

# Escherichia coli Infections

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## Educational Gap

Virulent strains of *Escherichia coli* are responsible for most diarrheal infections, meningitis, septicemia, and urinary tract infections in children worldwide. Clinicians must learn to recognize, treat, and prevent these infections.

## Objectives

After completing this article, readers should be able to:

1. Describe the epidemiology of *E coli* infections.
2. Recognize the clinical features of *E coli* infections, including the O157:H7 strain.
3. Appropriately treat children with various types of *E coli* infections.
4. Understand ways to prevent *E coli* infections.

## INTRODUCTION

*Escherichia coli* are normal inhabitants of the human large intestine. Most strains are harmless, but some strains acquire bacteriophage or plasmid DNA-encoding enterotoxins or invasion factors and become pathogenic. These virulent strains are responsible for diarrheal infections worldwide, as well as neonatal meningitis, septicemia, and urinary tract infections (UTIs).

## MICROBIOLOGY

*E coli* are gram-negative bacilli of the family Enterobacteriaceae. They are facultative anaerobes and nonsporulating. *E coli* strains with the K1 capsular polysaccharide antigen cause approximately 40% of cases of septicemia and 80% of cases of meningitis.

Different strains of *E coli* are associated with a number of distinctive diarrheal illnesses (Table). Among these are the enterotoxigenic *E coli* (ETEC), enteroinvasive *E coli* (EIEC), and Shiga toxin-producing *E coli* (STEC). Of the STEC, *E coli* O157:H7 is the prototypic strain. Each class of *E coli* has distinct somatic (O) and flagellar (H) antigens and specific virulence characteristics. (1)

## EPIDEMIOLOGY

Diarrheogenic *E coli* strains are worldwide in distribution. The route of infection is fecal-oral, predominantly via contaminated water and food. STEC, especially

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### ABBREVIATIONS

EIEC	enteroinvasive <i>Escherichia coli</i>
ESBL	extended-spectrum $\beta$ -lactamase
ETEC	enterotoxigenic <i>Escherichia coli</i>
HUS	hemolytic uremic syndrome
STEC	Shiga toxin-producing <i>Escherichia coli</i>
UPEC	uropathogenic <i>Escherichia coli</i>
UTI	urinary tract infection

TABLE. Classification of *Escherichia coli* Associated With Diarrhea

PATHOTYPE	EPIDEMIOLOGY	TYPE OF DIARRHEA	MECHANISM OF PATHOGENESIS
Shiga toxin-producing <i>E coli</i>	Hemorrhagic colitis and hemolytic uremic syndrome in all ages	Bloody or nonbloody	Shiga toxin production, large-bowel attachment, coagulopathy
Enteropathogenic <i>E coli</i>	Acute and chronic endemic and epidemic diarrhea in infants	Watery	Small-bowel adherence and effacement
Enterotoxigenic <i>E coli</i>	Infant diarrhea in resource-limited countries and traveler's diarrhea in all ages	Watery	Small-bowel adherence, heat stable/heat-labile enterotoxin production
Enteroinvasive <i>E coli</i>	Diarrhea with fever in all ages	Bloody or nonbloody; dysentery	Adherence, mucosal invasion, and inflammation of large bowel
Enteroaggregative <i>E coli</i>	Acute and chronic diarrhea in all ages	Watery, occasionally bloody	Small- and large-bowel adherence, enterotoxin and cytotoxin production

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*E coli* O157:H7, is shed in feces of cattle, sheep, deer, and other ruminants. Human infection is acquired via contaminated food or water or via direct contact with an infected person. Outbreaks have been linked to ground beef, exposure to animals in public settlements (petting zoos), contaminated apple cider, and contamination of water in recreational areas. The incubation period for most *E coli* strains is 10 hours to 6 days. For *E coli* O157:H7, the incubation period is usually 3 to 4 days.

The source of *E coli* and other gram-negative bacterial pathogens in neonatal infections is often through the maternal genital tract. Hospital acquisition of gram-negative organisms through person-to-person transmission from nursery personnel or environmental sites can occur. The incubation period is variable with time of onset of infection ranging from birth to several weeks after birth.

## CLINICAL ASPECTS

### Septicemia and Meningitis in Neonates

Neonates, both term and preterm, are susceptible to septicemia and meningitis. Presentation in the first week after birth (early onset) and particularly in the first 2 days after birth reflects vertical transmission, whereas late-onset infection suggests nosocomial or community acquisition. The corresponding organisms are different; early-onset meningitis is more likely to be caused by group B *Streptococcus*, *E coli*, and *Listeria monocytogenes*, whereas late-onset meningitis may be caused by other gram-negative organisms and staphylococcal species. The *E coli* pathotype responsible for meningitis and sepsis is called neonatal meningitis-associated *E coli*. Neonatal meningitis-associated *E coli* have a K1 capsule

that contains sialic acid, which potentiates the bacteria's ability to invade through the blood-brain barrier. (2) Neonatal septicemia or meningitis caused by *E coli* cannot be differentiated clinically from infection caused by other agents. Clinical signs of septicemia include fevers, temperature instability, heart rate abnormalities, respiratory distress, apnea, cyanosis, lethargy, irritability, jaundice, vomiting, diarrhea, and abdominal distention. Predisposing factors in neonatal gram-negative bacterial infections include maternal intrapartum infection, gestation of less than 37 weeks, low birth weight, and prolonged rupture of membranes. Neonates with defects in the integrity of their skin or mucosa or abnormalities of gastrointestinal or genitourinary tracts are at increased risk as well.

### Diarrheal Infections

ETEC strains have been associated with self-limited gastrointestinal illness characterized by abdominal cramping and watery stools lasting 1 to 5 days. ETEC is common in infants in resource-limited countries, but it is rare as a cause of diarrhea in the United States. These strains are however a major cause of traveler's diarrhea, with infection typically resulting from ingestion of contaminated food or water.

STEC strains produce toxins similar to those found in *Shigella dysenteriae* type 1. These organisms are associated with diarrhea, hemorrhagic colitis, hemolytic uremic syndrome (HUS), and postdiarrheal thrombocytopenic purpura (usually in adults). STEC O157:H7 is the most virulent member of the *E coli* prototype. Illness caused by STEC can consist of bloody diarrhea or occult positive diarrhea. Severe abdominal pain is typical, and fever occurs in a third of the cases.

EIEC strains resemble *Shigella* biochemically and invade intestinal epithelial cells to produce disease. Like *Shigella*, these strains can cause watery diarrhea, fever, crampy abdominal pain, and tenesmus.

Enteropathogenic *E coli* strains cause watery diarrhea and often severe dehydration in children younger than 2 years. These illnesses predominantly occur in resource-limited countries. If the diarrhea is chronic, the children may also have growth retardation.

Diffusely adherent *E coli* causes watery diarrhea, sometimes bloody in children and adults. Pathogenicity has not clearly been determined, but it involves diffuse adherence of the bacteria to the epithelial cells of the large intestine.

### Hemolytic Uremic Syndrome

HUS, defined by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal failure, is a serious sequela of STEC enteric infections. In North America, *E coli* O157:H7 is the serotype responsible for most cases, usually developing during 2 weeks after the onset of diarrheal symptoms. It occurs in up to 20% of children with *E coli* O157:H7 diarrhea. A total of 50% of the cases are severe enough to require dialysis, and 3% to 5% of patients die of the illness.

### Urinary Tract Infections

UPEC strains are responsible for approximately 80% of community-acquired and 30% of nosocomial-acquired UTIs. Infections in children are often due to blockages in the urinary tract, resulting in pools of stagnant urine. UPEC can reside in the colon and then be introduced into the urethra. The first step in the development of a UTI is colonization of the periurethral area by enteric pathogens. A variety of virulence factors enable bacteria to ascend into the bladder and kidney. *E coli* possesses pili, hairlike appendages on the cell surface, which improve the bacteria's ability to adhere effectively to the uroepithelium. Furthermore, UPEC strains contain type 1 and P fimbriae, which enhance virulence and are involved in initial urethral colonization, and many UPEC strains produce hemolysin, which may be involved in potentiating kidney disease.

### Diagnostic Tests

The diagnosis of *E coli* septicemia, UTIs, and meningitis is established by growth of *E coli* from blood, urine, or cerebrospinal fluid. The diagnosis of infection caused by diarrhea-associated *E coli* usually is difficult because most clinical laboratories cannot differentiate diarrhea-associated *E coli* strains from stool flora *E coli* strains. The exception is *E coli* O157:H7,

which can be identified using selective media (eg, MacConkey agar base with sorbitol). Approximately 90% of human intestinal *E coli* strains rapidly ferment sorbitol, whereas the O157:H7 strains do not. In addition, serologic diagnosis using enzyme immunoassays to detect serum antibodies to the O157:H7 lipopolysaccharide is available at the Centers for Disease Control and Prevention for outbreak investigations.

### Treatment

Children, especially infants, who are suspected of having a systemic infection with *E coli* should receive intravenous antibiotic treatment pending isolation of the organism from cultures. Approximately 50% of *E coli* are resistant to amoxicillin or ampicillin, so an aminoglycoside or a third-generation cephalosporin is recommended as empiric therapy, pending sensitivity data. A more specific antibiotic can be selected once susceptibility results become available. Duration of therapy is based on clinical response of the patient and the site of the infection. The usual duration of therapy is 10 to 14 days for uncomplicated bacteremia, 7 to 14 days for UTIs, and a minimum of 21 days for meningitis.

Infections with multidrug resistant *E coli* are an increasing concern, with resistance mediated by extended-spectrum  $\beta$ -lactamase (ESBL) production. These isolates are most often isolated from hospitalized patients but are becoming an increased cause of community-acquired infections as well. Risk factors for infection include prior administration of an antibiotic, presence of urinary or vascular catheters, and longer hospital or intensive care unit stays. ESBLs are able to hydrolyze most of the  $\beta$ -lactam antibiotics, including third-generation cephalosporins. In addition, they can also have coresistance to trimethoprim-sulfamethoxazole, fluoroquinolones, and aminoglycosides. Carbapenems are generally considered the drug of choice for the treatment of ESBL-*E coli* infections. (3,4)

Treatment of *E coli*-associated diarrhea is primarily supportive, with particular attention paid to the status of hydration and electrolyte balance. Antimotility drugs should not be administered to children who have inflammatory or bloody diarrhea. ETEC diarrhea is usually self-limited, but if it is prolonged, antibiotic therapy may shorten the illness. Azithromycin or a fluoroquinolone, such as ciprofloxacin, are effective, but fluoroquinolones are not approved for routine pediatric use. A meta-analysis failed to confirm that children with hemorrhagic colitis caused by STEC have a greater risk of developing HUS if treated with an antimicrobial agent; however, most experts agree not to treat children with *E coli* O157:H7 enteritis with an antimicrobial agent.

## Prevention

Preventive measures for *E coli* infections involve good hand hygiene and contact isolation of those infected, especially those with ESBL infections. For prevention of *E coli* O157:H7 infections, all ground beef should be cooked thoroughly and raw milk should not be ingested. Because of the possible waterborne transmission of the illness, people with diarrhea caused by *E coli* O157:H7 should not use recreational venues, such as swimming pools and water slides, for 2 weeks after symptoms resolve. Because illness with O157:H7 is reportable, public health authorities should be notified of all outbreaks, especially in child care centers.

In the event of an *E coli* outbreak appearing in the media, physicians should advise families to check their refrigerators for recalled foods and not cook them if found. They should also practice food safety and not eat raw or undercooked beef; wash hands, kitchen work surfaces, and utensils with soap and water immediately after they have been in contact with raw ground beef; and avoid cross-contaminating other foods in their refrigerators. They should also be encouraged to contact the physician if they think they may have become ill from eating recalled food products, with symptoms usually occurring 2 to 7 days after ingestion.

For prevention of traveler's diarrhea, travelers should be advised to drink only bottled or canned beverages and to avoid using ice and eating raw produce and prepeeled fruits. They may, however, eat fruits they peeled themselves. Only bottled water should be used for brushing teeth. Antimicrobial agents are not recommended for prevention of traveler's diarrhea, but if diarrhea is severe or associated with bloody stools and/or fever, empiric antimicrobial therapy may be indicated.

Use of vaccines to protect against traveler's diarrhea is hindered by the varied pathogens that can cause diarrhea. A number of trials suggest that the oral, killed whole-cell vaccine given with the nontoxic B subunit of cholera toxin (Dukoral) provides protection for travelers against ETEC infection. This vaccine was approved in the United States in late 2006 for use as a traveler's diarrhea vaccine. However, a conservative estimate that took into account the incidence of ETEC infection throughout the world and the efficacy of the vaccine suggested that it may prevent 7% or less of traveler's diarrhea cases. (5)

## Summary

- On the basis of strong research evidence, *Escherichia coli* are normal inhabitants of the human large intestine. Virulent strains are responsible for diarrheal infections worldwide, as well as neonatal meningitis, septicemia, and urinary tract infections (UTIs). (7)
- On the basis of strong research evidence, *E coli* is the most common bacterial cause of UTIs. Uropathogenic *E coli* possess pili and type 1 and P fimbriae, which potentiate the bacteria to adhere effectively to the uroepithelium. (7,8)
- On the basis of strong research evidence, hemolytic uremic syndrome occurs in up to 20% of children with *E coli* O157:H7 diarrhea. (7)
- On the basis of strong research evidence, the diagnosis of *E coli* septicemia, UTIs, and meningitis is established by growth of *E coli* from blood, urine, or cerebrospinal fluid. Most clinical laboratories cannot differentiate diarrhea-associated *E coli* strains from stool flora *E coli* strains. The exception is *E coli* O157:H7, which can be identified using selective media (eg, MacConkey agar base with sorbitol). (6,7)
- On the basis of strong research evidence, children, especially infants, who are suspected of having a systemic infection with *E coli* should receive intravenous antibiotic treatment pending isolation of the organism from cultures. Aminoglycosides or third-generation cephalosporins are recommended as empiric therapy, pending sensitivity data. (7)
- On the basis of strong research evidence, community-acquired UTIs with extended-spectrum  $\beta$ -lactamase producing *E coli* have been reported in recent years. Carbapenems are generally considered the drug of choice. (9)
- On the basis of some research evidence and consensus, treatment of *E coli*-associated diarrhea is primarily supportive. Antimotility agents and antimicrobial therapy are not usually indicated. (7)
- On the basis of strong research evidence, preventive measures for *E coli* infections involve hand hygiene and contact isolation. For prevention of *E coli* O157:H7 infections, all ground beef should be cooked thoroughly and raw milk should not be ingested. For prevention of traveler's diarrhea, travelers should be advised to drink only bottled or canned beverages and avoid ice, raw produce, and prepeeled fruits. (7,10)

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## PIR Quiz

1. An 18-month-old child adopted from an underdeveloped country is seen in an outpatient clinic. He is underweight and short for age and has a history of chronic watery diarrhea. Initial laboratory examination has ruled out parasites and human immunodeficiency virus. You suspect *Escherichia coli* infection. Which of the following strains of *E coli* is the MOST likely cause of his diarrhea?
  - A. Enteroaggregative.
  - B. Enterohemorrhagic.
  - C. Enteroinvasive.
  - D. Enteropathogenic.
  - E. Enterotoxigenic.
2. A 3-year-old child is admitted with acute renal failure, anemia, and thrombocytopenia after a course of bloody diarrhea 2 weeks ago. What strain of *E coli* is the MOST likely cause of this child's illness?
  - A. Enteroaggregative.
  - B. Enterohemorrhagic.
  - C. Enteroinvasive.
  - D. Enteropathogenic.
  - E. Enterotoxigenic.
3. Which of the following is a correct treatment approach to a systemic *E coli* infection?
  - A. Ampicillin for 21 days for a febrile infant with suspected urinary tract infection (UTI).
  - B. Antimotility agents for 2 to 3 days for a child with chronic nonbloody diarrhea.
  - C. Carbapenems for 14 days for a teen with a UTI and suspected extended-spectrum  $\beta$ -lactamase-producing strain.
  - D. Ciprofloxacin for 7 days for a child with diarrhea from enterotoxigenic strain.
  - E. Third-generation cephalosporin for 14 days for a neonate with suspected meningitis.
4. Which of the following children is NOT at risk for a systemic *E coli* infection?
  - A. A 4-day-old infant born to a mother with prolonged rupture of membranes.
  - B. A 15-month-old child who pets baby sheep at a town fair.
  - C. A 3-year-old child who ingests unpasteurized apple juice.
  - D. A 5-year-old child who swam in a pool with a friend who had diarrhea 2 months ago.
  - E. A 12-year-old who likes to eat raw hamburger.
5. Which of the following is an accepted practice to prevent *E coli* infections and traveler's diarrhea?
  - A. Antibiotic prophylaxis for nurses caring for infected infants.
  - B. Antimicrobial agents for travelers to endemic areas.
  - C. Avoiding prepeeled fruits.
  - D. Making sure that recalled foods are thoroughly cooked before eating.
  - E. Requiring that children wear gloves at petting zoos.

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