Infectious Disease Epidemiology Section
Office of Public Health, Louisiana Dept of Health & Hospitals
800-256-2748 (24 hr number) – (504) 568-5005
www.oph.dhh.state.la.us

HEMOLYTIC UREMIC SYNDROME

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The hemolytic uremic syndrome (HUS) is an acute disorder characterized by:
1-acute renal failure,
2-hemolytic anemia,
3-thrombocytopenia.

Hemolytic uremic syndrome (HUS) is renal failure with or without oligoanuria, microangiopathic hemolytic anemia, and thrombocytopenia. These features usually appear several days to two weeks after a prodromal illness, which is commonly a gastroenteritis with diarrhea and less commonly an upper respiratory tract infection.

It may result from a reaction to some endotoxins or severe infections (gram negative bacteremias, typhoid fever, *Streptococcus pneumoniae* pneumonia, mumps, infectious mononucleosis, coxsackie A4, B2, B4, echo virus 22 and other viral infections) or appear as a result of a coagulation disorder and microangiopathic hemolytic anemia (Idiopathic HUS) where the kidney became the most extensively involved organ.

The most common gram negative bacteria are *Shigella dysenteriae* and a special serotype of *Escherichia coli*. These are isolated by stool cultures. A Shigella-like toxin plays a major part in the pathogenesis of this syndrome.

This is primarily a disease of children with few adult cases. In areas where HUS is common, children of middle socio-economic groups, beyond the neonatal period are at highest risk.

Clinical Description

The initial symptoms in children with HUS are digestive, respiratory and systemic. Bloody diarrhea and fever are the most common initial signs. Soon they develop acute anemia, signs of renal and central nervous system injury, gastrointestinal bleeding. Anemia is due to hemolysis following fragmentation of red blood cells. Platelet counts are severely depressed and it is accompanied by signs of intravascular coagulation.

HUS appears to be the most frequent cause of renal insufficiency in childhood.

In adults the prodrome resembles any acute viral infection. The clinical signs are similar to those in children but the prognosis is poorer. HUS should be differentiated from thrombotic thrombocytopenic purpura, renal cortical necrosis, severe vasculitis and necrotizing glomerulonephritis.

Laboratory Tests

Patients with HUS should be cultured for enteric pathogens, including *E.coli* O157:H7. The absence of EHEC in feces does not preclude the diagnosis of EHEC-associated HUS, since HUS typically is diagnosed a week after onset of diarrhea when the organism no longer may be detectable in stool.

The high frequency of isolation of *E.coli* O157 may be due to the ease of isolation of this type of *E.coli* since it does not ferment sorbitol unlike other *E.coli* on sorbitol McConkey. Routine laboratory studies can easily identify suspected colonies for further evaluation by reference laboratories. There are no such easy biochemical markers for other *E.coli* serotypes.

Surveillance

HUS is a condition reportable within one business day.

Case Definition

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 diarrhea).

Laboratory criteria for diagnosis

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/mm^3, 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 the preceding 3 weeks or
An acute illness diagnosed as HUS or TTP, that a) has onset within 3 weeks after onset of an acute 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 3 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 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.

Treatment

Management of HUS is supportive and includes meticulous attention to fluid and electrolyte balance; dialysis is often necessary. Therapy is primarily directed at management of the acute renal failure.

Intervention

The purpose of investigation is to identify cases, to differentiate any etiologic agent, to determine the mode of transmission (whether from person-to-person or by common vehicle), to identify the population exposed and at increased risk of infection and to institute disease control measures.

Upon receipt of a report of HUS, contact the physician and/or hospital to confirm the diagnosis. Inquire if testing for enteric pathogens (specifically, *E. Coli* 0157:H7) has been attempted. Patients with HUS should be cultured for enteric pathogens, including *E. Coli 0157:H7.*
If the case is suspected to be part of a foodborne outbreak, carry out a foodborne outbreak investigation.

Cases associated with a child care center:
- Contact the child care center owner/director to notify her of the case and to determine if any other cases have occurred.
- The normal procedure to follow includes testing symptomatic individuals if a second case has been confirmed. (Diarrhea is defined as two or more loose stools over and above what is normal for that child. It is recommended that the child be excluded until the diarrhea is gone or the child has been cleared by the child's physician or health department.

Cases involving a food handler or food establishment:
- If during completion of the case record, it is discovered that a case is a food handler, ascertain to what degree the person handles food, i.e., cook, waitress, etc. (Patients with HUS should be cultured for enteric pathogens, including *E. Coli* 0157:H7 or *Shigella*. The absence of Enterohemorrhagic *E. Coli* (EHEC) in feces does not preclude the diagnosis of EHEC-associated HUS, since HUS typically is diagnosed a week after onset of diarrhea when the organism may no longer be detectable in stool. HUS is considered to be part of a continuum of disease.)
- Notify the manager of the food establishment and indicate that the case should not engage in handling food until symptoms of illness has resolved. The employee may work in a non-food-handling capacity during this time if cleared by his physician.
- Identify any other employees who have symptoms of gastroenteritis and remove from the food-handling area. Refer the employee for stool screening by the Office of Public Health or by a private provider.
- Request the manager to notify OPH immediately if any additional cases occur.

Hospital precaution and isolation: contact precautions until one stool culture is negative for *E. Coli* 0157:H7, or, if these tests are not available, for at least ten days from onset of diarrhea.