

## Case Studies- Introduction to Digestive Tract Diseases

The major clinical manifestation of infections affecting the gastrointestinal tract is diarrhea. Diarrheal pathogens have two basic mechanisms by which they produce diarrhea. One is the production of toxins called enterotoxins, which cause physiologic changes in the intestinal epithelium that result in fluid and electrolyte secretion. *Vibrio cholerae*, which produces an enterotoxin called cholera toxin, is a classic example of a diarrheal pathogen which produces a secretory diarrhea due to the action of an enterotoxin. Microscopically, the intestinal epithelium appears normal in patients with enterotoxin-induced diarrhea.

The other major mechanism of diarrheal disease is direct damage to the intestinal epithelium caused by cytotoxin or organism invasion. The protozoan *Entamoeba histolytica* produces such a cytotoxin. This cytotoxin is responsible for the characteristic ulcerative lesions which can be seen in individuals with amebic dysentery. A number of gastrointestinal pathogens including *Salmonella* spp., *Shigella* spp., *Campylobacter* spp., and *Yersinia enterocolitiae* are capable of invading the intestinal epithelium. Inflammation frequently occurs in response to these pathogens. Patients with diarrhea due to organisms that damage the epithelium frequently will have white blood cells visible in their feces. However, these cells may also be present in feces of patients with noninfectious inflammatory bowel disease, so results of examination of feces for white blood cells should be interpreted cautiously.

Diarrheal diseases are almost always spread by the **fecal-oral route**. This means that individuals who become infected with diarrheal pathogens ingest either food or water which has been contaminated with human or animal feces containing the pathogens. Improper handling or preparation of food and contamination of water due to poor sanitation are major means by which diarrheal pathogens are spread. In the industrialized world, the spread of diarrheal disease is particularly problematic in day care centers for children. In addition to spread by contaminated food and water, infected children can pass the organisms directly, by placing contaminated hands in the mouths of other children, or indirectly, by using contaminated hands to handle toys which are then mouthed by other children. The infectious dose of diarrheal pathogens varies greatly, with the infectious doses of *Salmonella* spp. and *V. cholerae* in the hundreds of thousands to millions, while that for *Shigella* spp. is less than 100 organisms.

Because the major pathophysiologic effect of diarrhea is dehydration due to fluid and electrolyte loss, the most important treatment is **rehydration**. In recent years, simple solutions of glucose, salts, and water given orally have been developed which are proven to be highly effective in treating patients with even the most severe forms of diarrhea. The widespread use of **oral rehydration** in the past two decades, especially in the developing world, has been credited with saving literally millions of lives, primarily young children in whom diarrheal disease takes the greatest toll.

In addition to diarrheal disease, hepatitis is an important infection in the gastrointestinal system. The epidemiology of hepatitis A virus is the same as that of diarrheal pathogens. The virus is usually obtained by ingestion of raw shellfish taken from water contaminated by human sewage or of food handled by an infected food handler who has poor personal hygiene, i.e., individuals who fail to wash their hands after a bowel movement. Hepatitis B and C viruses are spread by contaminated blood. Contracting hepatitis used to be a major concern in individuals receiving blood transfusions. With the recognition of these agents and the development of screening tests for them, the epidemiology of hepatitis due to these two viruses has changed. Hepatitis B and C virus infections (and also human immunodeficiency virus [HIV] infections) are frequent in individuals who share needles while using illicit intravenous drugs. Hepatitis B virus is also spread sexually, especially in populations which practice anal intercourse. The frequency of spread of hepatitis C virus sexually is not well understood. Unlike hepatitis A virus, which causes a relatively mild self-limited disease, hepatitis B virus can cause fulminant, sometimes fatal disease. Hepatitis B and C viruses can also cause a chronic infection culminating in liver failure. Vaccines are available for hepatitis A and B but not C virus.

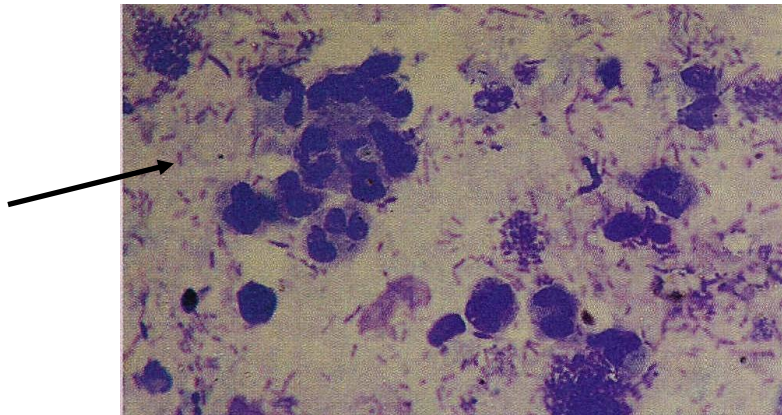
Other important types of gastrointestinal infection are ones in which the resident intestinal microflora or pathogens escape from the bowel and enter "sterile" tissues. One example is *Entamoeba histolytica* trophozoites, which enter the liver and cause an amebic abscess. Another is when there is penetrating trauma to the intestines, as might occur with a gunshot wound to the abdomen or during bowel surgery. In either situation, microbes can escape from the intestines into the peritoneum, where they can cause peritonitis or form an abscess. The organisms causing these infections are typically a mixture of both facultative and anaerobic bacteria that reside in the colon.

Organism	General characteristics	Usual source of infection	Disease manifestation
<b>Bacteria</b>			
<i>Baeteroides (ragilis</i>	Anaerobic, gram-negative bacillus	Endogenous	Abdominal abscess
<i>Campylobaeter</i> spp.	Microaerophilic, curved, gram-negative bacilli	Poultry	Invasive diarrhea, sepsis in AIDS patients
<i>Clostridium difficile</i>	Anaerobic, toxin-producing, gram-positive bacillus	Endogenous; nosocomial	Antibiotic-associated diarrhea, pseudomembranous colitis
<i>Clostridium perfringens</i>	Anaerobic, gram-positive bacillus	Endogenous; high-protein foods	Gangrenous lesions of bowel or gall bladder; food poisoning
Enterohemorrhagic <i>Escherichia coli</i>	Sorbitol-nonfermenting, gram-negative bacillus	Improperly cooked ground beef; apple juice/cider	Enterohemorrhagic colitis, hemolytic-uremic syndrome
Enterotoxigenic <i>Escherichia coli</i>	Lactose-fermenting, gram-negative bacillus	Fresh fruit and vegetables	Traveler's diarrhea, watery diarrhea
<i>Salmonella</i> spp.	Lactose-nonfermenting, gram-negative bacilli	Animal products; typhoid (human to human)	Invasive diarrhea, typhoid fever
<i>Shigella</i> spp.	Lactose-nonfermenting, gram-negative bacilli	Human to human; day care centers	Invasive diarrhea, dysentery
<i>Staphylococcus aureus</i>	Catalase-positive, gram-positive coccus	High-protein foods	Food poisoning
<i>Vibrio</i> spp.	Oxidase-positive, gram-negative bacilli	Raw fish and shellfish	Large-volume watery diarrhea
<i>Yersinia enterocolitica</i>	Lactose-nonfermenting, gram-negative bacillus	Meat and dairy products	Watery or invasive diarrhea
<b>Parasites</b>			
<i>Ascaris lumbricoides</i>	Roundworm	Food, soil	Diarrhea, abdominal discomfort, intestinal obstruction
<i>Cryptosporidium parvum</i>	Coccidian parasite	Fecally contaminated water; day care centers	Malabsorptive diarrhea (chronic in AIDS)
<i>Cyclospora</i> spp.	Coccidian parasite	Water, fresh fruits and vegetables	Malabsorptive diarrhea
<i>Echinococcus</i> spp.	Dog tapeworm	Ingestion of tapeworm eggs from infected dog	Hydatid cyst of liver
<i>Entamoeba histolytica</i>	Amoeba	Water, fresh fruits and vegetables	Diarrhea, amebic dysentery, liver abscess
<i>Giardia lamblia</i>	Flagellated trophozoite	Fecally contaminated water, day care centers	Malabsorptive diarrhea (acute; chronic)
<i>Necator americanus</i> , <i>Ancylostoma duodenale</i> ,	Hookworm	Skin contact with larvae in soil	Anemia, gastrointestinal discomfort
<b>Viruses</b>			
Enterovirus	Nonenveloped RNA virus	Fecal-oral	Diarrhea, respiratory disease, aseptic meningitis, exanthems
Hepatitis A virus	Nonenveloped RNA virus	Shellfish, infected food handlers	Acute, self-limited hepatitis
Hepatitis B virus	Enveloped DNA virus	Blood, direct sexual contact	Acute and chronic hepatitis, fulminant hepatitis, hepatic carcinoma

<b>Organism</b>	<b>General characteristics</b>	<b>Usual source of infection</b>	<b>Disease manifestation</b>
Hepatitis C virus	RNA virus	Blood	Acute and chronic hepatitis, fulminant hepatitis, hepatic carcinoma
Norwalk agent (calicivirus)	Nonenveloped RNA virus	Shellfish, common-source food outbreaks	"24-hour flu," vomiting, diarrhea
Rotavirus	Wheel-like, nonenveloped RNA virus	Human to human (day care center)	Diarrhea, vomiting

## Case One

The patient was an 80-year-old female who 10 days previously had had a cystocele repair performed. At the time of that hospital admission, a urine culture was obtained that revealed > 100,000 CFU/ml of an *Escherichia coli* strain that was susceptible to all antimicrobial agents against which it was tested. Postoperatively, she began a 7 day course of oral cephalexin. She was discharged after an uneventful postoperative course of 3 days. Ten days postoperatively, she presented with a 3-day history of diarrhea. The patient noted multiple, watery loose stools without blood, crampy abdominal pain, and vomiting. She presented with a temperature of 38.2°C, pulse rate of 90/min, respiratory rate of 20/min, and blood pressure of 116/53 mm Hg. Her white blood cell count was normal, but a large number (53%) of immature polymorphonuclear cells were seen. Physical examination, electrolytes, liver enzymes, and lipase were all within normal limits. A methylene blue stain for fecal leukocytes indicated presence of bacteria (arrow in figure below). Cultures for *Salmonella*, *Shigella*, *Yersinia*, and *Campylobacter* spp. were all negative. An enzyme immunoassay (EIA) test which was positive for the presence of a bacterial toxin in the stool established the patient's diagnosis.



1. What organism was causing this woman's diarrhea? How would you confirm this diagnosis? Why was toxin detection rather than culture used to establish the diagnosis of this patient's illness?
2. What in her history was a predisposing factor for her development of this infection? How did it predispose her?
3. What virulence factors does this organism produce, and what roles do these factors play in the pathogenesis of disease?
4. Why is this organism particularly problematic as a nosocomial pathogen?
5. Why are treatment failures and disease relapses thought to occur frequently with this organism?

## Case Two

Mr. D., a 33-year-old fully immunized, rather nervous accountant who is blood group O positive and taking H<sub>2</sub> blockers for ulcer disease; his 29-year-old healthy wife; and their 10-month-old baby boy returned from a 2-week trip to South America. The next morning Mr. D. passed a semisolid stool, which was quickly followed by a large watery bowel movement. Within an hour he passed another large watery stool, now opaque gray–white in color. He vomited several times and became slightly sweaty. After passing another large watery stool, Mr. D. called his physician, who advised him to go to the emergency department. When he arrived there Mr. D. was afebrile but had a rapid heart rate with a feeble pulse and low blood pressure. He complained of muscle cramps and dizziness. All these signs and symptoms were consistent with a significant loss of extracellular fluids. Laboratory studies showed a normal leukocyte count, a slightly elevated level of serum sodium, a normal serum potassium level, and an elevated blood urea nitrogen level, also consistent with dehydration.

Mr. D. was immediately given 2 liters of fluid intravenously and then started on oral rehydration solution. His stool volumes progressively diminished over 48 hours, and he was discharged. Because of the suspected diagnosis, special media were used to isolate organisms other than *E. coli* and they came back positive.

Mrs. D., a native Peruvian, had two loose bowel movements on the second day of her husband's illness. Her stool culture grew only *Escherichia coli*.

1. What is the most likely organism causing Mr. D's disease?
2. Are all enteric bacteria capable of causing disease, or are some more frequently pathogenic than others?
3. What are the clinical manifestations caused by the diagnosed pathogen?
4. Why did Mrs. D. not show the same symptoms?
5. What factors are involved in colonization? What factors are involved in causing symptoms?
6. What is the proper therapy for this disease?

### **Case Three**

A nonprofit day care center in Juneau, Alaska cared for about 30 children, both infants and toddlers. In late August 1982, five cases of diarrhea were identified when a nursery employee submitted stool samples from children with chronic diarrhea to the Southeastern Regional Lab, Division of Public Health. As part of the epidemiological investigation, the Juneau Health Center, in cooperation with the nursery, discovered an additional eight cases of diarrhea caused by the same pathogen from the nursery population. Nine of 10 infants less than 16 months old were affected, and 4 of 24 toddlers (aged 16 months through 3 years) were affected. Two cases of diarrhea caused by the pathogen were identified among siblings of positive children. Both had attended the nursery during July and were enrolled in the day care center.

Clinical signs and symptoms of the infected children showed that 52% had suffered from foamy diarrhea for more than 1 week during the summer, with bloating and loss of appetite in half of them. 48% of the infected children were asymptomatic. The pathogen was identified by microscopically examining fecal smears. Oval cysts were observed.

1. What is the pathogen causing the infection? List 4 additional pathogens that could cause the diarrhea?
2. How would you have treated those infected by the pathogen?
3. Describe an appropriate way to have managed the outbreak.