Hemolytic Uremic Syndrome (HUS)

(Postdiarrheal)

DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS

Per N.J.A.C. 8:57, healthcare providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of Hemolytic Uremic Syndrome to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.

CDS Communicable Disease Service

NEW JERSEY DEPARTMENT of HEALTH and SENIOR SERVICES

June 2008

Hemolytic Uremic Syndrome (HUS)

1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Hemolytic uremic syndrome (HUS) is a syndrome characterized by anemia, renal injury, and low platelet count. 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 Shiga toxin–producing *E. coli* (STEC). *Shigella dysenteriae* also produces Shiga toxin, and infection with this organism can also cause HUS.

B. Clinical Description

HUS is an acute illness characterized by the sudden onset of thrombocytopenia and hemolysis with fragmented red blood cells, and acute anuric renal failure. For HUS caused by infection with a Shiga toxin–producing organism, the syndrome will usually manifest itself three to 10 days after the onset of a diarrheal illness, often including bloody diarrhea. Approximately 2% to 7% of *E. coli* O157:H7 cases develop HUS. Thrombotic thrombocytopenic purpura (TTP) is another potential consequence of infection with a Shiga toxin–producing organism. TTP is similar to HUS but with 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 (GI) illness (usually diarrhea).

Because HUS and TTP have multiple causes, 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 STEC strains, other animals, such as deer, are also known to carry these bacteria. In contrast, humans are the only known reservoir for *S. dysenteriae* type 1.

D. Modes of Transmission

See the chapters on STEC and Shigellosis for modes of transmission for each organism.

E. Incubation Period

Onset of HUS usually occurs three to ten days after the onset of diarrhea. Diarrhea may have resolved and the patient may appear to be improving when the onset of HUS occurs. For the incubation periods of the specific bacteria, refer to the chapters on STEC and Shigellosis.

F. Period of Communicability or Infectious Period

People with HUS may be infectious if still shedding STEC or *Shigella* in their stool. Refer to the chapters on each of these organisms for information on their infectious periods.

G. Epidemiology

HUS is seen worldwide and may occur in 5% to 10% of *E. coli* O157:H7 infections of children under ten years of age. A bacterial pathogen is often not confirmed by a laboratory in cases of HUS and, therefore, the proportion of cases of HUS attributable to specific bacterial infections is difficult to ascertain. Cases of HUS have been attributed to non–O157:H7 *E. coli* serotypes (i.e., other STEC strains), but the importance of these other serotypes in the occurrence of HUS is not known at this time. Annually, the New Jersey Department of Health and Senior Services (NJDHSS) reports an average of three cases of HUS.

2 CASE DEFINITION

A. New Jersey Department of Health and Senior Services (NJDHSS) Case Definition

CONFIRMED
A clinically compatible case and laboratory evidence of

Anemia (acute onset) with microangiopathic changes (schistocytes, burr cells, or helmet cells) on peripheral blood smear, AND

Renal injury (acute onset) evidenced by either hematuria, proteinuria, and/or elevated creatinine level (i.e., > 1.0 mg/dL in a child younger than 13 years, or > 1.5 mg/dL in a person older than 13 years, or > 50% increase over baseline).

NOTE: A low platelet count can usually be detected early in the illness, but it may then become normal or even high.

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 bloody diarrhea in the preceding three weeks, OR

An acute illness diagnosed as HUS or TTP that began within three weeks of acute diarrhea AND meets the laboratory criteria except that microangiopathic changes are not confirmed.

POSSIBLE
Initially reported on the basis of clinical diagnosis, until laboratory confirmation is obtained; no "possible" case classifications are retained.

NOTE: 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 involvement and fever are not provided because patients diagnosed clinically as postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as postdiarrheal HUS.

B. Differences from CDC Case Definition

The Centers for Disease Control and Prevention (CDC) surveillance case definition for hemolytic uremic syndrome is the same as the criteria outlined in section 2A above. CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting. For reporting to NJDHSS, always refer to the criteria in section 2A.

3 LABORATORY TESTING AVAILABLE

Laboratory confirmation is based on identifying evidence of anemia with microangiopathic changes: presence of fragmented red blood cells (schistocytes, burr or helmet cells) on peripheral blood smear, and acute renal failure: hematuria, proteinuria, and/or elevated creatinine level. NJDHSS and Public Health and Environmental Laboratories (PHEL) will test stool specimens and culture isolates for the presence of Shiga toxin.

Specimens testing positive for this toxin will be tested for the presence of *E. coli* O157:H7 and other *E. coli* strains that produce this toxin. If toxin-producing organisms are isolated, they will be referred to CDC for further studies. For further information, contact the laboratory at 609.292.7368.

NOTE: PHEL requests that all laboratories submit within three days ALL isolates of STEC and *Shigella* spp cultured for typing to aid in public health surveillance.

4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS

A. Purpose of Surveillance and Reporting

- HUS has been clearly demonstrated as important sequelae 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. HUS is also an important event for assessing morbidity caused by *E. coli* O157:H7.
- To identify whether the patient 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 commercially contaminated food product) and to stop transmission from such sources.

B. Laboratory Reporting Requirements

The New Jersey Administrative Code (NJAC 8:57-1.6) stipulates that laboratories report (by telephone, confidential fax, or over the Internet using the Communicable Disease Reporting and Surveillance System [CDRSS]) all cases of HUS to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. The report shall contain, at a minimum, the reporting laboratory's name, address, and telephone number; the age, date of birth, gender, race, ethnicity, home address, and telephone number of the person tested; the test performed; the date of testing; the test results; and the healthcare provider's name and address.

C. Healthcare Provider Reporting Requirements

NJAC 8:57-1.4 stipulates that healthcare providers report (by telephone, confidential fax, or in writing) all cases of HUS to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. The report shall contain the name of the disease; date of illness onset; and name, age, date of birth, race, ethnicity, home address, and telephone number of the person they are reporting. Additionally, name, address, institution, and telephone number of reporting official and other information as may be required by NJDHSS concerning a specific disease should be included.

D. Health Officer's Reporting and Follow-Up Responsibilities

NJAC 8:57-1.7 stipulates that each local health officer must report the occurrence of any case of HUS within 24 hours of receiving a report from a laboratory or healthcare provider to

NJDHSS, Infectious and Zoonotic Diseases Program (IZDP). A report can be mailed or filed electronically using CDRSS.

5 CASE INVESTIGATION

A. Forms

- It is the health officer's responsibility to complete the HUS Reporting Form by interviewing the patient and others who may be able to provide pertinent information. Much of the clinical information on the form can be obtained from the patient's healthcare provider or the medical record.
- Be sure to obtain as much information as possible about foods and activities during the week prior to onset of the diarrheal illness (not HUS onset). See also the chapters on STEC and Shigellosis for more information on case follow-up.
- If there have been several unsuccessful attempts to obtain patient information, please fill out the worksheet with as much information as possible. Please note on the worksheet why it could not be filled out completely. After completing the report, attach lab report(s) and mail (in an envelope marked "Confidential") to IZDP or, alternatively, file the report electronically over the Internet using the confidential and secure CDRSS. The mailing address is:

  NJDHSS
  Division of Epidemiology, Environmental and Occupational Health
  Infectious and Zoonotic Diseases Program
  PO Box 369
  Trenton, NJ 08625-0369

B. Entry into CDRSS

The mandatory fields for all cases in CDRSS include: disease, last name, county, municipality, gender, race, ethnicity, case status, report status.

The following table can be used as a quick reference guide to determine which fields in CDRSS are necessary for accurate and complete reporting of *HEMOLYTIC UREMIC SYNDROME* cases. The first column represents the tabs along the top of the CDRSS screen. The Required Fields column reflects a detailed explanation of the essential data for each tab.

CDRSS Screen	Required Information
Patient Info	Enter disease name "HEMOLYTIC UREMIC SYNDROME (HUS)," patient demographics, patient onset and date report was made to the local health department. There are no subgroups for HUS.

CDRSS Screen	Required Information
Addresses	Determine whether the case-patient attends or works at a daycare facility and/or is a food handler. Use as needed for additional addresses (e.g., work address, school, temporary NJ address for out-of-state case). Use the Comments section in this screen to record any pertinent information about the alternate address (e.g., the times per week the case-patient attends daycare).Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction.
Clinical Status	Clinical information such as past medical history, any treatment that the patient received, name of medical facility(s) including date of initial healthcare evaluation and dates of hospitalization, treating physician(s), and mortality status are entered here. (**NOTE:** If the patient received care from two or more medical facilities, be sure all are recorded in the case including admit/discharge dates so the case can be accessed by all infection control professionals (ICPs) covering these facilities.)
Signs/Symptoms	Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient's illness. Check appropriate boxes for signs and symptoms and indicate their onset and resolution.
Risk Factors	Be sure to obtain as much information as possible about foods and activities during the week prior to onset of the diarrheal illness (not HUS onset). See also the chapters on STEC and Shigellosis for more information on case follow-up. Enter complete information about risk factors including complete food history, travel history, any gatherings or outdoor activities attended, questions about water supply, pet or other animal contact and record in the Comments section.
Laboratory Eval	There are no lab tests for HUS, please record all additional lab information including Lab Specimen ID, Specimen, Date specimen collected, Lab Name, Referring Physician Name, Referring Medical Facility name, Test Result i.e., Positive/reactive or Negative/no reactive in the Comments section.

CDRSS Screen	Required Information
Contact Tracing	All potentially exposed contacts are entered into the contact tracing tab for local, county and statewide surveillance efforts. CDRSS requires a "YES" response to one of the two *HEMOLYTIC UREMIC SYNDROME (HUS)* exposure questions in order to add case contacts. Contacts are added individually by selecting the Enter Contact By Name feature: Each contact record reflects the period of exposure, symptomatic or asymptomatic, contact demographics, telephone numbers, marital status, primary language, exposure risk i.e., close, casual, unknown, and LHD response activities are noted. An exposure setting is selected for each contact from the drop down to the right of the contact's name. A summary reflecting the following contact details: total number, name, age, relationship, exposure specifics as well as all LHD recommendations to prevent further transmission of illness are entered into the contact tracing text box.
Case Comments	Any additional case investigation findings that can not be entered in discrete data fields are documented in the general comment section.
Epidemiology	Select the route of transmission route, import status of infection i.e., whether the case was imported and from where (another county, state, country), LHD notification of illness and association with high-risk venue type, name, location and last day of attendance, whether case-patient is a daycare worker or attendee, foodhandler, or healthcare worker. The NJDHSS assigned outbreak or investigation number is selected for all involved cases which automatically populates a summary of the initial report.
Case Classification Report Status	Case status options are: "REPORT UNDER INVESTIGATION (RUI)," "CONFIRMED," "PROBABLE," "POSSIBLE," and "NOT A CASE." • All cases entered by laboratories (including LabCorp electronic submissions) should be assigned a case status of "REPORT UNDER INVESTIGATION (RUI)." • Cases still under investigation by the LHD should be assigned a case status of "REPORT UNDER INVESTIGATION (RUI)." Upon completion of the investigation, the LHD should assign a case

CDRSS Screen	Required Information
	status on the basis of the case definition. "CONFIRMED", "PROBABLE", "POSSIBLE" and "NOT A CASE" are the only appropriate options for classifying a case of *HEMOLYTIC UREMIC SYNDROME (HUS).* Report status options are: "PENDING," "LHD OPEN," "LHD REVIEW," "LHD CLOSED," "DELETE," "REOPENED," "DHSS OPEN," "DHSS REVIEW," and "DHSS APPROVED." • Cases reported by laboratories (including LabCorp electronic submissions) should be assigned a report status of "PENDING." • Once the LHD begins investigating a case, the report status should be changed to "LHD OPEN." • The "LHD REVIEW" option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing). • Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to "LHD CLOSED." • "LHD CLOSED" cases will be reviewed by DHSS and be assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to "REOPENED" and the LHD will be notified by e-mail. Cases that are "DHSS APPROVED" cannot be edited by LHD staff. If a case is inappropriately entered as a case of HEMOLYTIC UREMIC SYNDROME (HUS) the case should be assigned a report status of "DELETE." A report status of "DELETE" should NOT be used if a reported case of HEMOLYTIC UREMIC SYNDROME (HUS) simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.

C. Other Reporting/Investigation Issues

1. Case report forms (HUS Reporting Form and labs) DO NOT need to be mailed to NJDHSS as long as mandatory fields in CDRSS indicated in section B are completed.

2. Once LHD completes its investigation and assigns a report status of "LHD CLOSED," NJDHSS will review the case. NJDHSS will approve the case by changing the report status to "DHSS APPROVED." At this time, the case will be submitted to CDC and the case will be locked for editing. If additional information is received after a case has been placed in "DHSS APPROVED," you will need to contact NJDHSS to reopen the case. This should be done only if the additional information changes the case status of the report.

3. Every effort should be made to complete the investigation within three months of opening a case. Cases that remain open for three months or more and have no investigation or update notes will be closed by NJDHSS.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (NJAC 8:57-1.10)

Food handlers with HUS must be excluded from work, although people diagnosed with HUS are usually hospitalized and are too ill to be working.

NOTE: A case of HUS is defined by the reporting criteria in section 2A of this chapter.

Minimum Period of Isolation of Patient

After symptoms have resolved, food-handling facility employees may return to work only after producing two **consecutive** negative stool specimens obtained at least 24 hours apart. If a patient has been treated with an antimicrobial, the stool specimen shall not be submitted until at least 48 hours after completion of therapy.

NOTE: Because the onset of symptoms 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-patient and handled in the same fashion. No restrictions otherwise.

NOTE: A food handler is any person directly preparing or handling food. This can include a patientcare or childcare provider.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

1. 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 GI illness should be heightened and children with GI symptoms should be referred to their healthcare providers for appropriate testing. If the patient has been diagnosed with *E. coli* O157:H7 or Shigellosis, please refer to

the appropriate chapter of this manual for that disease. Contact IZDP at 609.588.7500 for assistance in managing the follow-up of a case of HUS in a daycare setting.

2. Schools

A case of HUS in a school setting may be a marker for additional infections with *E. coli* O157:H7 or Shigellosis within the school, especially among classes with younger children. Surveillance for GI illness should be heightened and students with GI symptoms should be referred to their healthcare providers for appropriate testing. If the individual has been diagnosed with *E. coli* O157:H7 or Shigellosis, please refer to the appropriate chapter for that disease. Contact IZDP at 609.588.7500 for assistance in managing the follow-up of a case of HUS in a school setting.

7 OUTBREAK SITUATIONS

If the number of reported cases of HUS in a city/town is higher than usual, or if an outbreak is suspected, investigate to determine the source of infection and mode of transmission. A common vehicle (such as 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 IZDP at 609.588.7500. IZDP staff can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several jurisdictions and therefore be difficult to identify at a local level.

8 PREVENTIVE MEASURES

A. Environmental Measures

Implicated food items must be removed from the environment. A decision about testing implicated food items can be made in consultation with IZDP and the Food and Drug Safety Program (FDSP). FDSP can help coordinate pickup and testing of food samples. If a commercial product is suspected, FDSP will coordinate follow-up with relevant outside agencies (e.g., Food and Drug Administration, US Department of Agriculture). Contact FDSP at 609.588.3123.

NOTE: The role of FDSP is to provide policy and technical assistance with the environmental investigation such as interpreting the New Jersey Food Code, conducting a hazardous analysis and critical control points risk assessment, initiating enforcement actions, and collecting food samples.

B. Personal Preventive Measures/Education

To avoid future exposure, advise individuals to do the following:

- Wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet, and after changing diapers.
- After changing diapers, wash the child's hands as well as their own.
- Dispose of feces in a sanitary manner, especially in daycare centers or other institutional settings.
- Scrub their hands thoroughly after assisting in the following: caring for someone with diarrhea; cleaning toilets; and changing soiled diapers, clothing, or bed linens.
- Send back all undercooked hamburger for further cooking.
- Cook all ground beef and hamburger thoroughly.
- Drink only pasteurized milk, juice, or cider.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.

Additional Information

A Hemolytic Uremic Syndrome Fact Sheet can be obtained at the NJDHSS Web site at http://www.state.nj.us/health.

References

American Academy of Pediatrics. *Red Book 2003: Report of the Committee on Infectious Diseases*. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003.

Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. *MMWR Morb Mortal Wkly Rep.* 1997;46:RR-10.

Chin J, ed. *Control of Communicable Diseases Manual*. 17th ed. Washington, DC: American Public Health Association; 2000.

Mandell G, Bennett J, Dolin R, eds. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 5th ed. Philadelphia, Pa: Churchill Livingstone; 2005

Massachusetts Department of Public Health, Division of Epidemiology and Immunization. *Guide to surveillance and reporting.* Massachusetts Department of Public Health, Division of Epidemiology and Immunization; Jamaica Plain, MA January 2001.