abstract

The principal causes of diarrhea are infectious and inflammatory in origin, but the diagnosis and management of diarrhea in older patients may be complicated by age-related vulnerabilities and comorbidities. Several studies have indicated that the bacterial composition of feces may change with increasing age[1] and that immune response at the mucosal surface may also diminish.[2] Outbreaks of infectious diarrhea, including Escherichia coli 0157:H7 and viral origins, have occurred in the long-term care setting.[3,4] It is also known that a wide spectrum of medications can cause diarrhea through various mechanisms. Older patients are at greater risk of developing mesenteric or colonic ischemia due to underlying atherosclerotic disease and risk of embolic events from atrial fibrillation, valvular heart disease, or cardiomyopathies.[7,8] This article highlights the age-related considerations for the diagnosis and management of diarrhea in the older adult.

Key words: *mesenteric ischemia, ischemic colitis, Escherichia coli 0157:H7, Clostridium difficile, microscopic colitis, radiation colitis*

Diarrhea in the Older Patient

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Introduction

Older patients with diarrhea have the capacity to become quite ill and, in some cases, they can progress to surgical or lethal disease. Important elements in the history of an older patient with diarrhea should establish the acuity of onset, the volume and frequency of diarrhea, as well as the presence of abdominal pain and / or bloody stools. Systemic symptoms such as fevers and chills might suggest an infectious etiology, while a review of the daily medications may hint at possible adverse drug reactions. An assessment of the patient's living situation, particularly if the patient is a long-term care resident or has undergone a recent hospitalization, can suggest an exposure to potential pathogens. A history of cardiac disease or abdominal / pelvic cancers can provide other clues to potential causes of diarrhea.

The differential diagnosis of diarrhea in older adults is extensive. This article will focus on clinical entities that highlight common or specific concerns for older patients, including ischemic bowel disease, Clostridium difficile infections, Escherichia coli 0157:H7 infections, microscopic colitis, and radiation colitis.

Ischemic Bowel Disease

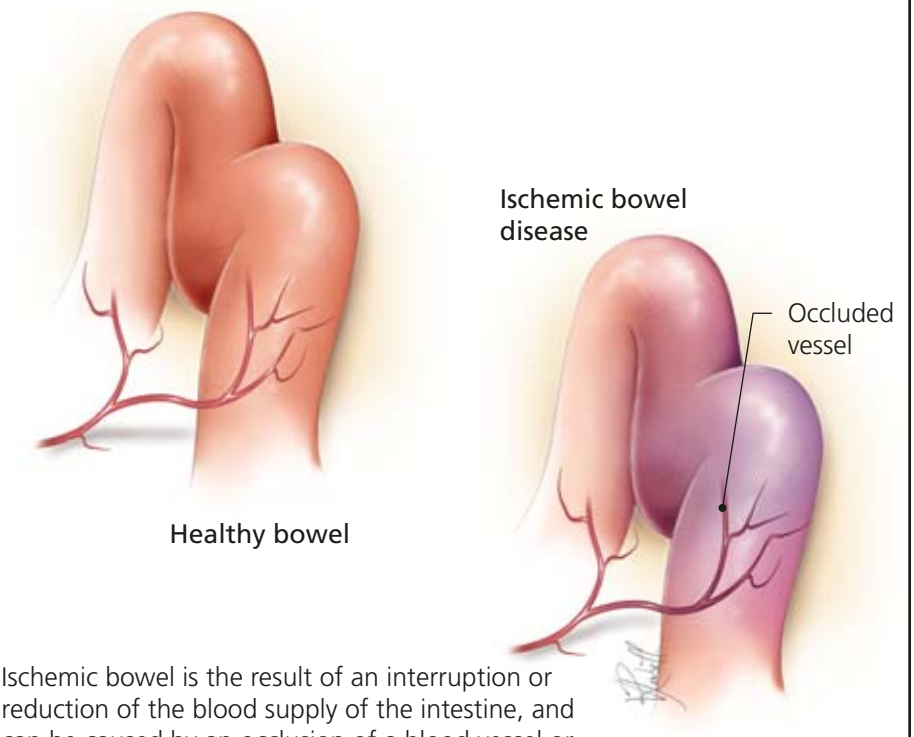
Ischemia of the bowel can be caused by an occlusion of an artery or a vein, or induced by a low-flow state leading to hypoxia of the intestinal mucosa (Figure 1). Acute mesenteric ischemia caused by a thrombus or an embolic event usually involves the celiac or the superior mesenteric artery. Older patients with underlying atherosclerosis, hypercoagulable states, atrial fibrillation, or valvular heart disease are at greatest risk for mesenteric ischemia. When mesenteric ischemia is a chronic condition, patients experience postprandial abdominal pain, fear of eating, and significant weight loss. In the acute setting, patients with mesenteric ischemia typically present with a severe mid-abdominal pain disproportionate to the physical exam findings. Magnetic resonance angiography, duplex Doppler ultrasound, and CT studies can help establish the diagnosis. Urgent angioplasty or surgical revascularization can prevent lethal outcomes; the overall mortality is estimated at 60–80%.[7]

In contrast, when a thrombus is formed in a mesenteric vein, the onset of pain is more insidious and may be associated with diarrhea and vomiting. Five to fifteen percent of all cases of intestinal ischemia are caused by a mesenteric vein thrombosis, most typically involving the superior mesenteric vein.[9] Recent abdominal surgery, cirrhotic liver disease, and hypercoagulable states increase the risk for mesenteric vein thrombosis. Selective mesenteric angiography, duplex Doppler ultrasound, and CT studies may help to establish this diagnosis. Anticoagulation can reduce the likelihood of recurrence and is associated with a decrease in mortality; surgery is indicated with bowel infarction.

Ischemic colitis is caused by a low-flow state often induced by episodes of hypotension and surgery, such as abdominal aortic aneurysm repairs. It generally involves the watershed areas at

the splenic flexure and the rectosigmoid junction, where collateral blood flow is weakest, and can result from infections such as Escherichia coli 0157:H7, Entamoeba histolytica, and cytomegalovirus.[10,11] Ergotomines, estrogens, and sodium polystyrene are well-known causes of colonic ischemia, while NSAIDs, pseudoephedrine, diuretics, and tricyclic antidepressants have also been linked to this condition.[12] Patients with colonic ischemia typically present with a sudden-onset mild abdominal pain and tenderness and / or guarding over the involved segment of bowel. They also have a variable amount of bloody diarrhea that begins within 24 hours of symptom onset. Diagnosis of ischemic colitis can be made by colonoscopy. Ischemic colitis typically resolves spontaneously, although urgent surgical intervention is occasionally required. Initial therapy is supportive and includes bowel rest with broad-spectrum antibiotics and close monitoring for complications.

Figure 1: Ischemic Bowel Disease



Ischemic bowel is the result of an interruption or reduction of the blood supply of the intestine, and can be caused by an occlusion of a blood vessel or induced by a low-flow state.

Escherichia coli

Escherichia coli 0157:H7 is commonly acquired by the ingestion of contaminated, undercooked ground beef (Table 1A). Outbreaks have also been associated with consumption of water, milk, juices, vegetables, and fruits likely contaminated by the feces of infected cattle. Outbreaks in the long-term care setting have followed exposure to contaminated food, and person-to-person transmission has also been documented.[3]

Patients with Escherichia coli 0157:H7 infections can be asymptomatic carriers or may have only mild flu-like symptoms. However, the classic presentation of a severe Escherichia coli 0157:H7 infection begins with severe abdominal cramping and watery diarrhea followed by rapid progression to bloody diarrhea, with or without fever. Fewer than 10% of these patients will go on to develop hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP) but the older patients (as well as young children) appear to be at greatest risk.[13]

Escherichia coli 0157:H7 infections are typically self-limited, with resolution of symptoms within a week. Patients should be offered supportive therapy and the older patient should be monitored for progression to HUS / TTP (Table 1B). Antidiarrheal therapy and antibiotics should be avoided as they are associated with an increased risk of HUS.

Clostridium difficile

Diarrhea develops in up to 25% of patients taking antibiotics and occurs most frequently with broad-spectrum antibiotics. Clostridium difficile is responsible for 10–20% of the cases of antibiotic-associated diarrhea.[14] Older patients are at increased risk for this infection. Hospitalized patients are also at increased risk, where colonization rates can be as high as 20–30%.

Patients with a Clostridium difficile infection typically present with watery diarrhea and abdominal cramps (Table 1A). Bloody diarrhea, fever, and abdominal pain are common in the most severe cases. Older patients can become dehydrated and may present with hypoalbuminemia and prerenal azotemia. Fulminant colitis can progress to megacolon, perforation, and death.

The diagnosis of Clostridium difficile infection can be established by a stool assay for toxin. Oral metronidazole or vancomycin should be prescribed for 10–14 days. Metronidazole is favoured as the first-line therapy because of its low cost and the growing concern that vancomycin use can promote the resistant enterococci strains. Intravenous

Table 1A: Indications and Dosages of Medications Used to Treat DLB and PDD

Diagnosis	Risk Factors	Clinical Features
Acute Mesenteric Ischemia	atherosclerosis hypercoagulable states atrial fibrillation valvular heart disease	acute and severe abdominal pain minimal physical exam findings
Venous Mesenteric Ischemia	oral contraceptive use recent abdominal surgery cirrhotic liver disease hypercoagulable states	abdominal pain nausea, vomiting, diarrhea
Ischemic Colon	hypotensive states surgery: abdominal aneurysm repair medications: ergotomines, estrogen, Kayexelate, NSAIDS	abdominal pain bloody diarrhea
Escherichia coli 0157:H7	ingestion of undercooked beef ingestion of contaminated water, milk, juice, fruit, and vegetables person-to-person transmission possible	variable presentation abdominal pain watery and/or bloody diarrhea fever may or may not be present
Clostridium difficile	antibiotic exposure older patients immunocompromised hospitalization history of prior C difficile infection	abdominal cramps and pain watery diarrhea hematochezia in severe cases fever
Microscopic Colitis	older patients' medications: NSAIDS and others	diarrhea for > one month 6-20 episodes diarrhea/24 hours
Chronic Radiation Colitis	history of abdominal/pelvic cancers history of radiation therapy	diarrhea rectal pain rectal bleeding

metronidazole, high-dose oral vancomycin, and vancomycin enemas are indicated in the most severe cases (Table 1B).

As many as 20% of patients with Clostridium difficile diarrhea will experience a recurrence within one week to two months following successful therapy and are likely to experience future relapses. The first recurrence is treated by repeating the initial therapy. Pulsed and/or tapering doses of antibiotics, probiotics to restore the colonic flora, and immunoglobulin therapy can also be effective in treating recurrent Clostridium difficile infections.

Microscopic Colitis (Collagenous Colitis and Lymphocytic Colitis)

There are two types of microscopic colitis: collagenous and lymphocytic. Both present with chronic watery diarrhea and a normal GI evaluation; diagnosis is made by findings on colon biopsy of normal appearing mucosa. The first case of collagenous colitis was reported in 1976 when a woman with chronic watery diarrhea had an abnormal colorectal biopsy showing a thickened subepithelial collagen band and a slight increase in lymphocytes in the lamina propria. This entity was named collagenous colitis. A second form of microscopic colitis, lymphocytic colitis, has similar histologic features but is differentiated by the absence of the subepithelial collagen band. Collagenous colitis and lymphocytic colitis cannot be distinguished clinically or by their treatment approach, and it is still unclear whether these entities represent

Table 1B: Indications and Dosages of Medications Used to Treat DLB and PDD

Diagnosis	Diagnostic Tests	Treatment Options
Acute Mesenteric Ischemia	magnetic resonance angiography duplex Doppler ultrasound CT scan	angioplasty surgical revascularization
Venous Mesenteric Ischemia	mesenteric angiography duplex Doppler ultrasound CT scan	anticoagulation surgery to resect infarcted bowel
Ischemic Colon	colonoscopy or flexible sigmoidoscopy barium enema	supportive therapy: bowel rest and antibiotics rarely requires surgical intervention
Escherichia coli 0157:H7	culture for Escherichia coli 0157:H7	supportive therapy monitoring for progression to HUS/TTP
Clostridium difficile	Clostridium difficile toxin assay	discontinue inciting antibiotic oral metronidazole or vancomycin severe cases: intravenous metronidazole, high dose oral vancomycin, or vancomycin enemas recurrent cases: pulsed or tapered antibiotics probiotics, immunogloubulin therapy
Microscopic Colitis	colonoscopy with biopsy	bismuth subsalicylate steroids cholestyramine
Chronic Radiation Colitis	colonoscopy	sulcrafate steroids 5-ASA compounds sulfasalazine antibiotics hyperbaric oxygen

a spectrum of the same disease. Collagenous colitis and lymphocytic colitis typically present in patients of average age 55–65 years and may account for 10% of patients with chronic diarrhea examined in referral centres.

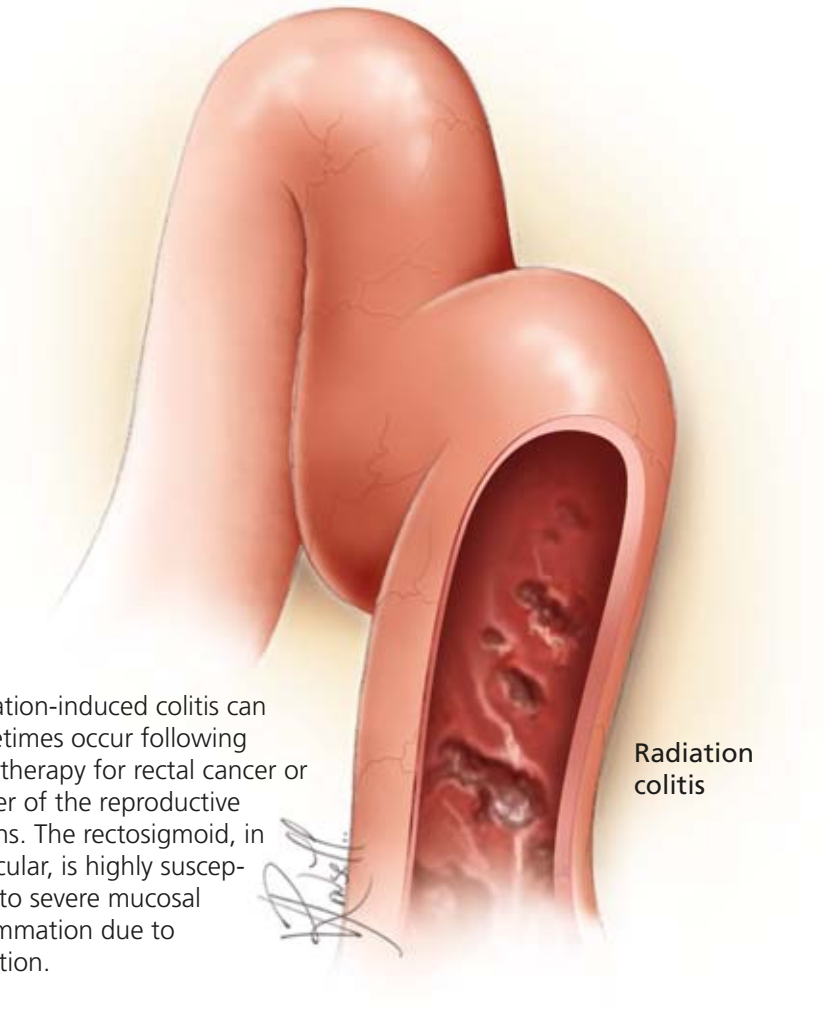
A diagnosis of microscopic colitis should be considered in patients with at least a one month history of watery, nonbloody diarrhea manifested by six to 20 bowel movements daily. The diarrhea can be associated with abdominal cramping, anorexia, and weight loss. Nocturnal stools are common. Drugs associated with microscopic colitis include: lansoprazole, nonsteroidal anti-inflammatory drugs (NSAIDs), ranitidine, ticlopidine, and carbamazepine (Table 1B).

The natural history of microscopic colitis may be chronic with recurrences or may spontaneously resolve. Bismuth subsalicylate and budesonide have proven efficacy in small trials. Steroid use is often limited by the return of symptoms following discontinuation of the medication, necessitating stronger immunosuppressants such as methotrexate or azathioprine. Other treatment options include antidiarrheals or cholestyramine alone, sulfasalazine, mesalamine, and 5-acetylsalicylic acid. Surgical intervention is rarely indicated.

Radiation Colitis

Radiation injury to the colon typically occurs after treatment of rectal, cervical, uterine, prostate, urinary bladder, and testicular cancer (Figure 2). The colon, especially the rectosigmoid, is highly susceptible to radiation injury because it is relatively immobile. Diarrhea can develop shortly after radiation therapy

Figure 2: Radiation Colitis



Radiation-induced colitis can sometimes occur following radiotherapy for rectal cancer or cancer of the reproductive organs. The rectosigmoid, in particular, is highly susceptible to severe mucosal inflammation due to radiation.

begins, but chronic symptoms of radiation colitis and proctitis can occur three months to as late as decades following the initial radiation exposure. Approximately five percent of patients exposed to more than 40 Gy will develop late-onset complications of radiation therapy. The primary symptoms associated with chronic injury to the colon and rectum include diarrhea, rectal pain, and rectal bleeding. Colonoscopy findings may vary from mild friability to fibrosis and epithelial atrophy with obliterative endarteritis.

Treatment of radiation colitis should be directed by the severity of symptoms (Table 1B). Oral and topical sucralfate, oral and topical steroids, 5-ASA compounds, sulfasalazine, hyperbaric oxygen, pentosan polysulfate, topical formalin, and antibiotics have been used to treat this condition with variable success. Thermal coagulation therapy has been used to treat bleeding associated with radiation colitis. Surgery is reserved for the most severe and refractory cases.

Conclusion

The initial evaluation of older patients with the acute onset of diarrhea should include stool studies to culture for common enteric pathogens (Campylobacter, Shigella, and Salmonella) and Escherichia coli 0157:H7 cultures should be analyzed in all cases of bloody diarrhea. In the case of Clostridium difficile toxin, stool should be sent in the presence of recent antibiotic use, recent hospitalization, or a prior history of Clostridium difficile infections. Ischemic colitis may present with similar features of Escherichia coli 0157:H7 infections and should always be considered in the older patient with bloody diarrhea. The diagnosis of microscopic colitis is not uncommon in older patients with chronic diarrhea and may be related to NSAID use. Radiation colitis can develop many years after radiation exposure.

Once diarrhea develops, older patients are at increased risk to develop dehydration and electrolyte imbalances as their ability to maintain fluid and sodium homeostasis deteriorates with age. Functionally, older patients may not recognize their dehydration or may not have their dehydration recognized; they can also be challenged by mobility issues that limit adequate hydration. The prevalence of hypernatremic dehydration increases with age and is associated with a significant mortality. Cautious and slow correction of hypernatremia is critical to prevent the osmotic shifts that lead to cerebral edema causing seizures, brain injury, and death.

Initial treatment of diarrhea in the older patient may include empiric antibiotics and gentle rehydration with appropriate correction of volume and electrolyte abnormalities. Further testing by colonoscopy, MRI / MRA, CT, or ultrasound should be considered based on the clinical presentation of the patient as well as associated risk factors, comorbidities, and medication exposures.

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