Chapter 73: Disorders Presenting Primarily With Diarrhea

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FIGURE 73-1.

GENERAL ASSESSMENT OF PATIENTS WITH DIARRHEA

INTRODUCTION AND EPIDEMIOLOGY

This chapter discusses the general assessment of patients with diarrhea and the special considerations of acute infectious and traveler's diarrhea, *Clostridium difficile* diarrhea and colitis, inflammatory bowel disease, ileitis and colitis, and ulcerative colitis.

Acute diarrhea is the sudden onset of an increase in the normal water content of stool. In general, humans lose approximately 10 mL/kg/day of fluids in stool. The increased water content of diarrhea results in an increased frequency of stools from 3 or more times daily to more than 20 bowel movements in a 24-hour period. Diarrhea is an increased frequency of defecation, usually greater than 3 bowel movements per day for a daily stool weight exceeding 200 grams.[1,2] Practically speaking, however, diarrhea is present when the patient is making more stools of lesser consistency more frequently.

PATHOPHYSIOLOGY

There are four basic mechanisms of diarrhea: increased intestinal secretion, decreased intestinal absorption, increased osmotic load, and abnormal intestinal motility. Normally, the jejunum receives between 6 and 8 L per day of fluid in the form of oral intake and gastric, pancreatic, and biliary secretions. Dietary intake actually constitutes a small portion of the jejunal load (1.5 L). A healthy small intestine absorbs nearly 75% of the fluid to which it is exposed. The 2 L of fluid not absorbed by the small intestine then enters the colon, where fluid is absorbed at an even higher rate. The absorptive power of the colon approaches 90% efficiency and far exceeds that of the small intestine. In fact, the colon can make up for a decrease in small intestinal absorption. Under normal conditions, very little fluid (<100 mL) is lost in the stool each day.[3]

In diarrheal states, normal intestinal physiology is disrupted. At a cellular level, intestinal absorption occurs through the villi, and secretion occurs through the crypts. Fluids are absorbed by two mechanisms: passively with the transport of sodium and actively with the absorption of glucose. Selected enterotoxins block the passive sodium resorption and specifically stimulate sodium excretion, resulting in a net loss of fluid. The glucose-dependent mechanism of water absorption, however, is unaffected by these toxins and can be exploited by including glucose in the rehydration treatments. The composition of oral rehydration therapies recommended by the World Health Organization is based largely on this physiology. In addition, diarrheal states, enterotoxins, inflammation, or ischemia disrupt the structure of the intestinal villi preferentially with less involvement in the crypts. As a result, diarrhea occurs because of diminished intestinal villi absorption *and* unopposed crypt secretion (the crypts are more resilient after injury).[4]

Another mechanism by which disease processes cause diarrhea is by the delivery of an osmotic load to the intestine. For example, administration of a laxative results in the collection of an osmotically active, nondigestible agent within the intestinal lumen. Other substances such as diet products and medications (e.g., colchicine) have similar effects. Osmosis occurs, drawing fluid into the intestinal lumen, and results in diarrhea. Increased intestinal motility also causes diarrhea. This mechanism is responsible for diarrhea in patients with irriTable bowel syndrome, neuropathies, or a shortened intestine secondary to surgery.

Diarrheal illness is primarily a viral infection (norovirus), but can also be caused by bacteria and parasites. Antibiotic and nosocomial diarrhea is most often caused by *C. difficile*. Many drugs affect gastrointestinal function. Erythromycin accelerates gastric emptying. Clavulanate stimulates small bowel motility. Other drugs that cause diarrhea are laxatives, sorbitol, lactose, nonsteroidal anti-inflammatory drugs, and cholinergics. Inflammatory bowel disease, ulcerative colitis, and Crohn's disease are characterized by diarrhea. **If patients have fecal evidence of inflammation and *Shigella*, *Salmonella*, *Campylobacter*, *C. difficile*, or *Entamoeba histolytica* have been excluded, suspect inflammatory bowel disease.** Less common causes of severe diarrhea include gastrointestinal bleeding, thyrotoxicosis, toxin exposure, and mesenteric ischemia, which are addressed elsewhere in the text.

CLINICAL FEATURES

History

After confirming a diarrheal illness, focus on identifying the cause. Determine whether the diarrhea is acute (<3 weeks) or chronic (>3 weeks). The acute diarrheas are of greatest concern to the emergency physician as they are more apt to be a manifestation of an immediately life-threatening illness (infection, ischemia, intoxication, or inflammation).[2] In the United States, most infectious diarrheal illnesses are caused by noroviruses or rotaviruses and occur in the winter.[5]

Ask directed questions to characterize the diarrhea: Is the diarrhea bloody or melenic? Is it associated with possible food poisoning or the ingestion of certain foods, such as milk or sorbitol? Does it resolve or persist with fasting? If so, this can indicate an osmotic or secretory diarrhea, respectively. Are the stools of smaller volume, localizing to the large intestine, or of larger volume, indicating small intestine pathology? What symptoms accompany the diarrhea? Is there fever or abdominal pain, which may suggest diverticulitis, infectious gastroenteritis, or inflammatory bowel disease? Seizures accompanying diarrhea often point toward shigellosis but could also indicate theophylline toxicity or hyponatremia. Does the patient have heat intolerance and anxiety, suggesting thyrotoxicosis, or paresthesias and reverse temperature sensation, suggesting ciguatera poisoning?

Next, define the host by obtaining the medical and surgical history. The differential diagnosis for diarrhea is broadened if the patient is immunocompromised. Is the patient taking medication that may cause diarrhea? Has the patient recently traveled outside the United States or to a rural area? Rural hiking places the patient at risk for *Giardia,* particularly if water-purification procedures were not strictly followed, and travel to third-world countries increases the chances of parasitic infection and traveler's diarrhea. A patient's occupation may be a clue to a diagnosis of organophosphate poisoning.

Physical Examination

Some examination findings helpful for diagnosis include thyroid enlargement, masses, oral ulcers, erythema nodosum, episcleritis, or an anal fissure, which would point toward inflammatory bowel disease. Reiter's syndrome, the triad of arthritis, conjunctivitis, and urethritis or cervicitis, should cause concern for *Salmonella, Shigella, Campylobacter,* or *Yersinia* infection.

Abdominal and rectal examinations are critical. Especially in the elderly, fecal impaction may result in diarrhea as liquid stool passes around the impaction. Pay attention to the presence or absence of surgical scars, tenderness, masses, or peritoneal signs. Check the stool for blood, because bloody diarrhea can be caused by inflammation, infection, or ischemia. An elderly patient with bloody diarrhea and abdominal pain out of proportion to the physical examination may have mesenteric ischemia—a true emergency.

DIAGNOSTIC STOOL EVALUATION

Diagnostic testing is rarely immediately helpful in the ED, but it can be helpful at patient follow-up. Since most diarrheal illnesses are self-limited, viral, or last less than 24 hours, most patients who present within 24 hours of onset need no microbiologic examination. **Patients who have severe abdominal pain, fever, and diarrhea that is voluminous, purulent, or bloody may have acute infectious diarrhea associated with the following pathogens: *Salmonella*, *Campylobacter*, *Shigella*, shiga toxin-producing *Escherichia coli*, *Yersinia*, *Vibrios*, or *C. difficile*.**[5] Patients fitting this subset will require microbiologic evaluation, as described next.

Wright's Stain

When applied to a stool sample, Wright's stain allows detection of fecal leukocytes. A positive Wright's stain has a sensitivity of 52% to 82% and a specificity of 83% for the presence of bacterial pathogens by stool culture.[6] Historically, Wright's stain for fecal leukocytes has been used to differentiate invasive from noninvasive infectious diarrheas. In the past, this was an important distinction: physicians were reluctant to prescribe antibiotics for patients with infectious diarrhea because of the fear of prolonging the *Salmonella* carrier state. They therefore reserved antimicrobial treatment for the toxic patients who they felt *truly* had invasive diarrhea. Many physicians now treat patients with diarrheal illness with antibiotics regardless of whether or not the diarrhea is invasive or bacterial in origin.[7]

Bacterial Stool Culture

Bacterial stool culture is expensive and labor intensive and plays a minor role in the ED evaluation of diarrhea. The diagnostic yield of stool cultures is probably <5%, unless there is careful patient selection.[1] Obtain stool cultures for bacteria in ill children; toxic, dehydrated, or febrile patients; patients with a diarrheal illness >3 days; patients with blood or pus in the stool; and the immunocompromised. For systemic illness, fever, or bloody stools, test for *Salmonella*, *Shigella*, *Campylobacter*, Shiga toxin-producing *E. coli*, or amoebic infection.[1,4,5] Many laboratories culture for only three common bacterial pathogens: *Salmonella, Shigella,* and *Campylobacter.* If other enteric pathogens are suspected, notify the laboratory so that appropriate testing may be performed.

Ova and Parasite Evaluation

Suspect parasitic infection and evaluate stool for ova and parasites in travelers exposed to untreated water and those presenting with diarrhea for more than 7 days. Stool tests for ova and parasites lack sensitivity, because many parasites are fastidious, and shedding of the organisms is intermittent. Multiple samples may need to be collected for a positive result. Direct immunofluorescence staining improves the sensitivity for detecting *Giardia* and *Cryptosporidium.*[8]

Clostridium difficile Toxin Assay

C. difficile infection is the commonest cause of antibiotic-associated or nosocomial diarrhea. Diagnosis is by the *C. difficile* toxin assay. Unfortunately, this assay has a 10% false-negative rate, and the turnaround time on the test approaches 24 hours.[9]

Other Diagnostic Tests

If diarrhea is not infectious in origin, data acquisition should be dictated by the differential diagnosis. Severely dehydrated patients need serum electrolyte and renal function measurements. Serum drug levels can assist the physician in making the diagnosis of theophylline, lithium, or heavy metal intoxication. In patients with a history of abdominal surgery, abdominal films may help rule out partial obstruction as a cause of diarrhea. A chest radiograph may help diagnose *Legionella* pneumonia in a patient with diarrhea and a cough. For patients in whom mesenteric ischemia is suspected, obtain a serum lactate, IV contrast CT scan, or mesenteric angiography.

Treatment

Severely dehydrated patients need IV hydration. Oral rehydration with a glucose-based electrolyte solution can be initiated in patients without associated nausea or vomiting and without severe dehydration. Glucose-containing, caffeine-free beverages are the fluids of choice. The glucose transport mechanism is unaffected by enterotoxins, allowing for water absorption in the small intestine. For patients who can afford to buy it, Gatorade® is a good rehydration choice for patients with mild dehydration. The World Health Organization recommends a solution with a higher sodium concentration for more extensive dehydration. Mildly dehydrated patients should aim to drink 30 to 50 mL/kg over the first 4 hours. For moderate dehydration, patients should drink 100 mL/kg over the next 4 hours.[2]

Counsel patients to avoid caffeine, which stimulates gastric motility, and sorbitol-containing chewing gum or raw fruits, which can worsen osmotic diarrhea. Initially, avoid lactose until the colonic villi are able to recover and produce the necessary digestive enzymes. Encourage patients to attempt early solid food intake, but with the previously mentioned restrictions, because eating expedites the recovery from diarrheal illnesses.[10]

ACUTE INFECTIOUS AND TRAVELER'S DIARRHEA

INTRODUCTION AND EPIDEMIOLOGY

Viruses cause the vast majority of infectious diarrheas, followed by bacterial and parasitic organisms. **Norovirus causes 50% to 80% of all** infectious diarrhea in the United States, followed with much less frequency by non–Shiga toxin producing *E. coli*, *C. difficile*, invasive bacteria, Shiga toxin-producing *E. coli*, and protozoa.[1,5]

Approximately 40% of the 50 million Americans who travel annually to developing countries develop diarrhea in the first 2 weeks of travel.[11] **A history of foreign travel is associated with an 80% probability of bacterial diarrhea.**[5] The most important risk factor for traveler's diarrhea is the destination of travel, with the risk increasing with travel to areas of lower socioeconomic status. Countries in Asia, Africa, Latin America, and parts

of the Middle East are considered high-risk destinations for traveler's diarrhea, with incidence rates ranging between 20% and 75%.[12] Other risk factors include the level of food contamination, the season of travel (rainy seasons are associated with a higher risk of traveler's diarrhea), use of a proton pump inhibitor, previous contraction of traveler's diarrhea (suggests genetic susceptibility), and the type of travel (adventure travel, camping, backpacking, and living with native inhabitants are associated with higher risk).[13] The major bacteria responsible are the toxin and non–toxin-producing strains of *E. coli*. These strains of *E. coli* make up most identifiable cases in Mexico and South America. The invasive bacteria, such as *Campylobacter jejuni*, *Shigella*, and S*almonella,* are more commonly seen in travelers to southern Asia.[5,12]

CLINICAL FEATURES

The presence of severe abdominal pain, fever, or bloody stool requires microbiologic studies to rule out bacterial or amoebic infection.[11] Assess stool for polymorphonuclear white blood cells or fecal leukocytes by microscopy or by immunoassay for the neutrophil protein lactoferrin.[5] The presence of fecal leukocytes increases the likelihood of a bacterial pathogen. However, bloody stool without white blood cells is a common feature of Shiga toxin–producing *E. coli* or *E. coli* O157:H7 and colitis that is due to *E. histolytica*.[1,5]

Laboratory

Testing Obtain stool culture for *Salmonella*, *Shigella*, *Campylobacter*, and *E. coli* O157:H7; assay for Shiga toxin; and obtain microscopy or antigen assay for *E. histolytica*.[5]

Exposure of a traveler or hiker to untreated water and illness that persists for more than 7 days should prompt evaluations for protozoal pathogens. Test stool for *E. histolytica* antigen, *Giardia intestinalis* antigen, and *Cryptosporidium parvum* antigen by enzyme immunoassay.[1,5] Rarely, helminthes such as *Ascaris, Enterobius,* and *Strongyloides* have been implicated.[14]

TREATMENT

Treatment of infectious diarrhea includes antibiotics, antimotility agents, restoration of fluid balance, and avoidance of agents that worsen diarrhea (Table 73-1). Loperamide and antibiotics improve outcome.[15,16]

TABLE 73-1

Empiric Treatment of Traveler's Diarrhea in the Adult

Rehydration			
Fluids: chicken broth with fruit juices, Gatorade®, noncaffeinated sodas, packages of salts and glucose to be reconstituted with boiled or treated water, CeraLyte 90®, Pedialyte® Foods: complex carbohydrates (bananas, bread, rice, apple juice, and tortillas), potatoes, crackers, *Lactobacillus*-containing yogurt			
	Trade Name	**Dosage**	**Comments**
Antimotility Agents			
Bismuth subsalicylate	Pepto-Bismol®	30 mL or 2 tablets every 30 min for 8 doses; repeat on day 2	Salicylate toxicity may occur with excessive dosing; may cause bismuth encephalopathy in HIV-positive patients.
Loperamide	Imodium®	4 milligrams initially, then 2 milligrams after each unformed stool for no more than 2 days; maximum, 16 milligrams per day	Preferred first-line agent for antimotility, with minimal central opiate effects. Can be used with antibiotics.
Diphenoxylate and atropine	Lomotil®	4 milligrams four times a day for 2 days	Second-line agent with more central opiate effects (narcotic related to meperidine); may potentiate the action of barbiturates, tranquilizers, and alcohol.
Antibiotics			

Ciprofloxacin	Cipro®	500 milligrams single dose or 500 milligrams twice a day for 3 days	For moderately severe illness in adults; complete 3-day course if single dose fails; significant drug–drug interactions may occur.
Azithromycin	Zithromax®	1000 milligrams in a single dose	Safe for children and pregnant women
Trimethoprim/sulfamethoxazole (see sulfamethoxazole-trimethoprim)	Bactrim®	160 milligrams/800 milligrams for single dose, 160 milligrams/800 milligrams twice a day for 3 days	For moderately severe illness; resistance limits reliable effectiveness.
Rifaximin[13,22]	Xifaxan®, Salix®	200 milligrams PO three times daily for 3 days	For moderately severe illness; do not use for fever or bloody stools; class C in pregnancy.

Abbreviation: HIV = human immunodeficiency virus.

For years, physicians avoided antibiotic use in the treatment of infectious diarrhea because of a fear of prolonging the *Salmonella* carrier state. This fear arose from an article published in 1969 in which the duration of *Salmonella* excretion was felt to be prolonged after antibiotic treatment.[17] Contemporary literature has put this to rest. Antibiotics shorten the duration of illness by about 24 hours.[7,17] Regardless of the causative agent, all patients—even those who had a negative Wright's stain, negative stool culture, and a low diarrheal illness score, suggesting less clinically significant disease and/or a viral cause—improve on ciprofloxacin.[18] Even though most cases of infectious diarrhea are self-limited, because of the inconveniencing and debilitating nature of the disease, **we recommend ciprofloxacin treatment for all patients believed to have an infectious diarrhea who do not have a contraindication to the drug** (e.g., children, allergy, pregnancy, or drug interaction). There are reports of growing fluoroquinolone resistance in bacterial pathogens.[19] Trimethoprim/sulfamethoxazole also shortens the duration of infectious diarrhea in adults but may be inferior to a course of ciprofloxacin because of resistant organisms.[18] Concerns remain about the impact of ciprofloxacin on the intestinal flora[20] and its side effect profile, and other non–gastrointestinal-absorbed agents such as rifaximin are an option.[21] (See **Table 73-2** for specific treatments.)

TABLE 73-2

Antimicrobial Recommendations for Infectious Pathogens in Adults

Organism	Primary Treatment	Alternative Treatment
Empiric treatment—but not for bloody diarrhea; not for Shiga toxin *E. coli* 0157:H7	Ciprofloxacin 500 milligrams PO twice a day for 5 days	Trimethoprim-sulfamethoxazole DS, 1 tab PO twice a day for 5 days
C. difficile	Metronidazole 500 milligrams PO 3 times a day for 14 days	Vancomycin, 125 milligrams PO four times a day for 14 days
E. coli 0157:H7	No antibiotics	No antibiotics
Listeria monocytogenes	No antibiotics	No antibiotics
Yersinia	No antibiotics; usually self-limited	Ciprofloxacin 500 milligrams PO twice a day for 3 days; or trimethoprim-sulfamethoxazole DS,1 tab PO twice a day for 3 days
Salmonella non-typhi	Ciprofloxacin 750 milligrams PO twice a day for 5 days	Azithromycin 500 milligrams PO once a day for 7 days
Shigella	Ciprofloxacin 750 milligrams PO twice a day for 3 days	Azithromycin 500 milligrams PO once a day for 3 days
V. cholerae	Doxycycline 500 milligrams PO for one dose *OR* Azithromycin 1 gram PO for one dose	Trimethoprim-sulfamethoxazole DS,1 tab PO twice a day for 3 days

Organism	Primary Treatment	Alternative Treatment
E. histolytica	Metronidazole 750 milligrams PO three times a day for 10 days *AND* Paromomycin 10 milligrams/kg three times a day PO for 7 days	Metronidazole *AND* iodoquinol 650 milligrams PO three times a day for 20 days *OR* Tinidazole 2 grams PO once a day for three days *AND* paromomycin or iodoquinol
Cyclospora	Trimethoprim-sulfamethoxazole DS, 1 tab PO twice a day for 10 days	
Giardia	Tinidazole 2 grams PO for one dose	Nitazoxanide 500 milligrams PO twice a day for 3 days *OR* Metronidazole 750 milligrams PO three times a day for 10 days *OR* Paromomycin 10 milligrams/kg/day PO three times a day for 10 days

Note: Length of treatment often varies with different sources.

Loperamide shortens the duration of symptoms when combined with an antibiotic regimen. Loperamide, bismuth subsalicylate, and kaolin are the only agents that are labeled as antidiarrheals. **Do not use antimotility** agents in the subset of patients with bloody diarrhea or suspected inflammatory diarrhea because of the possibility of prolonged fever, toxic megacolon in *C. difficile* patients, and hemolytic uremic syndrome in children infected with Shiga-toxin producing *E. coli*.[1]

Probiotics are safe and beneficial when used alongside rehydration therapy.[23] Proton pump inhibitors are not effective.[15]

DISPOSITION

Admit the toxic patient and any patient who cannot comply with oral rehydration. Be conservative in admitting those at extremes of age. Most patients with diarrhea can be discharged home.

The best way to combat many infectious diarrheas is with prevention. Counsel families about frequent hand washing to minimize spread of disease. Counseling families about the proper selection and preparation of food and beverages consumed while traveling is a cornerstone of prevention.[12] Encourage the use of boiled, bottled, and carbonated water for drinking, brushing teeth, and preparing food and infant formula. Water can be made safe by boiling, treating it chemically, or filtering.[12] A quick phrase for prevention is, "Peel it, boil it, cook it, or forget it!"

In addition, vaccines against the most common etiologic agent, rotavirus, are now available.[24]

Provide work excuses for patients employed in the food, day-care, and healthcare industries.

CLOSTRIDIUM DIFFICILE–ASSOCIATED DIARRHEA AND COLITIS

INTRODUCTION AND EPIDEMIOLOGY

C. difficile is a spore-forming obligate anaerobic bacillus that causes infection ranging from mild diarrhea to severe pseudomembranous colitis. ***C. difficile* infection is the most common cause of bacterial diarrhea in hospitalized patients in Europe and North America.** The incidence and severity of disease has increased at an alarming rate of 25% per year since 2000.[25] A more virulent strain of *C. difficile* called North American pulsed-field type 1 or B1/NAP1/027 affects hospitalized patients, but can also occur in community-dwelling healthy adults.[26] This strain causes more severe disease that more often progresses to toxic megacolon.

The organism secretes two toxins, A and B, that cause a secretory diarrhea. At the most severe end of the spectrum, three different syndromes have been described: neonatal pseudomembranous enterocolitis, postoperative pseudomembranous enterocolitis, and antibiotic-associated pseudomembranous colitis. In pseudomembranous colitis, membrane-like yellowish exudative plaques overlie and replace necrotic intestinal mucosa. Recent antibiotic use, gastrointestinal surgery or manipulation, severe underlying medical illness, chemotherapy, and advancing age are risk factors for pseudomembranous colitis. Transmission of the organism is by direct human contact as well as contact with inanimate objects (commodes, telephones, rectal thermometers).

PATHOPHYSIOLOGY

Hospitalized patients are colonized with *C. difficile* in 10% to 25% of cases, so the development of diarrhea in recently discharged patients is suggestive of *C. difficile* infection. There is a linear relationship between the length of hospital stay, colonization with *C. difficile,* and the development of *C. difficile* diarrhea. Broad-spectrum antibiotics—most notably clindamycin, second- and third-generation cephalosporins, ampicillin/amoxicillin, and fluoroquinolones—reduce fecal anaerobes, which are needed for carbohydrate metabolism and bile acid breakdown. Accumulation of gut carbohydrates can cause osmotic diarrhea, and the accumulation of bile acids, which are colonic secretory agents, also results in diarrhea. Toxin-producing *C. difficile* then flourishes within the colon. Almost any antibiotic (including metronidazole and vancomycin) can lead to pseudomembranous colitis, and chemotherapeutic agents, proton pump inhibitors, and antiviral agents have also been implicated. Bowel ischemia, inflammatory bowel disease, recent bowel surgery, uremia, malnutrition, shock, advanced age, peripartum status, and Hirschsprung's disease also contribute to the development of *C. difficile* infection and pseudomembranous colitis.[26]

Most disease-producing strains of *C. difficile* produce two toxins: toxin A, an enterotoxin, and toxin B, a cytotoxin, that interact in a complex way to produce pseudomembranous colitis and its associated symptoms.

CLINICAL FEATURES

The disease typically begins 7 to 10 days after the institution of antibiotic therapy, although symptoms may occur up to 60 days after the antibiotic is discontinued. Pseudomembranous colitis results in a spectrum of clinical manifestations that vary from frequent, mucoid, watery stools to a toxic picture that includes profuse diarrhea (20 to 30 stools per day), crampy abdominal pain, fever, leukocytosis, and dehydration. Stool examination may demonstrate fecal leukocytes, which are not generally found in more benign forms of antibiotic-induced diarrhea.[27] In 1% to 3% of patients, toxic megacolon or colonic perforation may occur in patients with pseudomembranous colitis.[28]

DIAGNOSIS

The diagnosis is suggested by a history of diarrhea that develops during administration of antibiotics or within 2 weeks of their discontinuation.

Stool Assays

The diagnosis is confirmed by the demonstration of *C. difficile* in the stool and by the detection of the toxin in stool filtrates. The organism is best identified by stool culture using a selective growth medium. This technique has a sensitivity approaching 100%, but lacks specificity because the presence of *C. difficile* does not necessarily implicate it in the cause of the disease.

Instead, *C. difficile* toxins are detected directly using a number of techniques including tissue-culture assay, enzyme-linked immunosorbent assays, latex agglutination, dot-immunobinding assays, and polymerase chain reaction. Tests vary in their sensitivity, specificity, and time to completion. Although tissue-culture assays are considered the gold standard, most laboratories use the enzyme-linked immunosorbent assay technique to detect the clostridial toxins; it has a sensitivity of 63% to 94% and a specificity of 75% to 100%.[28] Five to 20% of patients require more than one stool specimen to detect toxin.

Colonoscopy

Colonoscopy reveals characteristic yellowish plaques within the intestinal lumen. Lesions may be seen throughout the entire alimentary tract, although they are typically limited to the right colon. Colonoscopy is not routinely needed to establish a diagnosis, but may be used in patients who require a rapid diagnosis and those who cannot produce a stool specimen due to ileus.

TREATMENT

Mild *C. difficile* infection in an otherwise healthy patient is treated by discontinuing the offending antibiotic.[25] This is effective in only about 20% of cases, however. Severely ill persons must be hospitalized. For specific antibiotic regimens, see **Table 73-3**.[29,30] Fidaxomicin (macrolide antibiotic) 200 milligrams PO twice a day for 10 days is also available for treatment.[31]

TABLE 73-3

Treatment of *Clostridium difficile* Infection Based on Severity of Illness

Disease Severity	Treatment
Mild: WBC <15,000 mm^3	Metronidazole 500 milligrams PO three times a day for 14 days
Moderate: WBC >15,000 mm^3, patient able to tolerate PO	Vancomycin 125 milligrams PO four times a day for 14 days
First relapse	Metronidazole 500 milligrams PO three times a day for 14 days
Second relapse	Vancomycin 125 milligrams PO four times a day for 14 days; then taper dose over 4 weeks
Severe disease with toxic megacolon	Metronidazole 500 milligrams IV every 6 hours *and* vancomycin 500 milligrams PO every 6 hours (PO preferred to IV)

Note: Assume the offending antibiotic is discontinued.

Rarely, emergency colectomy may be required for patients with severe *C. difficile* infection. Indications for emergency colectomy based on 30-day mortality include leukocytosis greater than 20,000 mm^3, lactate >5 mmoL/L, age >75 years, immunosuppression, shock, toxic megacolon, colonic perforation, or multiorgan system failure.

Relapses occur in 20% to 30% of patients.[29] Patients with prolonged antibiotic use, prolonged hospitalization, advanced age, diverticulosis, or multiple comorbidities are at increased risk for relapse.[26] The addition of monoclonal antibodies against the toxin to antibiotics reduces infection recurrence.[32] Probiotic treatment is not a useful adjunct for *C. difficile* infection.[33] The use of antidiarrheal agents is controversial.[34] Steroids are rarely needed.

Ensure contact isolation, use of personal protective equipment, and good hand washing with soap and water when caring for patients with suspected *C. difficile*–associated disease. Alcohol-based rubs are not effective in eliminating the spores of *C. difficile.*

DISPOSITION

Hospitalize patients with severe diarrhea, clinical toxicity, or symptoms that persist despite appropriate outpatient management. Consult the surgeon for suspected toxic megacolon or intestinal perforation for consideration of colectomy. For those patients who are discharged, discontinue antibiotics and encourage good oral hydration. Follow the antibiotic recommendations in Table 73-3

INFLAMMATORY BOWEL DISEASE/ILEITIS/COLITIS CROHN'S DISEASE

INTRODUCTION AND EPIDEMIOLOGY

Crohn's disease is a chronic granulomatous inflammatory disease of the gastrointestinal tract of unknown origin. **Crohn's disease can involve any part of the gastrointestinal tract from the mouth to the anus.** The ileum is involved in the majority of cases. In 20%, the disease is confined to the colon, making differentiation from ulcerative colitis difficult. The terms *regional enteritis, terminal ileitis, granulomatous ileocolitis,* and *Crohn's disease* are all used to describe the same disease process.

The peak incidence of Crohn's disease occurs between 15 and 22 years of age, with a secondary peak from 55 to 60 years. It is more common in women. The incidence is increasing, especially in children.[35] The disease is four times more common among Jews than non-Jews and is more common in whites than blacks, Asians, or Native Americans. A family history of inflammatory bowel disease is present in 10% to 15% of patients, particularly with early onset of disease. Ulcerative colitis as well as Crohn's disease may be present in other family members, and siblings of patients with Crohn's disease have a higher incidence of the disease. Smoking, oral contraceptive use, and the use of nonsteroidal anti-inflammatory agents worsen the course of the disease.

PATHOPHYSIOLOGY

The most important pathologic feature of Crohn's disease is the involvement of all the layers of the bowel and extension into mesenteric lymph nodes. The disease is discontinuous, with normal areas of bowel ("skip areas") located between one or more involved areas. Longitudinal, deep mucosal ulcerations are characteristic. If ulcerations penetrate the bowel wall, fissures, fistulas, and abscesses result. Late in the disease, a cobblestone appearance of the mucosa results from the criss-crossing of ulcers with intervening normal mucosa.

CLINICAL FEATURES

The clinical course of Crohn's disease varies and in the individual patient is unpredictable. Abdominal pain, anorexia, diarrhea, and weight loss are present in most cases. Chronic abdominal pain, fever, and diarrhea may be present for several years before definitive diagnosis is established. Perianal fissures or fistulas, hematochezia, abscesses, or rectal prolapse can develop, particularly with colonic involvement.[36,37] Patients may also present with complications of the disease, such as obstruction with vomiting, crampy abdominal pain, and obstipation, or an intra-abdominal abscess with fever, abdominal pain, and a palpable mass.

In 10% to 20% of patients, the extraintestinal manifestations of arthritis, uveitis, or liver disease may be presenting symptoms. Crohn's disease should also be considered in the differential diagnosis of patients with fever of unknown etiology.

The clinical course and manifestations of the disease appear to be related to its anatomic distribution: in 30% the disease involves only the small bowel, in 20% only the colon is involved, and in 50% both the small bowel and colon are involved. A small percentage of patients present with disease involving the mouth, esophagus, and stomach. Crohn's disease of the stomach may demonstrate symptoms of peptic ulcer disease.

Extraintestinal manifestations are seen in up to 40% of patients with Crohn's disease (**Table 73-4**),[38] and the incidence and types of extraintestinal complications are similar in patients with Crohn's disease and ulcerative colitis.

TABLE 73-4

Common Extraintestinal Manifestations of Inflammatory Bowel Disease

Manifestation	Description
Arthritic	
Peripheral arthritis	Migratory monoarticular or polyarticular pain in peripheral joints (hip, knee, ankle, wrist) with effusion
Ankylosing spondylitis	Pain and stiffness of spine, hips, neck, and rib cage with limitation in truncal motion, loss of lumbar lordosis; decreased chest expansion and forward cervical flexion in advanced disease
Sacroiliitis	Low back pain with morning stiffness, relieved by exercise; progressive joint sclerosis
Ocular	
Episcleritis	Eye burning or itching without visual changes or pain; scleral and conjunctival hyperemia
Uveitis	Acute blurring of vision, photophobia and pain; perilimbic scleral injection
Dermatologic	
Erythema nodosum	Painful, red, raised nodules on extensor surfaces of arms or legs
Pyoderma gangrenosum	Ulcerative lesions with a necrotic center and violaceous skin typically found in pretibial region or trunk
Hepatobiliary	
Cholelithiasis	Varies from asymptomatic stones to right upper quadrant pain, fever, vomiting

Manifestation	Description
Fatty liver	Mild right upper quadrant pain; hepatomegaly
Pericholangitis	Mild elevation in serum alkaline phosphatase, asymptomatic
Chronic active hepatitis	Autoimmune elevation of liver aminotransferase enzymes, may progress to cirrhosis
Primary sclerosing cholangitis	Pruritus progressing to jaundice, fatigue, and lethargy; laboratory findings vary from mild elevations of alkaline phosphatase to cirrhosis, portal hypertension, and liver failure; male predominance
Cholangiocarcinoma	Extrahepatic biliary mass, evidence of biliary obstruction, jaundice, right upper quadrant pain, fever, malaise
Pancreatitis	Varies from painless elevation of serum amylase to clinically apparent central abdominal pain radiating to back; may be associated with drugs such as azathioprine, 6-mercaptopurine, sulfasalazine, mesalamine, olsalazine, metronidazole
Vascular	
Thromboembolic disease	Symptoms of deep venous thrombosis and pulmonary emboli; portal vein, mesenteric vein, and hepatic venous thrombosis reported
Other	
Malnutrition	Fatigue, malaise, muscular wasting, cachexia
Chronic anemia	Fatigue, malaise, pallor, dyspnea; may be microcytic (blood loss), macrocytic (B_{12} deficiency), or autoimmune hemolytic
Nephrolithiasis	Flank pain, nausea, vomiting, hematuria; stones result from increased dietary oxalate absorption (calcium oxalate stones) and dehydration (urate stones)

DIAGNOSIS

In most patients, the definitive diagnosis of Crohn's disease is established months or years after symptom onset. A provisional diagnosis of appendicitis or pelvic inflammatory disease may change to Crohn's disease after imaging or at the time of surgery. A detailed history asking about previous bowel symptoms that preceded the onset of acute right lower quadrant pain provides clues to the correct diagnosis.

ED evaluation focuses on determining the severity of the attack; identifying significant complications such as obstruction, intra-abdominal abscess, life-threatening hemorrhage, or toxic megacolon; and eliminating other possible causes of the patient's complaints.

Laboratory Testing

Laboratory evaluation should include a CBC, serum electrolytes, BUN, creatinine, and a type and cross-match where appropriate. C-reactive protein levels can monitor disease activity.[39] Fecal markers of inflammation (calprotectin and lactoferrin) are other markers of disease activity.[40]

Imaging

Plain radiographs of the abdomen may demonstrate obstruction, perforation, or toxic megacolon. Abdominal CT scanning with PO and IV contrast identifies bowel wall thickening, segmental narrowing, destruction of the normal mucosal pattern, mesenteric edema, fistulas, and abscesses, which suggest the diagnosis of Crohn's disease. Extraintestinal complications such as gallstones, renal calculi, sacroiliitis, and osteomyelitis can also be seen on CT scan. Diagnosis is confirmed by colonoscopy.

Differential Diagnosis

The differential diagnosis of Crohn's disease includes lymphoma, ileocecal amebiasis, sarcoidosis, deep chronic mycotic infections involving the gastrointestinal tract, gastrointestinal tuberculosis, Kaposi's sarcoma, *Campylobacter* enteritis, and Y*ersinia* ileocolitis. Fortunately, most of these are uncommon conditions and can be differentiated by appropriate laboratory tests. *Yersinia* ileocolitis and *Campylobacter* enteritis may cause chronic abdominal pain and diarrhea similar to Crohn's disease, but can be diagnosed by appropriate stool cultures. It is not uncommon that a bout of acute bacterial diarrhea may uncover a diagnosis of inflammatory bowel disease.[41] Acute ileitis should not be confused with Crohn's disease. Young patients with acute ileitis usually recover without sequelae and should not undergo surgery. When Crohn's disease is confined to the colon, ischemic bowel disease (particularly in the elderly) and pseudomembranous colitis as well as ulcerative colitis must be included in the differential diagnosis.

TREATMENT

The aim of therapy for this incurable disease includes relief of symptoms, induction of remission, maintenance of remission, prevention of complications, optimizing timing of surgery, and maintenance of nutrition.[42,43]

Initial treatment (**Table 73-5**) consists of adequate fluid resuscitation and restoration of electrolyte balance. Place a nasogastric tube for obstruction, peritonitis, or toxic megacolon. Administer broad-spectrum antibiotics for fulminant colitis or peritonitis. Patients with severe disease should receive IV steroids such as hydrocortisone 300 milligrams per day or an equivalent dose of methylprednisolone (48 milligrams per day) or prednisolone (60 milligrams per day).

TABLE 73-5

Treatment of Fulminant Colitis

Restore fluid and electrolyte balance

Nothing by mouth

Nasogastric suction for

Obstruction

Adynamic ileus

Suspected toxic megacolon

Parenteral corticosteroids

Hydrocortisone 300 milligrams per day or methylprednisolone 48 milligrams per day or prednisolone 60 milligrams per day

Broad-spectrum antibiotics

Piperacillin-tazobactam 4.5 grams IV four times a day *OR*

Ampicillin 2 grams IV four times a day + metronidazole 500 milligrams IV three times a day + levofloxacin (Levaquin®) 750 milligrams IV once a day

Observe for complications

Obstruction

Perforation

Toxic megacolon

Life-threatening hemorrhage

Intra-abdominal abscess

Outpatient management (nontoxic patients)

Liquids only for first 48 h

Oral antibiotics

Ampicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, cephalexin, or rifaximin

and

Metronidazole or clindamycin

Salicylates

Sulfasalazine 3 to 5 grams per day is for mild to moderate Crohn's disease. Sulfapyridine is a byproduct of the colonic breakdown of sulfasalazine. Many of the toxic side effects of sulfasalazine (vomiting, anorexia, nausea, headache, diarrhea, epigastric distress, etc.) are attribuTable to sulfapyridine.

The active moiety in sulfasalazine is mesalamine. Many of the newer 5′-acetyl salicylic acid drugs feature a derivative of mesalamine without the sulfapyridine component. Pentasa®, Asacol®, Claversal®, Salofalk®, and Lialda® are mesalamine derivatives. Olsalazine (Dipentum®) and balsalazide (Colazide®) are 5-aminosalicylic molecules. The mesalamine formulations are most effective in patients with colonic disease and particularly in those with mild disease.

Corticosteroids

Oral glucocorticoids such as prednisone (40 to 60 milligrams per day) have traditionally been reserved for more severely affected patients but are now used as induction therapy. An ileal-released form of budesonide (9 milligrams per day) may be beneficial in patients with ileal and right colon disease. Glucocorticoids are not preferred for maintaining remission because of their complications and concerns about effectiveness.

Immunosuppressives

Immunosuppressive drugs such as 6-mercaptopurine, azathioprine, and thioguanine are useful in maintenance, as steroid-sparing agents, in healing fistulas, and in patients in whom there are serious contraindications to surgery.[44] Both agents have been associated with leukopenia, fever, hepatitis, and pancreatitis, necessitating the need for close follow-up, particularly during the initial phase of therapy. The response to immunosuppressives should not be expected before 3 to 6 months following the initiation of therapy. Parenteral methotrexate (15 to 25 milligrams per week) is considered third line and has been used following steroid and thiopurine metabolite failure.

Antibiotics

Antibiotics are first-line agents for perianal disease and help induce remission. Ciprofloxacin (1.0 to 1.5 milligrams/kg per day) induces remission with rates (55%) similar to those in patients treated with mesalamine (4 grams per day).[45] Metronidazole (10 to 20 milligrams/kg per day) is also

effective for perianal complications and fistulous disease. Combination therapies with antibiotics and biologic agents (see next section) have produced dramatic improvements in response.[46] Rifaximin is a broad-spectrum antibiotic that is not absorbed from the gastrointestinal tract. Rifaximin 800 milligrams twice daily for 12 weeks is effective for mild to moderate disease.[45] However, antibiotics raise concerns about precipitating *C. difficile* colitis infection.

Biologics

Patients with medically resistant moderate to severe Crohn's disease may benefit from the antitumor necrosis factor antibody, infliximab (Remicade®) or adalimumab (Humira®).[45,47,48] All biologics increase the risk of infections, especially those caused by intracellular pathogens such as tuberculosis. Concern about the emergence of lymphomas and progressive multifocal leukoencephalopathy has limited the long-term use of these agents.

Maintenance therapy and the effectiveness of various therapeutic agents in Crohn's disease are variable. Glucocorticoids are not used for maintaining a remission because of the lack of sufficient evidence of their efficacy and the potential for long-term complications. A reduced dose of 5-aminosalicyclic acid derivatives is used for the maintenance of remission of colonic disease. The addition of sulfasalazine, azathioprine, and 6-mercaptopurine to prednisone does not improve the response rate and increases side effects. Infliximab or adalimumab and an immunosuppressive (azathioprine, 6-mercaptopurine, and methotrexate) can maintain remission.[45]

Antidiarrheal Agents

Diarrhea can be controlled by loperamide (Imodium®) 4 to 16 milligrams per day, diphenoxylate (Lomotil®) 5 to 20 milligrams per day, and in some cases, cholestyramine (Questran®) 4 grams one to six times a day. The mechanism of action of cholestyramine is binding bile acids and eliminating their known cathartic action.

DISEASE COMPLICATIONS

More than three out of four patients with Crohn's disease will require surgery within the first 20 years of the onset of initial symptoms. **Abscess and fissure formation** is common. Abscesses can be characterized as intraperitoneal, visceral, retroperitoneal, interloop, or intramesenteric. Signs and symptoms are worsening abdominal pain and tenderness, fever, and possibly a palpable mass. Retroperitoneal abscesses may cause hip or back pain and difficulty ambulating.

Fistulas are the result of extension of the intestinal fissures seen in Crohn's disease into adjacent structures. The most common sites are between the ileum and the sigmoid colon, the cecum, another ileal segment, urinary bladder, vagina, or the skin. Suspect an internal fistula when there are changes in the patient's symptom complex, such as bowel movement frequency, amount of pain, or weight loss.

Obstruction is the result of both stricture formation due to the inflammatory process and of edema of the bowel wall. The distal small bowel is the most common site of obstruction. Symptoms include crampy abdominal pain, distention, nausea, and bloating.

Perianal complications include perianal or ischiorectal abscesses, fissures, fistulas, rectovaginal fistulas, and rectal prolapse. These are more commonly seen in patients with colonic involvement.

Major gastrointestinal bleeding is rare. Bleeding results from erosion into a vessel in the bowel wall. Toxic megacolon is also uncommon, but is associated with massive gastrointestinal bleeding in over half the cases.

When bowel symptoms are present, malnutrition, malabsorption, hypocalcemia, and vitamin deficiency can be severe. In addition to the complications of the disease itself are complications associated with the treatment of the disease with mesalamine, steroids, immunosuppressive agents, and antibiotics. These include leukopenia, thrombocytopenia, fever, infection, profuse diarrhea, pancreatitis, renal insufficiency, and liver failure.

The incidence of malignant neoplasm of the gastrointestinal tract is three times higher in patients with Crohn's disease than for the general population.

DISPOSITION

Patients with colitis, peritonitis, or complications such as obstruction, significant gastrointestinal hemorrhage, severe dehydration, or fluid/electrolyte imbalance should be hospitalized. Hospital admission should be considered in less severe cases that cannot be managed successfully with outpatient management. Surgical intervention is indicated in those patients with complications of the disease, including intestinal obstruction or hemorrhage, perforation, abscess or fistula formation, toxic megacolon, and perianal disease.

Before discharging patients with Crohn's disease, discuss alterations in the therapeutic regimen with the gastroenterologist. Assure close follow-up after discharge.

ULCERATIVE COLITIS

INTRODUCTION AND EPIDEMIOLOGY

Ulcerative colitis is a chronic inflammatory disease of the colon. The inflammation tends to be progressively more severe from the proximal to the distal colon. The rectum is involved nearly 100% of the time. The characteristic symptom is bloody diarrhea. The cause is unknown.

The disease is more prevalent in the United States and northern Europe than in other parts of the world, and peak incidence occurs in the second and third decades of life. It is more common in men. First-degree relatives of patients with ulcerative colitis have a 15-fold risk of developing ulcerative colitis and a 3.5-fold risk of developing Crohn's disease.

PATHOPHYSIOLOGY

Ulcerative colitis involves primarily the mucosa and submucosa. Microscopically, the disease is characterized by mucosal inflammation with the formation of crypt abscesses, epithelial necrosis, and mucosal ulceration. The submucosa, muscular layer, and serosa are usually spared. In the usual case, the disease increases in severity more distally, the rectosigmoid being involved in the vast majority of cases. In the early stages of the disease, the mucous membranes appear finely granular and friable. In more severe cases, the mucosa appears as a red, spongy surface dotted with small ulcerations oozing blood and purulent exudate. In very advanced disease, one sees large, oozing ulcerations, and pseudopolyps (areas of hyperplastic overgrowth surrounded by inflamed mucosa).

CLINICAL FEATURES

The clinical features and course of ulcerative colitis vary and depend on the anatomical distribution of the disease in the colon. Crampy abdominal pain, bloody diarrhea, and tenesmus are typical symptoms. The disease is classified as mild, moderate, or severe depending on the clinical manifestations. Patients with mild disease have fewer than four bowel movements per day, no systemic symptoms, and few extraintestinal manifestations. Of all patients with ulcerative colitis, 60% have mild disease; in 80% of cases, the disease is limited to the rectum. Occasionally, constipation and rectal bleeding are the presenting complaints. Progression to pancolitis occurs in 10% to 15% of patients with mild disease.

Moderate disease is seen in 25% of patients. Patients demonstrate a good response to therapy. These patients usually have colitis extending to the splenic flexure (left-sided colitis), but may develop pancolitis.

Patients with severe disease constitute 15% of those with ulcerative colitis. Severe disease is associated with frequent bowel movements, anemia, fever, weight loss, tachycardia, low serum albumin, and more frequent extraintestinal manifestations. Patients with severe disease account for 90% of the mortality from ulcerative colitis. Virtually all severely affected patients have pancolitis.

Ulcerative colitis is usually characterized by intermittent attacks of acute disease with complete remission between attacks. Sometimes, the first attack is followed by a prolonged period of inactivity, or the disease is chronically active. The factors associated with an unfavorable prognosis and increased mortality include higher severity and extent of disease, a short interval between attacks, systemic symptoms, and onset of the disease after 60 years of age.

Extraintestinal complications are listed in **Table 73-4**.

DIAGNOSIS

Laboratory findings in patients with ulcerative colitis are nonspecific and may include leukocytosis, anemia, thrombocytosis, decreased serum albumin, and abnormal liver function studies. There are many biomarkers for diagnosis and prognosis,[40] but none are available in the ED. Therefore, the diagnosis of ulcerative colitis rests on the following: a history of abdominal cramps and diarrhea, mucoid stools, stool examination negative for ova and parasites, stool cultures negative for enteric pathogens, and confirmation of diagnosis by colonoscopy.

Differential Diagnosis

The major diseases that should be considered in the differential diagnosis of ulcerative colitis include infectious colitis, Crohn's colitis, ischemic colitis, radiation colitis, toxic colitis from antineoplastic agents, and pseudomembranous colitis. When the disease is limited to the rectum, consider rectal syphilis, gonococcal proctitis, lymphogranuloma venereum, and inflammations caused by herpes simplex virus, *Entamoeba histolytica, Shigella,* and C*ampylobacter.*

TREATMENT

Patients with severe ulcerative colitis should be treated with IV steroids, replacement of fluids, correction of electrolyte abnormalities, broad-spectrum antibiotics, mesalamine, and steroids (**Table 73-5**). IV cyclosporine (4 milligrams/kg per day) or infliximab can be effective in fulminant colitis nonresponsive to IV corticosteroids.[45]

When toxic megacolon is suspected, place a nasogastric tube and obtain imaging and surgical consultation.

The majority of those with mild and moderate disease can be treated as outpatients. In the treatment of patients with mild active proctitis, proctosigmoiditis, and left-sided colitis (<60 cm of active disease), topical treatment with mesalamine suppositories or enemas is effective. Although not as effective for inducing remission as mesalamine, topical steroid preparations (beclomethasone, hydrocortisone, tixocortol, and

budesonide) are successful and better tolerated.[45] If topical therapy is unsuccessful, glucocorticoids are effective in inducing a remission in the majority of cases. Daily doses of 40 to 60 milligrams of prednisone are usually sufficient and can be adjusted depending on the severity of the disease.

A combination of oral (2.4 grams/day) and topical mesalamine is used in the treatment of acute mild to moderate attacks but is inferior to steroids in the more severe cases. In addition to sulfasalazine, the newer 5-aminosalicylic derivatives are quite effective in inducing remission of ulcerative colitis as well as maintaining it. The choice of agents available for the treatment of ulcerative colitis is very similar to that in Crohn's disease (mesalamine [Pentasa®, Asacol®, Lialda®], olsalazine [Dipentum®], and balsalazide). Topical glucocorticoid enemas or 5-aminosalicylic enemas (Rowasa®, 2 to 4 grams/60 mL per day for 3 weeks) or suppositories (500 milligrams twice a day) are quite effective in distal proctosigmoiditis and have lower systemic side-effect profiles.

Infliximab (5 milligrams/kg) is the only biologic indicated for ulcerative colitis. It should be considered for use in patients with mild to moderate disease who are corticosteroid dependent or refractory and in patients who have immunomodulator refractory disease.[47]

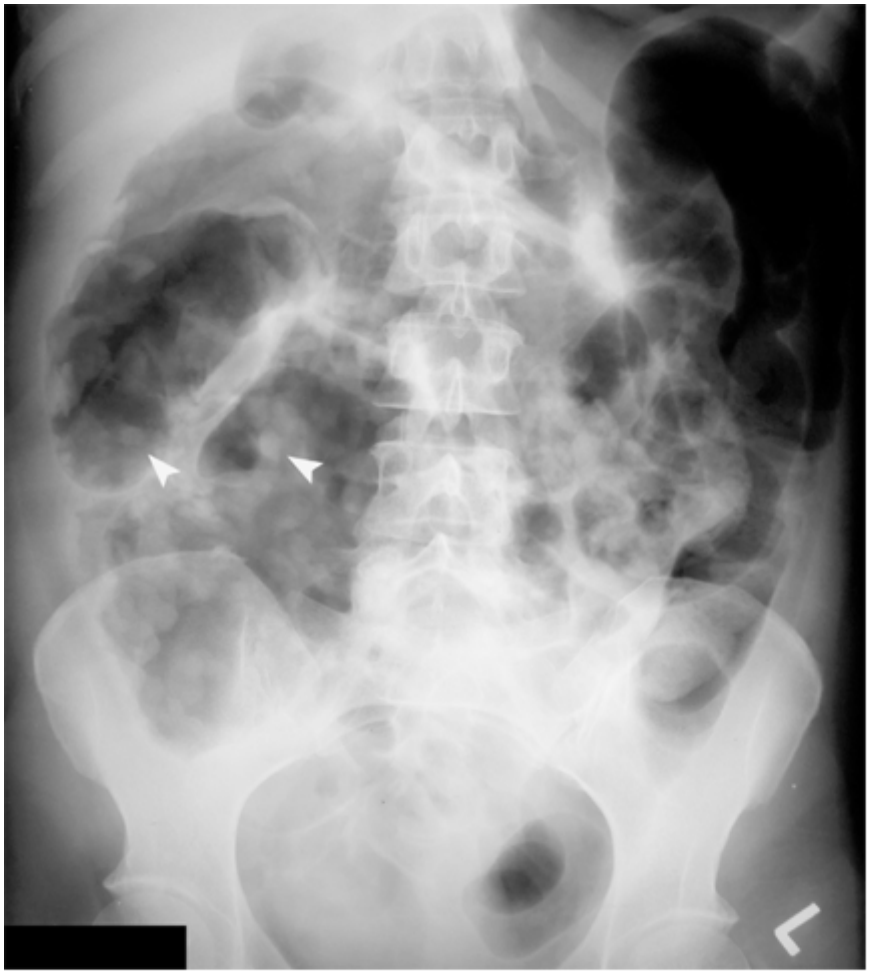
Hydrophilic bulk agents such as psyllium (Metamucil®) can be used in some patients to improve stool consistency. Antidiarrheal agents are generally ineffective and may precipitate toxic megacolon.

DISEASE COMPLICATIONS

Blood loss from sustained hemorrhage is the most common complication, but toxic megacolon must not be missed.

Toxic megacolon develops in advanced cases of colitis when the disease process extends through all layers of the colon (**Figure 73-1**).The result is a loss of muscular tone within the colon, with dilatation and localized peritonitis. If the colon continues to dilate without treatment, signs of toxicity will develop. Plain radiography of the abdomen demonstrates a long, continuous segment of air-filled colon greater than 6 cm in diameter. Loss of colonic haustra and "thumb printing," representing bowel wall edema, may also be seen. The distended portion of the atonic colon can perforate, causing peritonitis and septicemia. Mortality is high.

FIGURE 73-1.
Abdominal distention due to toxic megacolon. Arrows point to mucosal nodules. [Reproduced with permission from Schwartz DT (Ed): *Emergency Radiology: Case Studies.* © McGraw-Hill, Inc., 2008. Chapter II-2, Fig. 23.]



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A patient with toxic megacolon appears severely ill; the abdomen is distended, tender, and tympanic. Severe diarrhea (>10 bowel movements per day) is often seen but may have ceased. Fever, tachycardia, and hypotension are typically part of the clinical picture. Leukocytosis, anemia, electrolyte disturbances, and hypoalbuminemia are the supporting laboratory results.

Some of the more prominent features of toxic megacolon, such as leukocytosis and peritonitis, can be masked in the patient taking corticosteroids. Antidiarrheal agents, hypokalemia, narcotics, cathartics, pregnancy, enemas, and recent colonoscopy have been implicated as precipitating factors in toxic megacolon. Medical therapy with nasogastric suction, IV prednisolone 60 milligrams per day, or hydrocortisone 300

milligrams per day, parenteral broad-spectrum antibiotics active against coliforms and anaerobes, and IV fluids should be attempted as initial therapy, along with early surgical consultation.

Perirectal fistulas and abscesses may occur in up to 20% of patients with ulcerative colitis. Massive gastrointestinal hemorrhage, obstruction secondary to stricture formation, and acute perforation are other complications of the disease.

There is a 10- to 30-fold increase in the development of carcinoma of the colon in patients with ulcerative colitis. The major risk factors for the development of carcinoma of the colon are extensive involvement and prolonged duration of the disease. The cumulative risk of cancer after 20 and 30 years is 5% to 10% and 12% to 20%, respectively. Additional factors that constitute increased risk of cancer in patients with ulcerative colitis include early onset of the disease and a family history of colon cancer.

DISPOSITION

Patients with fulminant attacks of ulcerative colitis need hospitalization for aggressive fluid and electrolyte resuscitation and careful observation for the development of complications. Patients with complications such as gastrointestinal hemorrhage, toxic megacolon, and bowel perforation should also be admitted with consultation to both a gastroenterologist and a surgeon. In addition to toxic megacolon, the indications for surgery include colonic perforation, massive lower gastrointestinal bleeding, suspicion of colon cancer, and disease that is refractory to medical therapy (large doses of steroids required to control the disease).

Patients with mild to moderate disease can be discharged from the ED. Close follow-up should be arranged with the patient's physician or gastroenterologist, and any adjustment in medical therapy should be discussed prior to discharge.

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REFERENCES

1. Thielman NM, Guerrant RL: Acute infectious diarrhea. *N Engl J Med* 350: 38, 2004. [PubMed: 14702426]

2. Kroser JA, Metz DC: Evaluation of the adult patient with diarrhea. *Primary Care* 23: 629, 1996. [PubMed: 8888349]

3. Binder HJ: Pathophysiology of acute diarrhea. *Am J Med* 88 (Suppl 6A): 2S, 1990. [PubMed: 2356845]

4. Park SI, Giannella RA: Approach to the adult patient with acute diarrhea. *Gastroenterol Clin North Am* 22: 483, 1993. [PubMed: 8406726]

5. Goodgame R: A Bayesian approach to acute infectious diarrhea in adults. *Gastroenterol Clin N Am* 35: 249, 2006.

6. Savola KL, Baron EJ, Thompkins LS, Passaro DJ: Fecal leukocyte stain has diagnostic value for outpatients but not inpatients. *J Clin Microbiol* 39: 266, 2001. [PubMed: 11136781]

7. Salam I, Katelaris P, Leigh-Smith S et al.: Randomized trial of single-dose ciprofloxacin for travellers' diarrhoea. *Lancet* 344: 1537, 1994. [PubMed: 7983954]

8. Hines J, Nachamkin I: Effective use of the clinical microbiology laboratory for diagnosing diarrheal diseases. *Clin Infect Dis* 23: 1292, 1996. [PubMed: 8953074]

9. Bartlett JG: Antibiotic-associated diarrhea. *N Engl J Med* 346: 334, 2002. [PubMed: 11821511]

10. Sullivan P: Nutritional management of acute diarrhea. *Nutrition* 14: 758, 1998. [PubMed: 9785356]

11. DuPont HL: New insights and directions in travelers' diarrhea. *Gastroenterol Clin North Am* 35: 337, 2006. [PubMed: 16880069]

12. Kamat D, Mathur A: Prevention and management of travelers' diarrhea. *Dis Mon* 52: 289, 2006. [PubMed: 17046431]

13. de la Cabada Bauche J, Dupont HL: New developments in traveler's diarrhea. *Gastroenterol Hepatol* 7: 88, 2011.

14. de Saussure PH: Management of the returning traveler with diarrhea. *Therap Adv Gastroent* 2: 367, 2009.

15. Riddle MS, Arnold S, Tribble DR: Effect of loperamide in combination with antibiotics on treatment outcomes in traveler's diarrhea: a systematic review and meta-analysis. *Clin Infect Dis* 47: 1007, 2008. [PubMed: 18781873]

16. Akalin HE: Role of quinolones in the treatment of diarrhoeal diseases. *Drugs* 49 (Suppl 2): 128, 1995. [PubMed: 8549281]

17. Aserkoff B, Bennett JV: Effect of antibiotic therapy in acute salmonellosis on the fecal excretion of Salmonellae. *N Engl J Med* 281: 636, 1969. [PubMed: 4897014]

18. Ericsson CD, DuPont HL, Mathewson JJ et al.: Treatment of traveler's diarrhea with sulfamethoxazole and trimethoprim and loperamide. *JAMA* 263: 257, 1990. [PubMed: 2403603]

19. Ouyang-Latimer J, Jafri S, Vantassel A et al.: In vitro antimicrobial susceptibility of bacterial enteropathogens isolated from international travelers to Mexico, Guatemala, and India from 2006 to 2008. *Antimicrob Agents Chemother* 55: 874, 2011. [PubMed: 21115800]

20. McDonald LC, Killgore GE, Thompson A et al.: An epidemic, toxin gene-variant strain of Clostridium difficile. *N Engl J Med* 353: 2433, 2005. [PubMed: 16322603]

21. DuPont HL, Jiang ZD, Ericsson CD et al.: Rifaximin versus ciprofloxacin for the treatment of traveler's diarrhea: a randomized, double-blind clinical trial. *Clin Infect Dis* 33: 1807, 2001. [PubMed: 11692292]

22. Koo HL, DuPont HL, Huang DB: The role of rifamixin in the treatment and chemoprophylaxis of travelers' diarrhea. *Therap Clin Risk Manag* 5: 841, 2009.

23. Allen SJ, Martinez EG, Gregorio GV, Dans LF: Probiotics for treating acute infectious diarrhoea. *Cochrane Database Syst Rev* 11: CD003048, 2010. [PubMed: 21069673]

24. Dennehy PH: Rotovirus vaccine—an update. *Vaccine* 25: 3137–3141, 2007. [PubMed: 17321017]

25. Kelly CP: A 76-year-old man with recurrent *Clostridium difficile* associated diarrhea: review of *C. difficile* infection. *JAMA* 301: 954, 2009. [PubMed: 19190304]

26. Hookman P, Barkin JS: *Clostridium difficile* associated infection, diarrhea, and colitis. *World J Gastroenterol* 15: 1554, 2009. [PubMed: 19340897]

27. Bartlett JG: Antibiotic-associated diarrhea. *N Engl J Med* 346: 334, 2002. [PubMed: 11821511]

28. Gerding DN, Johnson S, Peterson LR et al.: *Clostridium difficile*-associated diarrhea and colitis. *Infect Control Hosp Epidemiol* 16: 459, 1995. [PubMed: 7594392]

29. Kelly CP, LaMont JT: *Clostidium difficile*—more difficult than ever. *N Engl J Med* 359: 1932, 2008. [PubMed: 18971494]

30. Zar FA, Bakkanagari SR, Moorthi KM, Davis MB: A comparison of vancomycin and metronidazole for the treatment of *Clostridium difficile*-associated diarrhea, stratified by disease severity. *Clin Infect Disease* 45: 302, 2007.

31. Louie TJ, Miller MA, Mullane KM, Weis K et al.: Fidaxomicin versus vancomycin for *Clostridium difficile* infection. *N Engl J Med* 364: 422, 2011. [PubMed: 21288078]

32. Lowy I, Molrine DC, Leav BA et al.: Treatment with monoclonal antibodies against *Clostridium difficile* toxins. *N Engl J Med* 362: 197, 2010. [PubMed: 20089970]

33. Pillai A, Nelson R: Probiotics for treatment of *Clostridium difficile*-associated colitis in adults. *Cochrane Database Syst Rev* 1: CD004611, 2008. [PubMed: 18254055]

34. Koo HL, Koo DC, Musher DM, DuPont HL: Anti-motility agents for the treatment of *Clostridia difficile* colitis and diarrhea. *Clin Infect Dis* 48: 606, 2009. [PubMed: 19191647]

35. Benchimol EI, Fortinsky KJ, Gozdyra P, Van den Heuvel M, Van Limbergen J, Griffiths AM: Epidemiology of pediatric inflammatory bowel disease: a systematic review of international trends. *Inflam Bowel Dis* 17: 423, 2011.

36. Schwartz DA, Maltz BE: Treatment of fistulizing inflammatory bowel disease. *Gastroent Clin North Am* 38: 595, 2009.

37. Devlin SM, Panaccione M: Evolving inflammatory bowel disease treatment paradigms: top-down versus step-up. *Gastroent Clinics N Am* 38: 577, 2009.

38. Levine JS, Burakoff R: Extraintestinal manifestations of inflammatory bowel disease. *Gastroent Hepatol* 7: 235, 2011.

39. Vermeire S, Van Assche G, Rutgeerts P: Laboratory markers in IBD: useful, magic, or unnecessary toys? *Gut* 55: 426, 2006. [PubMed: 16474109]

40. Zisman TL, Rubin DT: Novel diagnostic and prognostic modalities in inflammatory bowel disease. *Gastroent Clin North Am* 38: 729, 2009.

41. Porter CK, Tribble DR, Aliaga PA, Halvorson HA, Riddle MS: Infectious gastroenteritis and risk of developing inflammatory bowel disease. *Gastroent* 135: 781, 2008.

42. Kornbluth A, Sachar DB: Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol* 99: 1371, 2004. [PubMed: 15233681]

43. Travis SP, Stange EF, Lemann M et al.: European evidence-based consensus on the diagnosis and management of Crohn's disease: current management. *Gut* 55 (Suppl 1): i16, 2006. [PubMed: 16481629]

44. Dubinsky MC, Hassard PV, Abreu MT et al.: Thioguanine (6-TG): a therapeutic alternative in a subgroup of IBD patients failing 6-mercaptopurine. *Gastroenterology* 118: A891, 2000.

45. Tamboli CP: Current medical therapy for chronic inflammatory bowel diseases. *Surg Clin N Am* 87: 697, 2007. [PubMed: 17560421]

46. West RL, van der Woude CJ, Hansen BE, Felt-Bersma RJ, van Tilburg AJ, Drapers JA, Kuipers EJ: Clinical and endosonographic effect of ciprofloxacin on the treatment of perianal fistulae in Crohn's disease with infliximab: a doubleblind placebo-controlled study. *Aliment Pharmacol Ther* 20: 1329, 2004. [PubMed: 15606395]

47. Rutgeerts P, Sandborn WJ, Feagan BG et al.: Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 353: 2462, 2005. [PubMed: 16339095]

48. Schreiber S, Rutgeerts P, Fedorak RN et al.: A randomized, placebo-controlled trial of certolizumab pegol (CDP870) for treatment of Crohn's disease. *Gastroenterology* 129: 807, 2005. [PubMed: 16143120]