ESCHERICHIA COLI (E.COLI) INFECTIONS

Revised 11/28/2016

There are hundreds of strains of the bacterium Escherichia coli. Most are harmless, living in the intestines of healthy humans and animals. Each group of E.coli strains has a distinct group of somatic (O) and flagellar (H) antigens and has specific virulence characteristics that usually are plasmid-mediated.

- **Enterohemorrhagic E.coli (EHEC)** strains: Hemorrhagic colitis is caused by E.coli 0157:H7 and less frequently, by other serotypes of E.coli (O26:H11) that produce cytotoxins resembling those found in Shigella dysenteriae, type 1. These toxins are referred to as shigalike toxins or verotoxins.

- **Enteroinvasive E.coli (EIEC)** strains include specific serotypes of E.coli (O28, O112, O115, O124, O136, O143, O144, O147, O152, O164 and O167) that are different from EPEC serotypes. The EIEC strains resemble Shigella biochemically and can invade intestinal epithelial cells.

- **Enteropathogenic E.coli (EPEC):** The EPEC strains traditionally have been defined as members of specific E.coli serotypes that have been epidemiologically incriminated as causes of infantile diarrhea and include the following somatic (O) serogroups: O44, O55, O86, O111, O114, O119, O125, O126, O127, O128, O142 and O158. More recently, EPEC has been defined according to specific virulence properties. Enteropathogenic E.coli strains adhere to intestinal mucosa and produce a characteristic lesion in the gastrointestinal tract. Enteropathogenic E.coli do not produce enterotoxins and are not invasive.

- **Enterotoxigenic E.coli (ETEC):** The ETEC strains colonize the small intestine without invading and produce either or both heat-labile and/or heat-stable enterotoxins. Some of these strains are O6:H16, O8:H9 or O8:H-, O15:H11 or other H-

- **Enteroaggregative E.coli** are defined by their characteristic adherence pattern in tissue-culture-based assays. Unlike EPEC, which demonstrates localized adherence, these strains exhibit a "stacked brick" adherence pattern on HEP-2 or HeLa cells. An additional group of E.coli that adhere diffusely to these cell lines needs further clarification.

<table>
<thead>
<tr>
<th>E.coli</th>
<th>Epidemiology</th>
<th>Diarrhea</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHEC</td>
<td>Hemorrhagic colitis and hemolytic uremic syndrome in all ages and thrombotic thrombocytopenic purpura in adults</td>
<td>Bloody or non-bloody diarrhea</td>
<td>Cytotoxin production and adherence</td>
</tr>
<tr>
<td>EPEC</td>
<td>Acute and chronic endemic and epidemic diarrhea in infants</td>
<td>Watery</td>
<td>Adherence effacement</td>
</tr>
<tr>
<td>ETEC</td>
<td>Infantile diarrhea in developing countries and travelers' diarrhea</td>
<td>Watery</td>
<td>Adherence, enterotoxin production</td>
</tr>
<tr>
<td>EIEC</td>
<td>Diarrhea with fever in all ages</td>
<td>Bloody or not</td>
<td>Adherence, invasion of mucosa</td>
</tr>
<tr>
<td>EAggEC</td>
<td>Chronic diarrhea in infants</td>
<td>Watery</td>
<td>Adherence</td>
</tr>
</tbody>
</table>
EHEC (E.coli O157 H7)
Hemorrhagic Uremic Syndrome (HUS)

The E. coli O157:H7 strain produces a toxin that can cause severe illness. Infection often leads to bloody diarrhea with severe abdominal pain. Occasionally other complications such as hemorrhagic colitis, hemolytic-uremic syndrome and thrombotic thrombocytopenic purpura (TTP) may occur.

Epidemiology

EHEC E.coli O157:H7 has a bovine reservoir. Typically, EHEC is detectable in bovine feces of no less than 5% at any point in time. The agent has been detected at similar, or slightly higher, prevalence among cattle being held at slaughter plants and on the external surface of the hides of recently slaughtered animals. EHEC also has been found in feces from several species other than cattle, including deer, sheep, dogs, horses, flies and birds. Colonization of cattle with EHEC typically is of short duration - one to two months. EHEC is not associated with any recognizable disease in cattle but instead appears to behave as transient normal flora. The typical pattern of O157 shedding in a herd followed over time is one of epidemic shedding interspersed with longer periods of rare or no shedding.

EHEC is transmitted by undercooked ground beef and unpasteurized milk. Part of the reason is that hamburger meat comes from a large number of animals; up to 100 cows may contribute to a pack of hamburgers. Outbreaks from contaminated apple cider, raw vegetables, salami, yogurt and water also have occurred.

EHEC also spreads from person-to-person by fecal-oral transmission.

Infectious dose: In a 1992-1993 large outbreak in the western U.S. associated with consumption of ground beef patties, infectious doses as low as 700 microorganisms were estimated. The cattle were initially colonized and their slaughter caused surface contamination of meat. These low infectious doses suggest a zero tolerance for E.coli O157H7.

Incubation period for most E.coli strains is from ten hours to six days; for E.coli O157:H7, it is usually three to four days, but can be as long as eight days.

Clinical Description

The duration of excretion of the bacteria is usually up to a week but has been observed for much longer periods, particularly in children. Asymptomatic carriage of O157 has also been reported.

EHEC strains are associated with

- diarrhea
- hemorrhagic colitis
- hemolytic-uremic syndrome (HUS)
- post-diarrheal thrombotic thrombocytopenic purpura.

The illness usually begins as non-bloody diarrhea and may progress to grossly bloody diarrhea. Severe abdominal pain is typical; fever occurs in one third of cases. The average duration of illness is eight days.

Hemolytic-uremic syndrome (HUS) is defined by the triad of

- microangiopathic hemolytic anemia
- thrombocytopenia
- acute renal dysfunction.

The frequency of HUS as a complication of EHEC in children has been estimated to be 5% to 10% of those infected with EHEC.
Many children with hemorrhagic colitis caused by *E. coli* 0157:H7 develop mild, self limited, microangiopathic hematologic changes and/or nephropathy in the week after onset of diarrhea.

Thrombotic thrombocytopenic purpura (TTP) occurs in adults, may follow EHEC infection and is part of a disease spectrum often designated as TTP-HUS. While the vast majority of cases of childhood HUS are caused by *E. coli* 0157:H7, most cases of TTP in adults are of unknown etiology.

**Laboratory Tests**

A case of *E. coli* 0157:H7 is diagnosed by:

1) isolation of *E. coli* 0157:H7 from a specimen; isolates can be identified presumptively by lack of sorbitol fermentation on MacConkey-sorbitol agar culture plates

or

2) isolation of Shiga toxin-producing *E. coli* 0157 from a clinical specimen.

Stool specimens should be collected on cotton tipped swabs and then placed in tubes of Carey-Blair transport medium. These can be obtained from the regional laboratories. Specimens in Carey-Blair should be refrigerated and transported to the laboratory under refrigerated conditions as soon as possible. (If necessary to hold 48 hours or longer, freeze sample at -7ºC and transport to the laboratory in the frozen state). If fresh stools need to be collected for concurrent viral testing, a clean, unbreakable, leak-proof container can be used (supplied by the Office of Public Health, or be innovative and use a margarine tub container from home), and should be kept refrigerated upon arrival to the laboratory. (DO NOT FREEZE FRESH STOOL!)

Submit at least 100 grams (approximately 4 oz.-5 oz.) of each suspected food item. Place each food item in appropriate leak-proof containers provided in the Rapid Response Team laboratory kit and label each container. Be sure to keep food refrigerated (not frozen), and ship as soon as possible. Also complete the Food and Drug Lab requisition for each food item submitted.

Results of cultures will not be available for at least 72 hours. In order to adequately investigate and identify the cause of the outbreak, it is very important to obtain samples of the suspected food and several stool specimens. Confirmation of the causative organism(s) cannot be made with just one of these components.

**Surveillance**

*E. coli* 0157:H7 and EHEC are reportable conditions to be reported within one business day.

**Case Definition**

- Enterohemorrhagic *Escherichia coli* (E. coli)
- Enterohemorrhagic *Escherichia coli* O157: H7
- Enterohemorrhagic *Escherichia coli* shiga toxin positive (not serogrouped)
- Enterohemorrhagic *Escherichia coli* shiga toxin positive (serogroup non-O157)

**Clinical description**

An infection of variable severity characterized by diarrhea (often bloody), and abdominal cramps. Illness may be complicated by HUS. (Note, some clinicians still use the term thrombotic thrombocytopenic purpura [TTP for adults with post-diarrheal HUS.) Asymptomatic infections also may occur, and the organism may rarely cause extra-intestinal infections.

**Laboratory criteria for diagnosis**

- Isolation of STEC from a clinical specimen. *Escherichia coli* O157 isolates that produce the H7 antigen may be assumed to be Shiga toxin-producing. For all other *E. coli* isolates, Shiga toxin production or the presence of Shiga toxin genes must be determined to be considered STEC.
Both asymptomatic infections and infections at sites other than the gastrointestinal tract, if laboratory confirmed, are considered confirmed cases that should be reported.

**Supportive laboratory results**
- A case with isolation of *E. coli* O157 from a clinical specimen, without confirmation of H antigen or Shiga toxin production
- Identification of an elevated antibody titer to a known STEC serotype from a clinically compatible case
- Identification of Shiga toxin in a specimen from a clinically compatible case without the isolation of STEC
- Identification of *E. coli* O157 or EHEC using a non-culture based method

**Epidemiologic linkage**
A clinically compatible case that is epidemiologically linked to a confirmed or probable case.

**Case definition**

**Confirmed**
- A case that meets the confirmed laboratory criteria for diagnosis. When available, O and H antigen serotype characterization should be reported

**Probable**
- A case with isolation of *E. coli* O157 from a clinical specimen, without confirmation of H antigen or Shiga toxin production. **OR**
- A clinically compatible case that is a contact of an STEC case or is a member of a defined risk group during an outbreak. **OR**
- Identification of an elevated antibody titer to a known STEC serotype from a clinically compatible case

**Suspect**
- A case of post-diarrheal HUS (see HUS case definition) **OR**
- Identification of Shiga toxin in a specimen from a clinically compatible case without the isolation of STEC **OR**
- Identification of *E. coli* O157 or EHEC using a non-culture based method

**Investigation**

The purpose of investigation is to identify cases, to differentiate between other infections that cause diarrhea, to identify the source(s) of illness and to institute disease control measures to prevent further spread of the disease.

- Upon receipt of a report of *E. coli* O157:H7, contact the physician and/or hospital to confirm the diagnosis.
- If the case is suspected to be part of a foodborne outbreak, notify the RRT coordinator and/or the Infectious Disease Epidemiology Section immediately. The first concern would be to determine the source(s) of the infection. Check recent food history and recover all suspected foods for appropriate testing.
- Symptomatic individuals should be excluded from foodhandling and from direct care of hospitalized and institutionalized patients and child care centers. The recommendation is that individuals do not return until one negative culture is obtained.
- If the case is associated with a child care center (either attendee or staff member), contact the owner/director to notify her/him 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. Once the laboratory test results are available on those persons, a decision can be made regarding further testing and referral. This should be discussed with the Infectious Disease Epidemiology Section. The Office of Public Health has developed guidelines and recommendations for licensing standards regarding exclusion of children with certain disease conditions. Diarrhea is defined as two (2) or more loose stools over and above what is normal for that child. The recommendation is that the child or staff member be excluded until the diarrhea is gone, and one negative culture is obtained, or the child has been cleared by the child’s physician or health department.

Case Management - Treatment

Most persons recover without antibiotics or other treatment within five to ten days. Orally administered solutions to correct dehydration and electrolyte abnormalities may be given.

Hospital precaution and isolation: Contact precaution should be used during the acute illness and until stool cultures become negative.

Prevention

- Educate the public on the importance of cooking all ground beef or hamburger thoroughly. The meat should be brown throughout (with no pink), and hot on the inside. *E. coli* is killed by thorough cooking, as long as the food exceeds 72°C for at least two minutes.
- Raw milk should be avoided; only pasteurized milk and milk products should be consumed.
- Fruit juices should also be pasteurized
- Drinking water should be treated.
- Stress the importance of hand washing with soap to reduce transmission from infected persons, especially children.

**EIEC (Enteroinvasive *E. coli*)**

Epidemiology

EIEC are rare causes of diarrhea throughout the world. There were only two outbreaks in the U.S., both associated with contaminated food. Since this infection is rare, the dynamics of transmission not well known.

Clinical

EIEC can cause dysentery, similar to that caused by *Shigella*, characterized by fever, diarrhea, vomiting, crampy abdominal pain and tenesmus. Stools often contain blood and leukocytes. However, most patients experience watery diarrhea without blood or mucus. Outbreaks have occurred, usually secondary to ingestion or consumption of contaminated food.
EPEC (Enteropathogenic *E. coli*)

**Epidemiology**

EPEC typically occurs in neonates and children younger than or equal to two years of age (mostly ≤6 months) in developing countries, either sporadically or in epidemics. Outbreaks occurred in the 1940s and 1950s in U.S. hospital nurseries. EPEC are still often found in hospital outbreaks. In an epidemic, a single strain of EPEC is usually predominant. Attack rates observed during community epidemics range from 1% to 3% among infants (≤12 months old). Among older children, rates are much lower (0.1%). Besides cases, the strain may be isolated from pharyngeal or intestinal asymptomatic carriers (1%-30% of case associates). Half of the index households have at least one carrier. Outbreaks occur all year with an increase during summer or fall.

During hospital outbreaks, EPEC has been isolated in the excretors of asymptomatic nursing personnel and family members. In one outbreak 13% of mothers were carriers with a subsequent infection rate of 40% of their offspring.

Pharyngeal carriage is usually asymptomatic, but in some cases, mild upper respiratory symptoms are observed.

**Clinical**

EPEC is an important cause of chronic diarrhea that can cause failure to thrive. The illness is characterized by:

- Fever (60%)
- Watery diarrhea (90%+) that is often severe and can result in dehydration (30%)
- Abdominal distension, paralytic ileus

Symptoms usually last for one week.

**Prevention:**

In a newborn nursery, management of EPEC infection is based on the number of cases.

- If a single case occurs, the infant should be isolated in a unit separate from the nursery area.

- If multiple cases occur, the nursery room should be closed to admissions and not reopened until all infants in the room have been discharged and the room has been cleaned. Infants should be discharged home or, if not possible, transferred to a designated isolation area and not to other infant wards. Personnel caring for infants in the closed nursery cohort should not have duties in other open nursery rooms.

- If epidemic disease involves more than one room in a nursery, the entire nursery should be closed and not reopened until a strict cohort system has been established in each room of the nursery for the duration of the epidemic. Admissions to a room should be limited to infants born in a one to two day period. The room should then be closed to admissions until all infants have been discharged and the room has been cleaned. Personnel should be cohorted with the infants.
**ETEC (Enterotoxigenic E.coli)**

**Epidemiology**

ETEC, “the Traveler’s E.coli” was first described during an outbreak of diarrhea occurring among a group of British soldiers in the Middle East.

In the U.S., it is not a common cause of endemic diarrhea and is isolated mostly during outbreaks. It occurs in persons of all ages. Outbreaks have occurred in adults, usually from ingestion of contaminated food or water.

ETEC is very common in tropical areas. It is the major cause of travelers' diarrhea (approximately 40%). It is a very common cause of infantile diarrhea in developing countries. In Mexico, during the first three years of life, children show a gradual increase of anti-LT antibody (reflecting prior exposure to LT-producing ETEC).

Food seems to play a major part in the spread of ETEC. Food and water make it possible for ETEC to achieve the large inoculum necessary to produce symptoms (approximately 100 million bacteria).

**Clinical**

Diarrhea caused by enterotoxigenic E.coli (ETEC) is a self-limiting illness of moderate severity with watery stools and abdominal cramps. Fever, if present, is usually low grade. The usual “turista” produces ten loose stools over five days.

**Prevention of Traveler’s Diarrhea**

Travelers' diarrhea has been associated with many entero pathogens, usually is acquired by ingestion of contaminated food or water and is a significant problem. Persons traveling in developing countries should be advised to drink only carbonated beverages and boiled or carbonated (bottled) water; they should avoid ice, salads and fruit they have not peeled themselves. Foods should be eaten hot. Antimicrobial agents usually are not recommended for prevention of travelers' diarrhea in children. Although several antimicrobial agents, such as trimethoprim-sulfamethoxazole, doxycycline and ciprofloxacin are effective prophylactically in decreasing the incidence of travelers' diarrhea, the benefit usually is outweighed by the potential risks, including allergic drug reactions, antibiotic-associated colitis and the selective pressure of widespread use of antimicrobial agents leading to antimicrobial resistance.

If diarrhea does occur, packets of oral rehydration salts can help maintain fluid balance and anti-spasmodic drugs can relieve symptoms. In children use of anti-peristalsis drugs is not advocated. If diarrhea is moderate or severe, or is associated with fever or bloody stool, empirical antimicrobial treatment is indicated. In children, the recommended drug is trimethoprim-sulfamethoxazole; in adults, a fluoroquinolone (eg, ciprofloxacin or ofloxacin) is recommended. Therapy should continue until symptoms resolve, but not for more than three days.

**Shiga Toxin producing E.coli (STEC)**

Shiga toxin–producing E. coli (STEC) is a denomination used to characterize all Entero-hemorrhagic E.coli without having to determine their O and H types. Most reported STEC infections in the U.S. are caused by E. coli O157:H7. Non-O157 STEC bacteria also are important causes of diarrheal illness in the United States; at least 150 STEC serotypes have been associated with outbreaks and sporadic illness. In the U.S., six non-O157 serogroups (O26, O45, O103, O111, O121 and O145) account for the majority of reported non-O157 STEC infections.
The toxins produced by STEC were named based on their similarity in structure and function to Shiga toxins produced by Shigella dysenteriae type 1. Shiga toxin 1 (Stx1) is neutralized by antibodies against Shiga toxin, whereas Shiga toxin 2 (Stx2) is not neutralized by antibodies against Shiga toxin but is neutralized by homologous antibodies. STEC are also referred to as verocytotoxigenic E. coli; STEC that cause human illness are also referred to as enterohemorrhagic E. coli. In this report, all E. coli that produce a Shiga toxin are referred to as STEC. STEC serotypes are named according to their somatic (O) and flagellar (H) antigens. In this report, all STEC with the O antigen 157 are referred to as O157 STEC, regardless of whether the H7 antigen has been identified or Shiga toxin production has been confirmed. STEC with other O antigens are referred to as non-O157 STEC or by their specific O antigen.

**Infectious dose**

Both O157 STEC and O111 STEC have a low infectious dose (less than 100 organisms); the infectious dose of other serogroups is not known.

**Clinical**

STEC infection causes acute, often bloody, diarrhea. Approximately 8% of persons who receive a diagnosis of O157 STEC infection develop hemolytic uremic syndrome (HUS), a life-threatening condition characterized by thrombocytopenia, hemolytic anemia and renal failure. Thrombotic thrombocytopenic purpura (TTP), a syndrome with signs and symptoms that are similar to those of HUS, is typically diagnosed in adults. When TTP is diagnosed after a diarrheal illness, the condition is usually caused by infection with O157 STEC or another STEC.

Although most persons with diarrhea-associated HUS have an O157 STEC infection, certain non-O157 STEC strains also can lead to HUS. The virulence of non-O157 STEC is partly determined by the toxins they produce; non-O157 STEC strains that produce only Stx2 are more often associated with HUS than strains that produce only Stx1 or that produce both Stx1 and Stx2.

**Laboratory**

Most O157 STEC isolates can be readily identified in the laboratory when grown on sorbitol-containing selective media because O157 STEC cannot ferment sorbitol within 24 hours. However, many clinical laboratories do not routinely culture stool specimens for O157 STEC.

Recently, the increased use of enzyme immunoassay (EIA) or polymerase chain reaction (PCR) to detect Shiga toxin or the genes that encode the toxins (stx1 and stx2) has facilitated the diagnosis of both O157 and non-O157 STEC infections. Although EIA and other nonculture tests are useful tools for diagnosing STEC infection, they should not replace culture; a pure culture of the pathogen obtained by the clinical laboratory (O157 STEC) or the Public Health laboratory (non-O157 STEC) is needed for serotyping and molecular characterization (e.g., pulsed-field gel electrophoresis [PFGE] patterns), which are essential for detecting, investigating and controlling STEC outbreaks.

Because virtually all O157 STEC have the genes for Stx2 (stx2), and intimin (eae), which are found in strains that are associated with severe disease, detection of O157 STEC should prompt immediate initiation of steps such as parenteral volume expansion to reduce the risk for renal damage in the patient and the spread of infection to others.
Escherichia coli Septicemia and Meningitis in Neonates

*Escherichia coli* strains with the K1 capsular polysaccharide antigen cause approximately 40% of cases of septicemia and 75% of cases of meningitis caused by *E. coli*. Other important gram-negative bacilli that can cause neonatal septicemia include non-K1 strains of *E. coli* and *Klebsiella, Enterobacter, Proteus, Citrobacter, Salmonella* and *Pseudomonas* species.

**Epidemiology:** The source of *E. coli* and other gram-negative bacterial pathogens in neonatal infections usually is the maternal genital tract. In addition, nosocomial acquisition of gram-negative flora through person-to-person transmission among nursery personnel and from nursery environmental sites, such as fluid reservoirs of incubators, has been documented, especially in preterm infants who require prolonged intensive care management.

**Clinical signs** of septicemia include fever, temperature instability, apnea, cyanosis, jaundice, hepatomegaly, lethargy, irritability, anorexia, vomiting, abdominal distention and diarrhea. Meningitis may occur with septicemia.

Predisposing host factors in neonatal Gram-negative bacterial infections include maternal perinatal infections, low birth weight, prolonged rupture of membranes and septic or traumatic delivery. Metabolic abnormalities, such as galactosemia, fetal hypoxia and acidosis also have been implicated as predisposing factors. Neonates with defects in the integrity of skin or mucosa (e.g., myelomeningocele) are at increased risk for Gram-negative bacterial infections. In intensive care nurseries, sophisticated systems for respiratory and metabolic support, invasive procedures, indwelling vascular lines and the frequent use of antimicrobial agents enable selection and proliferation of multiple antimicrobial-resistant strains of pathogenic Gram-negative bacilli.

**Laboratory Tests:** The diagnosis is established by growth of *E. coli* or other Gram-negative bacilli from blood, cerebrospinal fluid, or other usually sterile sites.

**Surveillance:** Newborn meningitis or invasive diseases caused by *E. coli* or other Gram negative bacilli are not reportable unless occurring in a cluster (nursery for example).

**Investigation:** Several cases of infection caused by the same genus and species of bacteria occurring in infants in physical proximity or caused by an unusual pathogen indicate the need for an epidemiologic investigation.