats, refer to the Iowa Foodborne Illness Outbreak Investigation Manual.
  - 4) Ask questions about unpasteurized juices and the water supply.
  - 5) Ask what grocery stores they have bought food at.
  - 6) Household/close contact, pet or other animal contact, child care, and food handler questions are designed to examine the case's risk of having acquired the illness from, or potential for transmitting it to, these contacts. Determine whether the case attends or works at a child care facility or is a food handler.
  - 7) If several attempts have been made to obtain case information, but have been unsuccessful (*e.g.*, the case or healthcare provider does not return calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), complete the case report with as much information as possible. Note on the form the reason why it could not be filled out completely, or if using IDSS, select the appropriate reason under the Event tab in the Event Exception field.
- c. After completing the case investigation form, enter the data into IDSS, FAX or mail to CADE. Reports may be faxed to CADE's secured fax at 515 281-5698. The mailing address is:

Iowa Department of Public Health  
Center for Acute Disease and Epidemiology  
321 East 12<sup>th</sup> Street  
Des Moines, Iowa 50319

- d. Institution of disease control measures is an integral part of case investigation. It is the LPHA responsibility to understand, and, if necessary, institute the control guidelines listed below in Section 3), Controlling Further Spread.

## **3) CONTROLLING FURTHER SPREAD**

HUS and TTP are not spread person to person. If shigella or *E. coli* EHEC strains are determined to be the cause of the illness see chapters specifically dealing with those diseases.

*Note:* Because the onset of symptoms of HUS or TTP usually occur within 3 weeks after diarrheal illness, stool cultures taken at the time of HUS or TTP frequently fail to identify a causative agent.

## A. Isolation and Quarantine Requirements

Standard Precautions while hospitalized.

## B. Protection of Contacts of a Case

Persons caring for the case should practice good hygiene with attention to good handwashing practices.

## C. Managing Special Situations

See chapters on specific enteric disease.

### Reported Incidence Is Higher than Usual/Outbreak Suspected

If the number of reported cases in your city/town is higher than usual, or if an outbreak is suspected, an investigation is indicated and consideration should be given to early consultation with CADE. Investigate clustered cases in an area or institution to determine source of infection and mode of transmission. A common vehicle (such as water, food or association with a child care center) should be sought and applicable preventive or control measures should be instituted. Control of person-to-person transmission requires special emphasis on personal cleanliness and sanitary disposal of feces. Consult with the epidemiologist on-call at the CADE at (800) 362-2736. CADE can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several county lines and therefore be difficult to identify at a local level.

*Note:* Refer to the Iowa's *Foodborne Illness Outbreak Investigation Manual* for comprehensive information on investigating foodborne illness complaints and outbreak.

## 4) ADDITIONAL INFORMATION

The Council of State and Territorial Epidemiologists (CSTE) surveillance case definitions for HUS can be found at: [www.cdc.gov/osels/ph\\_surveillance/nndss/phs/infdis.htm#top](http://www.cdc.gov/osels/ph_surveillance/nndss/phs/infdis.htm#top)

CSTE case definitions should not affect the investigation or reporting of a case that fulfills the criteria in this chapter. (CSTE case definitions are used by the state health department and the CDC to maintain uniform standards for national reporting.)

## References

American Academy of Pediatrics. *2006 Red Book: Report of the Committee on Infectious Diseases, 27<sup>th</sup> Edition*. Illinois, American Academy of Pediatrics, 2006.

CDC Website. *Escherichia coli* O157:H7. [www.cdc.gov/ecoli/](http://www.cdc.gov/ecoli/)

Heymann, D.L., ed., *Control of Communicable Diseases Manual, 20<sup>th</sup> Edition*. Washington, DC, American Public Health Association, 2015.

## Additional Resources

Centers for Disease Control and Prevention: [www.cdc.gov/ecoli/general/index.html#what\\_shiga](http://www.cdc.gov/ecoli/general/index.html#what_shiga)

Iowa Division of Inspections and Appeals, Food Inspections:  
[www.state.ia.us/government/dia/index.html](http://www.state.ia.us/government/dia/index.html)