integrins. A pathogenicity island encodes an iron uptake system that mediates iron capture and transport; similar iron transport systems are also present in *E. coli*, *Klebsiella*, *Salmonella*, and enterobacteria. In *Yersinia*, iron enhances virulence and stimulates systemic dissemination, explaining why individuals with increased non-heme iron, such as those with certain chronic forms of anemia or hemochromatosis, are more likely to develop sepsis and are at greater risk for death.

MORPHOLOGY

Yersinia infections preferentially involve the ileum, appendix, and right colon (Fig. 17-28*B*). The organisms multiply extracellularly in lymphoid tissue, resulting in regional lymph node and Peyer patch hyperplasia as well as bowel wall thickening. The mucosa overlying lymphoid tissue may become hemorrhagic, and aphthous-like erosions and ulcers may develop, along with neutrophil infiltrates (Fig. 17-28*B*) and granulomas. This can result in diagnostic confusion with Crohn disease.

Clinical Features. People infected with *Yersinia* generally present with abdominal pain, but fever and diarrhea may also occur. Nausea, vomiting, and abdominal tenderness are common, and Peyer patch invasion with subsequent involvement of regional lymphatics can mimic acute appendicitis in teenagers and young adults. Enteritis and colitis predominate in younger children. *Extraintestinal symptoms of pharyngitis, arthralgia, and erythema nodosum occur frequently. Yersinia* can be detected by stool culture on *Yersinia*-selective agar. In cases with extraintestinal disease, cultures of lymph nodes or blood may also be positive. Postinfectious complications include reactive arthritis with urethritis and conjunctivitis, myocarditis, erythema nodosum, and kidney disease.

Escherichia coli

E. coli are gram-negative bacilli that colonize the healthy GI tract; most are nonpathogenic, but a subset cause human disease. The latter are classified according to morphology, mechanism of pathogenesis, and in vitro behavior. Subgroups with major clinical relevance include enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enterohemorrhagic *E. coli* (EHEC), enteroinvasive *E. coli* (EIEC), and enteroaggregative *E. coli* (EAEC).

***Enterotoxigenic* E. coli. ETEC organisms are the principal cause of traveler's diarrhea and spread via contaminated food or water.** In developing countries, children younger than 2 years of age are particularly susceptible. ETEC produce heat-labile toxin (LT) and heat-stable toxin (ST), both induce chloride and water secretion while inhibiting intestinal fluid absorption. The LT toxin is similar to cholera toxin and activates adenylate cyclase, resulting in increased intracellular cAMP. This stimulates chloride secretion and, simultaneously, inhibits absorption. ST toxins, which have homology to the mammalian regulatory protein guanylin, bind to guanylate cyclase and increase intracellular cGMP with resulting effects on transport that are similar to those produced by LT. Like cholera, the histopathology induced by ETEC infection is limited. The patients have secretory, noninflammatory diarrhea, dehydration, and, in severe cases, shock.

***Enteropathogenic* E. coli. EPEC** are prevalent in developed and developing countries, where they are an important cause of endemic diarrhea as well as diarrheal outbreaks particularly in children less than 2 years of age. EPEC are characterized by their ability to produce attaching and effacing (A/E) lesions in which bacteria attach tightly to the enterocyte apical membranes and cause local loss, i.e. effacement, of the microvilli. The proteins necessary for creating A/E lesions are all encoded by large genomic pathogenicity island, the locus of enterocyte effacement (LEE), which is also present in many EHEC strains. These proteins include Tir, which is inserted into the intestinal epithelial cell plasma membrane. Tir acts as a receptor for the bacterial outer membrane protein intimin, which is encoded by the *espE* gene and is used for molecular detection and diagnosis of EPEC infection. The locus of enterocyte effacement also encodes a type III secretion system, similar to that in *Shigella*, that injects bacterial effector proteins into the epithelial cell cytoplasm. All EPEC strains lack genes to produce Shiga toxin.

***Enterohemorrhagic* E. coli. EHEC are categorized as *E. coli* O157:H7 and non-O157:H7 serotypes.** Because cows are a natural reservoir, it is not surprising that large outbreaks of *E. coli* O157:H7 infection in developed countries are often associated with the consumption of inadequately cooked ground beef. However, contaminated milk and vegetables are also vehicles for infection. Both O157:H7 and non-O157:H7 serotypes produce Shiga-like toxins, and therefore lesions (Fig. 17-28*C*) and clinical symptoms are similar to those resulting from *S. dysenteriae* infection. O157:H7 strains of EHEC are more likely than non-O157:H7 serotypes to cause large outbreaks, bloody diarrhea, *hemolytic-uremic syndrome,* and ischemic colitis. Importantly, antibiotics are not recommended for treatment because killing the bacteria can lead to increased release of Shiga-like toxins that enhance the risk of hemolytic uremic syndrome, especially in children.

***Enteroinvasive* E. coli. EIEC organisms are bacteriologically similar to *Shigella* and are transmitted via food, water, or by person-to-person contact.** While EIEC do not produce toxins, they invade epithelial cells and cause nonspecific features of acute self-limited colitis (Fig. 17-28*D*). EIEC infections are most common among young children in developing countries and are occasionally associated with outbreaks in developed countries.

***Enteroaggregative* E. coli. EAEC organisms were identified on the basis of their unique pattern of adherence to epithelial cells.** These organisms are now recognized as a cause of diarrhea in children and adults in developed as well as developing countries. EAEC can also cause traveler's diarrhea. The organisms attach to enterocytes via adherence fimbriae and are aided by dispersin, a bacterial surface protein that neutralizes the negative surface charge of lipopolysaccharide. While the bacteria do produce enterotoxins related to *Shigella* enterotoxin and ETEC ST toxin, histologic damage is minimal and the characteristic adherence lesions are only visible by electron microscopy.

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