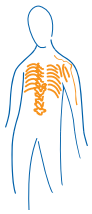
96

Infectious Diarrhea

Awewura Kwara



DEFINITION AND EPIDEMIOLOGY

Acute diarrhea is defined as an increase in frequency of bowel movements, to three or more times daily with at least 200 g of stool per day, lasting less than 14 days. In clinical practice, three or more loose stools per day is considered to represent diarrhea. *Infectious diarrhea* is diarrhea that has an infectious etiology and is often associated with symptoms and signs of enteric involvement, such as nausea, vomiting, abdominal cramps, passage of bloody stool (dysentery), or systemic symptoms. When diarrhea lasts longer than 14 days, it is considered to be *persistent diarrhea*. The term *chronic diarrhea* refers to illness that last longer than 1 month. Organisms responsible for infectious diarrhea include bacteria, viruses, and parasites.

Globally, there are an estimated 1.7 billion cases of diarrhea annually, with acute infectious diarrhea causing more than 2 million deaths per year. Infectious diarrhea is the second leading cause of death in children younger than 5 years of age, killing an estimated 760,000 such children every year. In the United States, an estimated 211 to 375 million episodes of acute diarrhea occur annually, with more than 900,000 hospitalizations and about 6000 deaths. Foodborne illnesses alone account for about 76 million cases and 5000 deaths in the US each year.

PATHOLOGY

Diarrhea is an alteration of movement of ions and water that leads to an increase in water content, volume, or frequency of stools. Under normal conditions, up to 9 L of fluid is passed through the adult gastrointestinal tract daily. Almost 98% of this fluid is absorbed, and only 100 to 200 mL is excreted in stools. Enteric pathogens or microbial toxins that are ingested can overcome host defenses and alter this balance toward a net secretion, leading to diarrhea. A large number of microorganisms are normally ingested with every meal. Host defense mechanisms against enteric pathogens include low gastric pH, rapid transit of bacteria through the proximal small intestine, cellular immune responses, and antibody production. In addition, large numbers of normal bacterial flora inhabit the intestines and prevent colonization by enteric pathogens.

Alteration of the normal defense mechanisms can put individuals at risk for infectious diarrhea. Individuals with gastric resection or achlorhydric states have increased frequency of infection due to *Salmonella*, *Giardia lamblia*, and helminths, whereas some organisms, such as *Shigella* or rotavirus, survive the extreme acidity of the gastric environment. Some viral, bacterial, and parasitic infections are more common in patients with impaired cellular or humoral immunity. More than 99% of the normal colonic flora is made up of anaerobic bacteria; they produce fatty acids and cause acidic pH, which is important for resistance to colonization. Alteration of the bacterial flora due to broad-spectrum antibiotic therapy predisposes some individuals to the development of *Clostridium difficile* infection.

The virulence factors employed by enteric pathogens include inoculum size, adherence factors, toxin production, and invasion. Organisms such as *Shigella*, enterohemorrhagic *Escherichia coli* (EHEC), *G. lamblia*, and *Entamoeba histolytica* need as few as 10 to 100 organisms to produce infection, whereas *Vibrio cholerae* needs 10^5 to 10^8 organisms to cause disease. Many pathogens, including *V. cholerae* and enterotoxigenic *E. coli* (ETEC), must adhere to the gastrointestinal tract to establish infection. They produce virulence factors that allow the organisms to attach to the brush border of the intestinal epithelium. Several enteric pathogens produce disease through the production of toxins. These include enterotoxins that cause secretory diarrhea, cytotoxins that cause cell destruction and inflammatory diarrhea, and neurotoxins that act on the nervous system. Other bacteria cause disease by invasion and destruction of mucosal epithelial cells.

Enterotoxin-Induced Secretory Diarrhea

Ingested enterotoxin-producing bacteria colonize the small bowel and multiply to large numbers. The bacteria then produce enterotoxin, which binds to the mucosa and causes watery diarrhea through hypersecretion of isotonic fluid that overwhelms the absorptive capacity of the colon. *V. cholerae* produces the cholera toxin, a heterodimeric protein composed of one A and five B subunits. The enterotoxin binds to the intestinal mucosa and activates adenylate cyclase to produce cyclic adenosine monophosphate (cAMP), which causes increased chloride secretion and decreased sodium absorption, leading to hypersecretion of fluid. ETEC, which causes traveler's diarrhea, produces both a heat-labile enterotoxin that acts by the same mechanism as the cholera toxin and a heat-stable enterotoxin that causes secretory diarrhea through activation of guanylate cyclase to produce cyclic guanosine monophosphate (cGMP).

Cytotoxin-Induced Diarrhea

In contrast to enterotoxins, cytotoxins elaborated by enteric pathogens destroy mucosal epithelial cells, causing bloody diarrhea with inflammatory cells (dysentery). *Shigella dysenteriae* produces the shiga toxin, which causes dysenteric diarrhea in patients with shigellosis. Other toxin-producing bacteria include *Vibrio parahaemolyticus*, *C. difficile*, and shiga toxin–producing strains of *E. coli* (STEC) that cause hemorrhagic colitis and hemolytic-uremic syndrome (HUS).