

HEMOLYTIC UREMIC SYNDROME (POST-DIARRHEAL)

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

Hemolytic Uremic Syndrome (HUS) is an acute illness involving the kidney and blood clotting. HUS includes microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Most cases of HUS follow an acute gastrointestinal illness (usually diarrhea).

About 5% of survivors will eventually develop end stage kidney disease and will need dialysis or transplantation. Another 5-10% of survivors will develop neurological or pancreatic problems.

Causative Agent:

HUS consists of anemia from red blood cell destruction and impaired renal function. Many different infections and disorders can cause HUS. Among children, the most common cause of HUS is infection with a Shiga toxin-producing organism, most commonly *Escherichia 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.

Differential Diagnosis:

Laboratory testing is necessary to determine the cause of HUS.

Laboratory identification:

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).

Hematuria (blood in the urine) can be microscopic or gross. 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.

Additional laboratory testing to identify the cause of HUS should be conducted, as well.

Treatment:

The mainstay of treatment of patients with HUS remains supportive care. There is no known therapy to halt the progression of Hemolytic Uremic Syndrome. Additional treatment for the cause of HUS may be necessary.

Case fatality:

HUS in children can be fatal.

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.

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.

Susceptibility:

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.

Incubation period:

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

Period of communicability:

Please refer to the appropriate disease plan for information on the period of communicability.

Epidemiology:

HUS is seen worldwide and may occur in 5–10% of *E. coli* O157:H7 infections in 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.

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

Prevention:

Personal Preventive Measures/Education

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

- Always wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet, after changing diapers, and after touching their pets or other animals.
- Wash their own hands as well as the child's hands after changing a child's diapers.
- In a child care setting, dispose of diapers in a closed-lid garbage can.
- Wash their hands thoroughly and frequently when ill with diarrhea or when caring for someone with diarrhea.
- Hands should be scrubbed for at least 15–20 seconds after cleaning the bathroom, after using the toilet or helping someone use the toilet, after changing diapers, before handling food, and before eating.
- 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.

Chemoprophylaxis:

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

Vaccine:

Please refer to the appropriate disease plan for information on vaccines.

Isolation and quarantine requirements:

Isolation: Food handlers with HUS must be excluded from work; however, individuals diagnosed with HUS are usually too ill to be working. After diarrhea has resolved, food handlers may return to food handling duties only after producing two negative stool specimens, taken at least 24 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.

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

Hospital: Enteric precautions.

Quarantine: Contacts who have diarrhea and are food handling facility employees shall be considered the same as a case and shall be handled in the same fashion. In outbreak circumstances involving a facility, asymptomatic contacts who are food handling employees may be required to submit stool specimens for testing.

✓ CASE INVESTIGATION

Reporting:

Since HUS can have multiple causes, only HUS that follows an acute diarrheal illness should be reported to public health.

Case definition:

Hemolytic Uremic Syndrome, Post-diarrheal (1996)

Clinical description

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thrombocytopenic 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 (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear
- AND
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., 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 7 days after onset of the acute gastrointestinal illness is not less than 150,000/mm³, other diagnoses should be considered.

Case classification

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 3 weeks,

OR

- has onset within three weeks after onset of an acute or bloody diarrhea and 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.

Criterion	Case Definition		
	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 thrombocytopenic 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 (i.e., NOT present) for the case to meet the classification criteria. O = At least one of these —O (Optional) criteria in each category (i.e., 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.			

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.

Case Investigation Process:

- Food handlers should be excluded from work until diarrhea has resolved and two stool specimens are negative.

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 is causing the disease be identified in order to link cases of HUS to each other.

Identification of case contacts and management: Neonatal Infection/ Maternal Infant Transmission

When neonate is less than one month of age, please use the following data entry procedure.

UTNEDSS/ Trisano Data Entry

- The mother is the case-patient, or “parent” CMR
 - Enter mother’s medical record number in parent CMR
 - Enter mother’s symptoms in the parent CMR
 - Enter mother’s exposure history in parent CMR
 - Add attachments and lab report(s) for mother on parent CMR.
- Neonate is entered as a contact of the mother
 - Enter neonate medical record number as a contact of the mother
 - Enter neonate symptoms as a contact of the mother
 - Enter neonate exposure as a contact of the mother
 - Add attachments and lab report(s) for neonate as a contact of the mother
- Neonate may be promoted to own CMR as appropriate
- When searching UTNEDSS/ Trisano for name of mother or neonate, both CMRs should come up in search results

Daycare

A case of HUS in a daycare 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 health care 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 health care 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.

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