UTAH DEPARTMENT OF HEALTH

Hemolytic Uremic Syndrome (Post-Diarrheal)

Disease Plan

Quick Links:

Last updated: February 18, 2016, by Laine McCullough.

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ WHY IS HEMOLYTIC UREMIC SYNDROME IMPORTANT TO PUBLIC HEALTH?

Hemolytic uremic syndrome (HUS) is a serious sequela of many different infections, most commonly *Escherichia coli* (*E. coli*). HUS is seen worldwide and in the United States (U.S.). Approximately 200–300 cases of HUS are reported in the U.S. each year. On average, Utah has less than 5 cases reported year. Occurrence of HUS could be indicative of additional cases of the source disease in the community. Correct diagnosis, confirmation of initial etiology, early detection of cases, and interview of ill persons is crucial in identifying sources of illness and preventing future cases and outbreaks.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

HUS is an acute illness involving the kidney and blood clotting system. HUS is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Most cases of HUS follow an acute gastrointestinal illness (usually diarrhea). Early symptoms of HUS following a gastrointestinal illness can include bloody stools, irritability, fever, lethargy, vomiting, and weakness. Later symptoms may include bruising, decreased consciousness, low or no urine output, pale or yellow skin, and bruising.

Causative Agent

HUS consists of anemia from red blood cell destruction and impaired renal function. Many different infections and disorders can cause HUS. The most common cause of HUS is infection with a Shiga toxin-producing organism, most commonly *E. coli*. Other bacterial agents that can cause HUS include: *Shigella*, *Salmonella*, *Yersinia*, and *Campylobacter*. Only HUS that follows an acute diarrheal illness should be reported to public health.

Differential Diagnosis

The differential diagnosis for HUS includes disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), and systemic vasculitis.

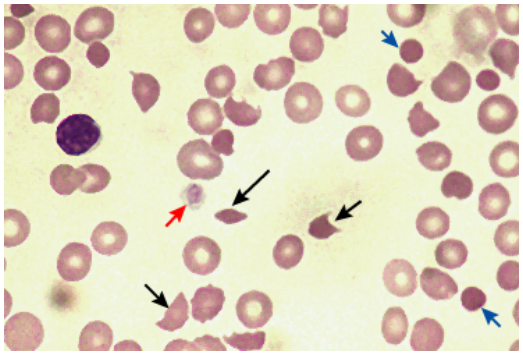
Laboratory Identification

There is no single laboratory test for HUS. A person with HUS will usually have a history of diarrhea for a few days, with development of bloody diarrhea, anemia, and kidney failure. If a doctor suspects HUS based on a patient's symptoms, he or she will request several laboratory tests. The diagnosis of HUS depends on laboratory demonstration of:

- Anemia with microangiopathic changes, and
- Renal injury evidenced by hematuria, proteinuria, or elevated creatinine level.

Anemia is determined by measuring the amount of iron in the patient's blood. A low amount of iron means the patient is anemic. Hematocrit, the test that determines the amount of iron in the patient's blood, is usually ordered as a part of the complete blood count (CBC).

Microangiopathic changes (changes in the structure of red blood cells), e.g. schistocytes, burr cells, helmet cells, etc., can be determined through a peripheral blood smear. A peripheral blood smear is usually ordered as a part of the complete blood count (CBC).



Peripheral smear in microangiopathic hemolytic anemia showing presence of schistocytes (UpToDate Photo, 2016)

Hematuria (blood in the urine) can be microscopic or visible. A chemical examination of urine using small test strips will measure the amount of blood in the urine. A positive test indicates an increased amount of red blood cells.

Proteinuria (protein in the urine) can be an early sign of kidney disease. A chemical examination of urine using small test strips will measure the amount of protein in the urine. A positive test indicates an increased amount of protein.

Creatinine test and blood urea nitrogen (BUN) tests are used as indicators of kidney function. Both are usually ordered as a part of the basic or comprehensive metabolic panel (BMP or CMP) run on blood samples. Increased levels of either indicate diseases or conditions that affect the kidneys.

NOTE: Additional laboratory testing, such as stool cultures, to identify the cause of HUS should be conducted as well to determine whether *E. coli* or another bacterium is present. The combination of clinical signs and symptoms and the laboratory results help a doctor determine the diagnosis of HUS.

Treatment

The mainstay of treatment of patients with HUS remains supportive care. Depending on the needs of the patient, this supportive care may involve red blood cell transfusions, platelet transfusion, appropriate fluid and electrolyte management, cessation of nephrotoxic drugs, initiation of dialysis, and/or provision of adequate nutrition. There is no known therapy to halt the progression of HUS. Antibiotics are usually not used because they may make symptoms worse. Most patients with HUS recover completely and kidney function returns to normal if they are treated quickly and properly. Additional treatment for the cause of HUS may be necessary.

Case Fatality

HUS is a serious illness in both children and adults. With proper treatment, most patients will recover; however, it can be fatal or produce long term sequelae (e.g., brain damage and kidney failure). The estimated case fatality rate is 3-5%. The prognosis can be influenced by the disease that preceded it. Rates can vary by disease and serotype; about 5% of patients who developed HUS as a result of *E. coli* O157:H7 die.

Reservoir

HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on reservoirs for these organisms.

Transmission

HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on transmission of these organisms.

Susceptibility

Those most at risk for developing HUS are children under the age of 5 years and people who have certain genetic characteristics that make them more susceptible.

HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on susceptibility to these organisms.

Incubation Period

HUS usually occurs during the two weeks following the onset of diarrhea. In some cases, diarrhea may have resolved, and the patient may appear to be improving, when the onset of HUS occurs. Please refer to the appropriate disease plan for more specific information on incubation period for associated organisms.

Period of Communicability

People with HUS may be infectious if still shedding *E. coli* or *Shigella* in their stool. Please refer to the appropriate disease plan for information on the period of communicability for specific associated organisms.

Epidemiology

HUS is seen worldwide and may occur in 5–15% of *E. coli* O157:H7 infections. Children younger than 5 years are at highest risk of HUS, which occurs in approximately 15% of those with laboratory-confirmed *E. coli* O157:H7 infection, compared with approximately 6% among people of all ages. 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. HUS occurs in approximately 1% of patients of all ages with laboratory confirmed non-O157:H7 *E. coli* infection.

In the past five years, there has been less than five cases of HUS reported each year in Utah. During this time period, Utah cases of HUS have primarily been a result of *E. coli* O157:H7 infection; however, illness has also been caused by *E. coli* O121, *E. coli* O26, and *Campylobacter*.

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Investigate all suspect cases of disease, and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.

- Identify cases and sources of infection to prevent further transmission.
- Identify clusters or outbreaks of this disease, and determine the source.

Prevention

Personal Preventive Measures/Education

To avoid exposure to bacteria that may cause HUS, individuals should:

- Always wash their hands thoroughly with soap and water for at least 20 seconds:
    - Before eating or preparing food;
    - After cleaning or using the toilet or helping someone use the toilet;
    - After changing diapers;
    - After touching their pets or other animals; and
    - Frequently when ill with diarrhea or when caring for someone with diarrhea.
- Wash their own hands, as well as the child's hands, after changing a child's diapers.
- In a childcare setting, dispose of diapers in a closed-lid garbage can.
- Keep food that will be eaten raw, such as fruits and vegetables, from becoming contaminated by animal-derived food products.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.
- Cook all ground beef and hamburgers thoroughly, and send back all undercooked hamburgers for further cooking.
- Drink only pasteurized milk, juice, or cider.

Chemoprophylaxis

Please refer to the appropriate disease plan for information on chemoprophylaxis for specific associated organisms.

Vaccine

Please refer to the appropriate disease plan for information on vaccine for specific associated organisms.

Isolation and Quarantine Requirements

Isolation: HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on isolation for specific associated organisms.

Hospital: Standard and contact precautions should be followed.

Quarantine: HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on quarantine for specific associated organisms.

✓ CASE INVESTIGATION

Reporting

Report any illness to public health authorities that meets any of the following criteria:

- Any person diagnosed as having hemolytic uremic syndrome.
- Any person diagnosed as having thrombotic thromobocytopenic purpura.
- Any person with hemolytic anemia and renal injury as evidenced by hematuria, proteinuria, or an elevated creatinine level.
- A person whose healthcare record contains a diagnosis of hemolytic uremic syndrome.
- A person whose death certificate lists hemolytic uremic syndrome as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures:

- All cases of hemolytic uremic syndrome (post-diarrheal) should be reported.
- Reporting should be ongoing and routine.
- Frequency of reporting should follow the state health department's routine schedule (in Utah, within three working days of identification).

Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Reporting
Clinical Evidence	
Diagnosis of Hemolytic Uremic Syndrome	S
Diagnosis of thrombotic thromobocytopenic purpura	S
Death certificate lists Hemolytic Uremic Syndrome as a cause of death or a significant condition contributing to death	S
Laboratory Evidence	
Anemia	N
Microangiopathic changes on peripheral blood smear (burr cells, helmet cells, schistocytes)	N
Hematuria	O
Proteinuria	O
Increased creatinine level	O

Notes:
S = This criterion alone is Sufficient to identify a case for reporting.
N = All "N" criteria in the same column are Necessary to identify a case for reporting.
O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to identify a case for reporting. (These optional criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.)

Case Definition

Hemolytic Uremic Syndrome (post-diarrheal) (2010)

Clinical Description

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thromobocytopenic purpura (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

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

- Anemia (acute onset) with microangiopathic changes (e.g., schistocytes, burr cells, or helmet cells) on peripheral blood smear, AND
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (e.g., 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 seven days after onset of the acute gastrointestinal illness is not less than 150,000/mm3, other diagnoses should be considered.

Case Classification

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.

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 three weeks, OR
- An acute illness diagnosed as HUS or TTP, that a) has onset within three weeks of onset of acute or bloody diarrhea and b) meets the laboratory criteria, except that microangiopathic changes are not confirmed.

Comment: 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 postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as postdiarrheal HUS. Most diarrhea-associated HUS is caused by Shiga toxin-producing *Escherichia coli*, most commonly *E. coli* (STEC) and HUS, the case should be reported for each of the conditions.

Classification Table

Criteria for defining cases of hemolytic uremic syndrome.

Criterion	Confirmed	Probable	
Clinical Evidence			
Diarrhea	N		N
Onset of illness <3 weeks after onset of diarrhea	N	A	N
Diagnosis of Hemolytic Uremic Syndrome		O	O
Diagnosis of thrombotic thromobocytopenic purpura		O	O
Laboratory Evidence			
Anemia	N	N	N
Microangiopathic changes on peripheral blood smear (burr cells, helmet cells, schistocytes)	N	N	
Hematuria	O	O	O
Proteinuria	O	O	O
Increased creatinine level	O	O	O

Notes:
N = All "N" criteria in the same column are Necessary to classify a case.
A = This criterion must be absent (e.g., NOT present) for the case to meet the classification criteria.
O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.

Case Investigation Process

HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on the case investigation process for specific associated organisms.

Outbreaks

CDC defines a food-borne outbreak as, "an incident in which two or more persons experience a similar illness resulting from the ingestion of a common food." Since HUS can have multiple causes, it is crucial that the agent which caused the disease is identified in order to link cases of HUS to each other.

Identify Case Contacts

HUS can be caused by a number of different organisms, although *E. coli* is the most common. Please refer to the appropriate disease plan for information on identifying case contacts for specific associated organisms.

Case Contact Management

Childcare

A case of HUS in a childcare setting may be a marker for additional *E. coli* or *Shigella* infections within the facility. Surveillance for gastrointestinal illness should be heightened, and children with gastrointestinal symptoms should be referred to their healthcare providers for appropriate testing. If the case has been diagnosed with *E. coli* or *Shigella*, please refer to the appropriate disease plan for additional information on case contact management.

School

A case of HUS in a school setting may be a marker for additional infections with *E. coli* 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 healthcare providers for appropriate testing. If the case has been diagnosed with *E. coli* or *Shigella*, please refer to the appropriate disease plan for additional information on case contact management.

✓ ACKNOWLEDGEMENTS

This document is a revision of the Utah Department of Health disease plan for hemolytic uremic syndrome. We would like to acknowledge Virginia Department of Health, New Jersey Department of Health and Senior Services, and Massachusetts Department of Public Health for select content of this document.

✓ REFERENCES

Council of State and Territorial Epidemiologists (CSTE) Position statements. Available from URL: http://www.cste.org/default.asp?page=PositionStatements.

E. coli Diarrheal Diseases. (2015). In D. Heymann (Ed.), *Control of communicable diseases manual* (20th ed.). Washington, DC: American Public Health Association.

Escherichia coli Diarrhea (Including Hemolytic-Uremic Syndrome). (2015). In L. Pickering (Ed.), *Red Book: 2015 Report of the Committee on Infectious Diseases* (30th ed.). Elk Grove Village, IL: American Academy of Pediatrics.

Hemolytic-uremic syndrome: MedlinePlus Medical Encyclopedia. (n.d.). Retrieved February 18, 2016, from https://www.nlm.nih.gov/medlineplus/ency/article/000510.htm.

Hemolytic uremic syndrome (HUS). (n.d.). Retrieved February 18, 2016, from http://www.mayoclinic.org/diseases-conditions/hemolytic-uremic-syndrome/basics/definition/con-20029487.

Massachusetts Department of Public Health, Bureau of Communicable Disease Control. (2006, June). Hemolytic Uremic Syndrome (HUS). Retrieved February 18, 2016.

New Jersey Department of Health and Senior Services. (2008, June). Hemolytic Uremic Syndrome (HUS). Retrieved February 18, 2016.

Niaudet, P. (2016, January 22). Clinical manifestations and diagnosis of Shiga toxin-producing Escherichia coli (STEC) hemolytic uremic syndrome (HUS) in children. Retrieved February 18, 2016, from http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-shiga-toxin-producing-escherichia-coli-stec-hemolytic-uremic-syndrome-hus-in-children?source=search_result&search=clinical+manifestations+and+diagnosis+of+shiga+toxin&selectedTitle=1~45.

Niaudet, P. (2016, January 22). Overview of hemolytic uremic syndrome in children. Retrieved February 18, 2016, from http://www.uptodate.com/contents/overview-of-hemolytic-uremic-syndrome-in-children?source=search_result&search=hemolytic+uremic+syndrome&selectedTitle=1~150.

UpToDate. (2016, January). Peripheral smear in microangionpathic hemolytic anemia showing presence of schistocytes [Photograph]. Retrieved from http://s0www.utdlab.com/contents/image.do?imageKey=HEME%2F70851.

Virginia Department of Health. (2013, June). Hemolytic Uremic Syndrome (HUS). Retrieved February 18, 2016.

Wanke, C. (2015, September 8). Pathogenic Escherichia coli. Retrieved February 18, 2016, from http://www.uptodate.com/contents/pathogenic-escherichia-coli?source=search_result&search=pathogenic+escherichia+coli&selectedTitle=1~150.

✓ VERSION CONTROL

Updated Nov 2014 – CSTE reporting criteria, case definition, and case classification swim lanes included.

Updated Feb 2016 – Added "Why is Hemolytic Uremic Syndrome Important to Public Health" section. Updated symptoms in "Clinical Description" section. Updated “Differential Diagnosis" and "Laboratory Identification." Updated "Treatment" to include supportive care examples. Updated “Susceptibility” and “Period of Communicability” sections. Updated “Epidemiology” section with Utah trends. Reorganized “Prevention measures and recommendations.” Updated “Isolation and Quarantine Requirements” and “Case Investigation Process” to refer back to appropriate disease plan. Updated "Identify Case Contacts" section and separated from "Case Contact Management.” Added "Acknowledgements,” "Version Control,” and "Minimum Data Set" sections. Deleted the symptoms from the Reporting Table swim lanes because there were no letter criteria associated with them and they were not in the narrative.

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic
- ☑ Last Name
- ☑ First Name
- ☑ State
- ☑ County
- ☑ Date of Birth
- ☑ Area Code
- ☑ Phone Number
- ☑ Birth Gender
- ☑ Ethnicity
- ☑ Race

Clinical
- ☑ Disease
- ☑ Onset Date
- ☑ Date Diagnosed
- ☑ Died
- ☑ Date of Death
- ☑ Diagnostic Facility
- ☑ Did patient have HUS or TTP?
    - ○ (if yes) Which
    - ○ (if yes) Date of diagnosis:

Laboratory
- ☑ Test Type
- ☑ Test Result
- ☑ Accession Number

Epidemiological
- ☑ Food Handler
- ☑ Group Living
- ☑ Childcare Association
- ☑ Occupation
- ☑ Imported From
- ☑ Risk Factors
- ☑ Risk Factor Notes

Reporting
- ☑ Date first reported to public health

Investigation
- ☑ Diarrheal onset date:
- ☑ HUS/TTP onset date:
- ☑ Is HUS/TTP onset date within 3 weeks of diarrheal onset date?
- ☑ Was diarrhea illness diagnosed with stool culture?
    - ○ (if yes) Cause of HUS/TTP:
        - • (if other) Specify:
- ☑ Was diarrhea treated with antibiotic(s)?
    - ○ (if yes) List Antibiotic(s):
    - ○ (if yes) Dose(s):
    - ○ (if yes) Start date(s):
    - ○ (if yes) End date(s):
      Note if antibiotic is not finished

Administrative
- ☑ State Case Status (completed by UDOH)
- ☑ Outbreak Associated
- ☑ Outbreak Name