Hemolytic Uremic Syndrome (HUS)

REPORT IMMEDIATELY

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Hemolytic uremic syndrome (HUS) consists of anemia from red blood cell destruction and impaired renal function. 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 infection with this organism can be accompanied by HUS.

B. Clinical Description

HUS is an acute illness involving the kidney and blood clotting. For HUS caused by infection with a Shiga toxin-producing organism, the syndrome usually manifests itself during the two weeks following the onset of a diarrheal illness, often with bloody diarrhea. Approximately 2–7% of infections with EHEC, such as *E. coli* O157:H7, develop HUS. HUS includes microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Thrombotic thrombocytopenic purpura (TTP) is another potential consequence of infection with a Shiga toxin-producing organism. TTP is similar to HUS, but it has more prominent neurologic signs. HUS is most commonly seen in children, whereas TTP is more commonly seen in adults. HUS in children 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. Vectors and 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* type 1.

D. Modes of Transmission

See the chapters on *E. coli* O157:H7 and *Shigella* for modes of transmission for each organism.

E. Incubation Period

HUS usually occurs during the two weeks following the onset of diarrhea. In some cases, diarrhea may have resolved when HUS occurs. (For the incubation periods of the specific bacteria, refer to the chapters on *E. coli* O157:H7 and *Shigella.*)

F. Period of Communicability or Infectious Period

People with HUS may be infectious if still shedding *E. coli* O157:H7 or *Shigella* in their stool. (Refer to the chapters on each of these organisms for more information on infectious periods.)

G. Epidemiology

HUS is seen worldwide and may occur in 5–10% of *E. coli* O157:H7 infections of children under ten years of age. A bacterial pathogen is often not laboratory-confirmed in cases of HUS, and therefore, the proportions of cases of HUS due to specific bacterial infections are difficult to ascertain. Cases of HUS have been attributed to non-O157:H7 *E. coli* serotypes (i.e., other EHEC strains), but the importance of these other serotypes in the occurrence of HUS is not clear.

H. Bioterrorist Potential

E. coli O157:H7 and *Shigella* are listed by the Centers for Disease Control and Prevention (CDC) as Category B bioterrorist agents. For information on *E. coli* O157:H7 and *Shigella*, please refer to the chapters on these organisms.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report the onset of acute renal disease within three weeks of acute bloody or non-bloody diarrhea.

Note: See Section 3C for information on how to report a case.

B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) does not provide laboratory services for diagnosing acute renal disease. However, the SLI Enteric Laboratory will test stool specimens for the presence of *Shigella, E. coli* O157:H7, or other Shiga toxin-producing organisms.

For more information on testing, contact the SLI Enteric Laboratory at (617) 983-6609.

The SLI Food Microbiology Laboratory at (617) 983-6610 will test implicated food items from case clusters or outbreaks for *Shigella* and *E. coli* O157:H7. See Section 4D for more information.

Section 3:
REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify whether the case may be a source of infection for other persons (e.g., a diapered child, daycare 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 contaminated food source or product), and to stop transmission from such sources.

B. Laboratory and Health Care Provider Reporting Requirements

HUS is reportable to the local board of health (LBOH). Due to the potential severity of HUS, the MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of HUS, as defined by the reporting criteria in Section 2A. If this is not possible, call the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

HUS is an important sequela of infection with *E. coli* O157:H7. Because HUS cases generally come to medical attention, surveillance for HUS can serve as a marker for *E. coli* O157:H7 activity in the community and may lead to the identification of outbreaks at the state or local level. Surveillance of HUS is important for assessing morbidity caused by *E. coli* O157:H7.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations *(105 CMR 300.000)* stipulate that HUS is reportable to the LBOH and that each LBOH must report any case of HUS or suspect case of HUS, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using an official MDPH *Hemolytic Uremic Syndrome (HUS) Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Case Investigation

1. If a LBOH learns of a suspect or confirmed case of HUS, it should call the MDPH Division of Epidemiology and Immunization immediately, any time of the day or night, at (617) 983-6800 or (888) 658-2850.
2. Following notification of the MDPH, it is the responsibility of the LBOH to complete a MDPH *Hemolytic Uremic Syndrome (HUS) Case Report Form* (found at the end of this chapter). Much of the information required on the form can be obtained from the case's health care provider or from the medical record. You may ask the health care provider to complete the information on the case report form.
3. It is helpful to complete a *HUS Case Investigation Worksheet* (found at the end of this chapter). Information for this worksheet should be obtained from the case or from the case's parent/guardian if the case is a child. Be sure to obtain as much information as possible about foods eaten and activities engaged in during the week prior to the onset of the diarrheal illness (not HUS onset). (See also, the chapters on *E. coli* O157:H7 and *Shigella* for more information on case follow-up.)

   Note: The HUS Case Investigation Worksheet does not replace the MDPH Hemolytic Uremic Syndrome (HUS) Case Report Form.

4. Remember the following sections when completing the case report form:
   a. Accurately record the demographic/personal information.
   b. Complete the HUS case information, including sections on HUS diagnosis, symptoms, laboratory findings, other medical information, and outcome.

5. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the forms with as much information as you have gathered. Please note on the forms the reason(s) why they could not be filled out completely.
6. After completing the case report form, attach laboratory report(s) indicating the causative agent, if identified (e.g., *E. coli* O157:H7), and the *HUS Case Investigation Worksheet* and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

7. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4:
CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

Food handlers with HUS must be excluded from work; people diagnosed with HUS are usually too ill to be working. A case of HUS is defined by the reporting criteria in Section 2A of this chapter.

Minimum Period of Isolation of Patient

After diarrhea has resolved, food handlers may return to food handling duties only after producing two negative stool specimens, taken at least 48 hours apart. If a case was treated with an antimicrobial, the stool specimen shall not be collected until at least 48 hours after cessation of therapy.

Because the onset of HUS usually occurs about a week after diarrheal illness, stool cultures frequently fail to identify a causative agent.

Minimum Period of Quarantine of Contacts

Contacts with diarrhea who are food handling facility employees shall be considered the same as a case and shall be handled in the same fashion. In outbreak circumstances, asymptomatic contacts who are food handling facility employees shall be required to produce two negative stool specimens, collected 24 hours apart. No restrictions otherwise.

Note: A food handler is any person directly preparing or handling food. This can include a patient care or childcare provider. See Glossary (at the end of this manual) for a more complete definition.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Daycare

A case of HUS in a daycare setting may be a marker for additional *E. coli* O157:H7 or *Shigella* infections within the facility. Surveillance for gastrointestinal illness should be heightened, and children with gastrointestinal symptoms should be referred to their health care providers for appropriate testing. If the case has been diagnosed with *E. coli* O157:H7 or *Shigella*, please refer to the appropriate section of this manual for information on that disease. Contact the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 for assistance in managing follow-up of a case of HUS in a daycare setting.

School

A case of HUS in a school setting may be a marker for additional infections with *E. coli* O157:H7 or *Shigella* within the school, especially among classes with younger children. Surveillance for gastrointestinal illness should be heightened, and students with gastrointestinal symptoms should be referred to their health care providers for appropriate testing. If the case has been diagnosed with *E. coli* O157:H7 or *Shigella*, please refer to the appropriate section of this manual for information on that disease. The MDPH's *Comprehensive School Health Manual* also provides guidelines for managing a gastrointestinal illness outbreak in a school setting. Contact the MDPH Division of Epidemiology and Immunization for assistance in managing follow-up of a case of HUS in a school setting.

Reported Incidence Is Higher Than Usual/Outbreak Suspected

If the number of reported cases of HUS in your city/town is higher than usual or if you suspect an outbreak, investigate to determine the source of infection and the mode of transmission. A common vehicle (e.g., water, food, or association with a daycare 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 MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases across town lines, that would otherwise be difficult to identify at the local level.

Refer to the MDPH's *Foodborne Illness Investigation and Control Reference Manual* for comprehensive information on investigating foodborne illness complaints and outbreaks. Copies of this manual have been made available to LBOH. It can also be located on the MDPH website in PDF format at www.mass.gov/dph/fpp/refman.htm. For the most recent changes to the Massachusetts Food Code, contact the MDPH Center for Environmental Health, Food Protection Program (FPP) at (617) 983-6712 or through the MDPH website at www.mass.gov/dph/fpp.

D. Preventive Measures

Environmental Measures

Implicated food items must be removed from the environment. A decision about testing implicated food items can be made in consultation with the FPP or the MDPH Division of Epidemiology and Immunization. The FPP can help coordinate pickup and testing of food samples. If a commercial product is suspected, the FPP will coordinate follow-up with relevant outside agencies. The FPP can be contacted at (617) 983-6712.

Note: The role of the FPP is to establish policy and to provide technical assistance with the environmental investigation, such as interpreting the Massachusetts Food Code, conducting a Hazard Analysis Critical Control Point (HACCP) risk assessment, initiating enforcement actions, and collecting food samples.

The general policy of the SLI is to test only food samples implicated in suspected outbreaks, not single cases (except when botulism is suspected). The LBOH may suggest that the holders of food implicated in a single case locate a private laboratory that will test food or store the food in their freezer for a period of time, in case additional reports are received. However, in certain circumstances, a single, confirmed case with leftover food that had been consumed within the incubation period may be considered for testing.

Personal Preventive Measures/Education

To avoid future exposure, advise individuals to:

- Wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet, and after changing diapers.
- Wash their hands as well as the child's hands after changing a diaper.
- Scrub their hands thoroughly after assisting in caring for someone with diarrhea, after cleaning toilets, and after changing soiled diapers, clothing, or bed linens.
- Dispose of feces in a sanitary manner, especially in daycare centers or other institutional settings.
- Keep food that will be eaten raw, such as vegetables, from becoming contaminated by animal-derived food products.
- Send back all undercooked hamburgers for further cooking.
- Cook all ground beef and hamburgers thoroughly.
- Drink only pasteurized milk, juice, or cider.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.

An *E. coli* 0157:H7 Public Health Fact Sheet and a *Shigella* Public Health Fact Sheet are available from the MDPH Division of Epidemiology and Immunization or on the MDPH website at www.mass.gov/dph. Click on the "Publications and Statistics" link, and select the "Public Health Fact Sheets" section under "Communicable Disease Control."

ADDITIONAL INFORMATION

The following is the CDC surveillance case definition for HUS. It is provided for your information only, and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting and may be used to uniformly define an outbreak of HUS.) For reporting to the MDPH, always use the criteria outlined in Section 2A of this chapter.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Laboratory Criteria for Diagnosis

The following are 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.
- Renal injury (acute onset), evidenced by hematuria, proteinuria, or elevated creatinine level (i.e., $\geq$1.0 mg/dL in a child aged <13 years, or $\geq$1.5 mg/dL in a person aged $\geq$13 years, or $\geq$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 seven days after onset of the acute gastrointestinal illness is not <150,000/mm^3, other diagnoses should be considered.

Clinical Description

Probable	◆ An acute illness diagnosed as HUS or TTP which meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding three weeks; or ◆ An acute illness diagnosed as HUS or TTP which: a) has onset within three weeks after onset of acute diarrhea 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 three weeks after onset of an episode of acute or bloody diarrhea.

Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of central nervous system (CNS) involvement and fever are not provided because cases diagnosed clinically as post-diarrheal TTP should also meet the criteria for HUS. These cases are simply reported as post-diarrheal HUS.

REFERENCES

American Academy of Pediatrics. [*Escherichia coli* Diarrhea Including Hemolytic-Uremic Syndrome.] In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Diseases, 26th Edition.* Elk Grove Village, IL, American Academy of Pediatrics; 2003: 275–279.

Centers for Disease Control and Prevention (CDC). Case Definitions for Infectious Conditions Under Public Health Surveillance. *MMWR*. 1997; 46(RR-10).

Heymann, D., ed. *Control of Communicable Diseases Manual, 18th Edition*. Washington, DC, American Public Health Association, 2004.

MDPH. *The Comprehensive School Health Manual*. MDPH, 1995.

MDPH. *Control Guidelines for Long-Term Care Facilities.* Massachusetts Department of Public Health. 2002. <www.mass.gov/dph/cdc/epii/ltcf/ltcf.htm>.

MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements.* MDPH, Promulgated November 4, 2005.

FORMS & WORKSHEETS

Hemolytic Uremic Syndrome (HUS)

Hemolytic Uremic Syndrome (HUS)

REPORT IMMEDIATELY

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to Hemolytic Uremic Syndrome (HUS) case investigation activities.

LBOH staff should follow these steps when HUS is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

- ❑ Immediately notify the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 to report a suspect or confirmed case(s) of HUS.
- ❑ Obtain laboratory confirmation.
- ❑ Complete a *HUS Case Investigation Worksheet.*
- ❑ Identify potential exposure sources, such as food or water.
- ❑ For HUS suspected to be the result of an *E. coli* O157:H7 infection related to food consumption, complete a MDPH *Foodborne Illness Complaint Worksheet* and forward to the MDPH Center for Environmental Health, Food Protection Program (FPP).
- ❑ Determine whether the case attends or works at a daycare facility and/or is a food handler.
- ❑ Identify other potentially exposed persons.
- ❑ Fill out the case report form (attach laboratory results).
- ❑ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).