Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults

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INTRODUCTION

Ulcerative colitis is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. It commonly involves the rectum and may extend in a proximal and continuous fashion to involve other parts of the colon.

This topic will review the clinical manifestations, diagnosis, and natural history of ulcerative colitis. The definition, epidemiology, pathogenesis, and treatment of ulcerative colitis are discussed in detail, separately. (See "Definitions, epidemiology, and risk factors for inflammatory bowel disease" and "Medical management of low-risk adult patients with mild to moderate ulcerative colitis" and "Management of the hospitalized adult patient with severe ulcerative colitis" and "Management of moderate to severe ulcerative colitis in adults".)

CLINICAL MANIFESTATIONS

Colitis — Patients with ulcerative colitis usually present with diarrhea, which may be associated with blood. Bowel movements are frequent and small in volume as a result of rectal inflammation. Associated symptoms include colicky abdominal pain, urgency, tenesmus, and incontinence [1]. Patients with mainly distal disease may have constipation accompanied by frequent discharge of blood and mucus.

The onset of symptoms is usually gradual, and symptoms are progressive over several weeks. Symptoms may be preceded by a self-limited episode of rectal bleeding that occurred weeks or months earlier.

The severity of symptoms may range from mild disease with four or fewer stools per day with or without blood to severe disease with more than 10 stools per day with severe cramps and continuous bleeding [1]. (See 'Disease severity' below.)

Patients may have systemic symptoms including fever, fatigue, and weight loss. Patients may also have dyspnea and palpitations due to anemia secondary to iron deficiency from blood loss, anemia of chronic disease, or autoimmune hemolytic anemia. The presence and severity of systemic symptoms depends on the clinical severity of the intestinal disease. (See 'Disease severity' below and 'Extraintestinal manifestations' below and "Anemia of chronic disease/anemia of inflammation" and "Vitamin and mineral deficiencies in inflammatory bowel disease", section on 'Iron'.)

Physical examination is often normal, especially in patients with mild disease. Patients with moderate to severe ulcerative colitis may have abdominal tenderness to palpation, fever, hypotension, tachycardia, and pallor. Rectal examination may reveal evidence of blood. Patients with prolonged diarrhea symptoms may have evidence of muscle wasting, loss of subcutaneous fat, and peripheral edema due to weight loss and malnutrition. (See 'Disease severity' below.)

Disease severity — The severity of disease in patients with ulcerative colitis is important in guiding clinical management and can predict long-term outcomes. The severity of disease activity can be objectively measured using a clinical disease activity index. The Montreal classification of severity of ulcerative colitis is one such index that stratifies ulcerative colitis severity into mild, moderate, and severe based on the frequency and severity of diarrhea, and the presence of systemic symptoms and laboratory abnormalities [2].

- **Mild** – Patients with mild clinical disease have four or fewer stools per day with or without blood, no signs of systemic toxicity, and a normal erythrocyte sedimentation rate (ESR). Mild crampy pain, tenesmus, and periods of constipation are also common, but severe abdominal pain, profuse bleeding, fever, and weight loss are not part of the spectrum of mild disease.

- **Moderate** – Patients with moderate clinical disease have frequent loose, bloody stools (>4 per day), mild anemia not requiring blood transfusions, and abdominal pain that is not severe. Patients have minimal signs of systemic toxicity, including a low-grade fever. Adequate nutrition is usually maintained, and weight loss is not associated with moderate clinical disease.

- **Severe** – Patients with a severe clinical presentation typically have frequent loose, bloody stools (≥6 per day) with severe cramps and evidence of systemic toxicity as demonstrated by a fever (temperature ≥37.5°C), tachycardia (HR ≥90 beats/minute), anemia (hemoglobin <10.5 g/dL), or an elevated ESR (≥30 mm/hour). Patients may have rapid weight loss.

Most patients with ulcerative colitis present with an attack of mild severity at presentation, approximately 27 percent of patients have moderate disease, and 1 percent have severe disease at presentation [3,4].

The Mayo scoring system can also be used to assess disease severity and monitor patients during therapy (calculator 1) [5]. Scores range from 0 to 12 with higher scores indicating more severe disease.

Acute complications

- **Severe bleeding** – Bleeding may be severe in up to 10 percent of patients. Massive hemorrhage occurs in up to 3 percent of patients with ulcerative colitis at some time in their disease course and may necessitate urgent colectomy [6].

- **Fulminant colitis and toxic megacolon** – Patients with ulcerative colitis may develop fulminant colitis with more than 10 stools per day, continuous bleeding, abdominal pain, distension, and acute, severe toxic symptoms including fever and anorexia. Patients with fulminant colitis are at high risk of developing toxic megacolon as the inflammatory process extends beyond the mucosa to involve the muscle layers of the colon.

  Toxic megacolon is characterized by colonic diameter ≥6 cm or cecal diameter >9 cm and the presence of systemic toxicity [7,8]. (See "Toxic megacolon", section on 'Clinical manifestations'.)

- **Perforation** – Perforation of the colon most commonly occurs as a consequence of toxic megacolon [3]. However, it may also occur in the absence of toxic megacolon in patients with the first episode of ulcerative colitis due to lack of scarring from prior attacks of colitis. Perforation with peritonitis has been associated with 50 percent mortality in patients with ulcerative colitis [9]. (See "Surgical management of ulcerative colitis", section on 'Surgical options'.)

Extraintestinal manifestations — Although ulcerative colitis primarily involves the bowel, it is associated with manifestations in other organ systems. Although less than 10 percent of patients with inflammatory bowel disease (IBD) have an extraintestinal manifestation (EIM) at initial presentation, 25 percent of patients have an EIM in their lifetime [10]. With the exceptions

of primary sclerosing cholangitis, uveitis, and ankylosing spondylitis, EIMs tend to follow the clinical course of the colitis (table 1).

- **Musculoskeletal** – Arthritis/arthropathy is the most frequent EIM of IBD. IBD is associated with both a nondestructive peripheral arthritis, which primarily involves large joints, and ankylosing spondylitis. Other musculoskeletal manifestations of IBD include osteoporosis, osteopenia, and osteonecrosis. The musculoskeletal manifestations of IBD are discussed in detail, separately. (See "Clinical manifestations and diagnosis of arthritis associated with inflammatory bowel disease and other gastrointestinal diseases".)

- **Eye** – The most frequent ocular manifestations of IBD include uveitis and episcleritis (picture 1A-B). Scleritis, iritis, and conjunctivitis have also been associated with IBD. Affected patients may be asymptomatic or complain of burning, itching, or redness of the eyes. The eye manifestations of IBD and their management are discussed in detail, separately. (See "Dermatologic and ocular manifestations of inflammatory bowel disease", section on 'Ocular disease'.)

- **Skin** – The most frequent skin lesions associated with IBD include erythema nodosum and pyoderma gangrenosum (picture 2A-C). The skin manifestations of IBD and their management are discussed in detail, separately. (See "Dermatologic and ocular manifestations of inflammatory bowel disease", section on 'Dermatologic disease'.)

- **Hepatobiliary** – Primary sclerosing cholangitis, fatty liver, and autoimmune liver disease have been associated with IBD. Patients with primary sclerosing cholangitis are usually asymptomatic and identified only due to an isolated elevation in the serum alkaline phosphatase concentration. Patients may present with fatigue, pruritus, fevers, chills, night sweats, and right upper quadrant pain. (See "Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis", section on 'Clinical manifestations'.)

- **Hematopoietic/coagulation** – Patients with IBD are at an increased risk for both venous and arterial thromboembolism (table 2) [11-17]. In one prospective cohort study, for example, the risk for development of venous thromboembolism was increased in both hospitalized and ambulatory patients with an IBD flare as compared with controls (hospitalized patients absolute risk 37.5/1000 person-years versus 13.9/1000 person-years, ambulatory patients with IBD flare 6.4/1000 person-years versus 0.4/1000 person-years) [18]. (See "Overview of acute pulmonary embolism in adults", section on 'Clinical presentation, evaluation, and diagnosis' and "Management of the hospitalized adult patient with severe ulcerative colitis" and "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity".)

Autoimmune hemolytic anemia has been associated with IBD. Patients with anemia may be asymptomatic or have nonspecific symptoms including dyspnea, fatigue, and palpitations. (See "Warm autoimmune hemolytic anemia (AIHA) in adults", section on 'Clinical manifestations'.)

- **Pulmonary** – Pulmonary complications of IBD, although rare, include airway inflammation, parenchymal lung disease, serositis, and thromboembolic disease. Symptoms range in severity from asymptomatic decreases in diffusion capacity to disabling bronchiectasis with cough and mucopurulent sputum production. The pulmonary manifestations of IBD and their management are discussed in detail, separately. (See "Pulmonary complications of inflammatory bowel disease".)

LABORATORY FINDINGS

Patients with severe ulcerative colitis may have anemia, an elevated erythrocyte sedimentation rate (≥30 mm/hour), low albumin, and electrolyte abnormalities due to diarrhea and dehydration [19-21]. (See 'Disease severity' above.)

Patients with ulcerative colitis and primary sclerosing cholangitis may have an elevation in serum alkaline phosphatase concentration. (See "Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis", section on 'Clinical manifestations'.)

Fecal calprotectin or lactoferrin may be elevated due to intestinal inflammation but are nonspecific [22]. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'General laboratory tests'.)

IMAGING

Abdominal imaging is not required for the diagnosis of ulcerative colitis but may be performed in patients who present with symptoms of colitis.

Abdominal radiography is usually normal in patients with mild to moderate disease, but may identify proximal constipation, mucosal thickening or "thumbprinting" secondary to edema, and colonic dilation in patients with severe or fulminant ulcerative colitis. (See 'Disease severity' above.)

Double contrast barium enema may be normal in mild ulcerative colitis. Findings on barium enema may include a diffusely reticulated pattern with superimposed punctate collections of

barium in micro ulcerations (image 1). In more severe disease, there may be spiculated collar button ulcers, shortening of the colon, loss of haustrae, narrowing of the luminal caliber, pseudopolyps, and filiform polyps (image 2A-C). Barium enema should be avoided in patients who are severely ill since it may precipitate ileus with toxic megacolon. (See "Toxic megacolon", section on 'Clinical manifestations'.)

Computed tomography (CT) and magnetic resonance imaging (MRI) may demonstrate marked thickening of the bowel wall, but this finding is nonspecific (image 3). CT and MRI have lower sensitivity than barium enema for the detection of subtle early mucosal disease, but are equivalent in patients with established and severe disease [23,24].

Ultrasound with Doppler may demonstrate a thickened hypoechoic mucosal layer in patients with active ulcerative colitis. More severe cases may be associated with transmural bowel wall thickening (image 4). However, these sonographic findings are not specific for ulcerative colitis and may be seen in colitis due to other causes. (See "Transabdominal ultrasonography of the small and large intestine", section on 'Ulcerative colitis' and 'Differential diagnosis' below.)

EVALUATION

Evaluation of a patient with suspected ulcerative colitis serves to exclude other causes of colitis, establish the diagnosis of ulcerative colitis, and to determine the extent and severity of the disease.

Diagnosis — The diagnosis of ulcerative colitis is based on the presence of chronic diarrhea for more than four weeks and evidence of active inflammation on endoscopy and chronic changes on biopsy [25] . Since these features are not specific for ulcerative colitis, establishing the diagnosis also requires the exclusion of other causes of colitis by history, laboratory studies, and by biopsies of the colon obtained on endoscopy.

History — A history of risk factors for other causes of colitis should be sought. This includes a history of recent travel to areas endemic for parasitic infections including amebiasis, recent antibiotic use that might predispose to an infection with *Clostridioides difficile*, a history of or risk factors for sexually transmitted diseases (eg, *Neisseria gonorrhoeae* and herpes simplex virus [HSV]) that are associated with proctitis. Atherosclerotic disease or prior ischemic episodes are suggestive of chronic colonic ischemia. A history of abdominal/pelvic radiation and NSAID/medication exposure should be sought as these may also be associated with colitis. In an immunocompromised patient, cytomegalovirus (CMV) can mimic ulcerative colitis. (See 'Differential diagnosis' below and "Radiation proctitis: Clinical manifestations, diagnosis, and

management" and "NSAIDs: Adverse effects on the distal small bowel and colon" and "Colonic ischemia".)

Laboratory studies — Stool studies should include stool polymerase chain reaction (PCR) for *C. difficile* toxin, routine stool cultures (*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*), and specific testing for *Escherichia coli* O157:H7 [26]. Microscopy for ova and parasites (three samples) and a *Giardia* stool antigen test should also be performed, particularly if the patient has risk factors such as recent travel to endemic areas.

In addition, testing for sexually transmitted infections, including *C. trachomatis, N. gonorrhoeae*, HSV, and *Treponema pallidum*, may be warranted, particularly in men who have sex with men or patients with severe rectal symptoms including urgency and tenesmus. (See "Evaluation of anorectal symptoms in men who have sex with men" and "Clinical manifestations and diagnosis of *Neisseria gonorrhoeae* infection in adults and adolescents".)

In addition, a complete blood count, electrolytes, albumin, and markers of inflammation (erythrocyte sedimentation rate or C-reactive protein [CRP]) should be obtained to assess disease severity. (See 'Laboratory findings' above and 'Disease severity' above.)

Endoscopy and biopsy — Endoscopic findings in patients with ulcerative colitis are nonspecific. Biopsies of the colon obtained on endoscopy are necessary to establish the chronicity of inflammation and to exclude other causes of colitis. An ileocolonoscopy allows for evaluation of the terminal ileum for inflammation that would be suggestive of Crohn disease and to determine the endoscopic extent and severity of colonic disease [27,28]. However, a colonoscopy should be avoided in hospitalized patients with severe colitis because of the potential to precipitate toxic megacolon. In such patients, a flexible sigmoidoscopy should be performed and evaluation limited to the rectum and distal sigmoid colon. (See 'Disease severity' above and "Endoscopic diagnosis of inflammatory bowel disease in adults" and "Toxic megacolon".)

The endoscopic findings in patients with ulcerative colitis include a loss of vascular markings due to engorgement of the mucosa, giving it an erythematous appearance. In addition, granularity of the mucosa, petechiae, exudates, edema, erosions, touch friability, and spontaneous bleeding may be present. More severe cases may be associated with macro ulcerations, profuse bleeding, and copious exudates (picture 3). Nonneoplastic pseudopolyps may be present in areas of disease involvement due to prior inflammation. (See "Endoscopic diagnosis of inflammatory bowel disease in adults", section on 'Differentiating ulcerative colitis from Crohn disease'.)

The biopsy features suggestive of ulcerative colitis include crypt abscesses, crypt branching, shortening and disarray, and crypt atrophy. Epithelial cell abnormalities, including mucin depletion and Paneth cell metaplasia, may be seen. Inflammatory features of ulcerative colitis include increased lamina propria cellularity, basal plasmacytosis, basal lymphoid aggregates, and lamina propria eosinophils. Although none of these features are specific for ulcerative colitis, the presence of two or more histologic features is highly suggestive of ulcerative colitis [29,30]. Basal plasmacytosis may also be a predictor of relapse in patients with seemingly well-controlled ulcerative colitis with complete mucosal healing [31]. (See "Endoscopic diagnosis of inflammatory bowel disease in adults", section on 'Histologic findings'.)

The inflammation usually involves the rectum and extends proximally in a continuous and circumferential pattern with a sharp cut off between involved and uninvolved mucosa (picture 4). The initial episode of ulcerative colitis is limited to the rectum or sigmoid colon in 30 to 50 percent of patients, 20 to 30 percent of patients have left-sided colitis, and only approximately 20 percent of patients have pancolitis with disease extending proximal to the splenic flexure and involving the cecum. Occasionally a subset of patients with ulcerative colitis have focal inflammation around the appendiceal orifice that is not contiguous with disease elsewhere in the colon (a "cecal patch") [20,32,33]. Ileal inflammation ("backwash" ileitis) may occasionally be seen in patients with ulcerative colitis with active right-sided colitis. Unlike the ileitis associated with Crohn disease which is patchy, backwash ileitis associated with ulcerative colitis is typically diffuse. However, patchy ileal inflammation can be seen in patients with UC who have been treated with systemic therapy (eg, glucocorticoids). (See "Endoscopic diagnosis of inflammatory bowel disease in adults", section on 'Direct visualization'.)

In patients with CMV colitis, conventional hematoxylin and eosin stains reveal enlarged (cytomegalic) cells that are often two- to fourfold larger than surrounding cells, usually with large eosinophilic intranuclear inclusions, sometimes surrounded by a clear halo, and smaller cytoplasmic inclusions [34]. Immunoperoxidase staining should be done to confirm suspected CMV. Cultures for *N. gonorrhoeae* and HSV should be performed in patients with severe rectal symptoms of urgency and tenesmus. (See "Clinical manifestations and diagnosis of *Neisseria gonorrhoeae* infection in adults and adolescents" and "Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus infection".)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of ulcerative colitis includes other causes of chronic diarrhea.

- **Crohn disease** – Crohn disease that involves the colon may have a similar clinical presentation to ulcerative colitis [33]. However, features that are suggestive of Crohn disease include absence of gross bleeding, presence of perianal disease (eg, anal fissures, anorectal abscess), and fistulas. The absence of rectal inflammation and the presence of ileitis, focal inflammation, and granulomas on endoscopy and biopsy are also suggestive of Crohn disease.

  Although ileal inflammation ("backwash" ileitis) may occasionally be seen in ulcerative colitis, these patients have active right-sided colitis. In addition, backwash ileitis associated with ulcerative colitis is diffuse and not patchy as seen in Crohn disease. (See "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults", section on 'Clinical features' and "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults", section on 'Diagnostic evaluation'.)

- **Infectious colitis** – Infectious colitis may have a similar clinical presentation and endoscopic appearance to ulcerative colitis (table 3). Infectious colitis must be excluded with stool and tissue cultures, stool studies, and on biopsies of the colon. (See 'Laboratory studies' above.)

- **Radiation colitis** – Radiation colitis may be seen weeks to years after abdominal or pelvic irradiation. Radiation colitis involving the rectum or sigmoid colon has a similar appearance to ulcerative colitis on endoscopy. Although not specific for radiation colitis, histologic findings suggestive of radiation colitis include eosinophilic infiltrates, epithelial atypia, fibrosis, and capillary telangiectasia. (See "Radiation proctitis: Clinical manifestations, diagnosis, and management", section on 'Clinical suspicion' and "Radiation proctitis: Clinical manifestations, diagnosis, and management", section on 'Clinical manifestations'.)

- **Diversion colitis** – Individuals with diversion colitis have a history of a surgically excluded bowel loop and prominent lymphoid hyperplasia on histology.

- **Solitary rectal ulcer syndrome** – Patients with solitary rectal ulcer syndrome may have bleeding, abdominal pain, and altered bowel habits. Mucosal ulceration may be seen on endoscopy similar to ulcerative colitis but solitary rectal ulcer syndrome has a characteristic appearance on histology with a thickened mucosal layer and distortion of crypt architecture. The lamina propria is replaced with smooth muscle and collagen leading to hypertrophy and disorganization of the muscularis mucosa. (See "Solitary rectal ulcer syndrome", section on 'Endoscopy and histology'.)

- **Graft versus host disease** – Graft versus host disease (GVHD) of the colon can cause chronic diarrhea in patients with a history of bone marrow transplantation. Patients may have symptoms due to involvement of the proximal gastrointestinal tract (eg, dysphagia, painful ulcers) or other organs (eg, liver involvement as suggested by elevated liver tests, skin involvement resembling lichen planus or scleroderma). There are no endoscopic features of chronic GVHD of the colon that distinguish it from ulcerative colitis. However, histologic examination in chronic GVHD is characterized by the presence of crypt cell necrosis with the accumulation of degenerative material in the dead crypts [35]. (See 'Clinical manifestations' above and "Clinical manifestations and diagnosis of chronic graft-versus-host disease", section on 'Clinical manifestations'.)

- **Diverticular colitis** – Diverticular colitis is characterized by inflammation in the interdiverticular mucosa without involvement of the diverticular orifices. In contrast, in patients with IBD and diverticulosis, the inflammation involves the colonic area harboring diverticula, as well as the diverticular orifices [36]. In addition, the distribution of the colitis in patients with diverticular colitis (ie, limitation to a segment of diverticular disease, sparing the rectum, terminal ileum, and other portions of the colon) also assist in differentiating it from ulcerative colitis [37]. (See "Segmental colitis associated with diverticulosis", section on 'Diagnosis'.)

- **Medication-associated colitis –** Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause chronic diarrhea and bleeding [38]. Other drugs that may cause a similar clinical presentation include retinoic acid, checkpoint inhibitors, mycophenolate, and gold [39]. The diagnosis is established by a history of medication use and the presence of nonspecific mucosal inflammation or mucosal erosions on biopsy that resemble ischemic changes. (See "NSAIDs: Adverse effects on the distal small bowel and colon" and "Immune checkpoint inhibitor colitis".)

- **Other disorders** – The clinical presentation of common variable immunodeficiency (CVID) may resemble inflammatory bowel disease (eg, chronic diarrhea, weight loss), and the diagnosis of CVID is discussed separately. (See "Clinical manifestations, epidemiology, and diagnosis of common variable immunodeficiency in adults", section on 'Gastrointestinal disease'.)

NATURAL HISTORY

Patients with ulcerative colitis usually present with attacks of bloody diarrhea that last for weeks to months. With treatment, the course of ulcerative colitis typically consists of intermittent

exacerbations alternating with long periods of complete symptomatic remission. However, a small percentage of patients have chronic symptoms and are unable to achieve complete remission [40,41]. Overall, patients who present initially with proctitis have a more benign disease course and frequently respond to topical therapy, whereas those who present with more extensive disease require systemic therapy and have a higher risk of colectomy.

- (See "Medical management of low-risk adult patients with mild to moderate ulcerative colitis".)
- (See "Management of moderate to severe ulcerative colitis in adults".)
- (See "Management of the hospitalized adult patient with severe ulcerative colitis".)
- (See "Surgical management of ulcerative colitis".)

Factors affecting disease course — Factors that may affect the disease course include age at diagnosis, smoking cessation, degree of and time course for mucosal healing in response to treatment, extent and severity of disease, and history of appendectomy.

Age at diagnosis — Approximately 67 percent of patients have at least one relapse within 10 years following the diagnosis, and the risk of relapse depends on the age at initial diagnosis [41-44]. In an observational study of 295 patients with ulcerative colitis, patients with late-onset ulcerative colitis (diagnosed at age 50 years or older) had a higher likelihood of steroid-free clinical remission (64 versus 49 percent) at one year as compared with those with early-onset ulcerative colitis (diagnosed between ages 18 and 30 years) [43]. A disease flare within two years of the diagnosis, the presence of fever or weight loss at diagnosis, and active disease in the preceding year increase the risk of subsequent relapse [40].

Mucosal healing — Mucosal healing in response to treatment is also important in predicting long-term clinical outcomes [45-47]. In an analysis of two multicenter, randomized controlled trials (ACT-1 and ACT-2) in which patients with moderate to severe ulcerative colitis were randomized to receive infliximab or placebo, early mucosal healing as defined by a Mayo endoscopy subscore of 0 or 1 at week 8 in patients treated with infliximab was associated with a lower risk of colectomy through 54 weeks and higher rates of symptomatic remission, steroid-free remission, and subsequent mucosal healing at weeks 30 and 54 [47]. (See 'Disease severity' above and "Overview of dosing and monitoring of biologic agents and small molecules for treating ulcerative colitis in adults".)

Extension of colitis — Extension of colonic disease is seen in up to 20 percent of patients within five years [41,48-50]. Patients with proctitis have a 50 percent chance of extension, and those with disease proximal to the sigmoid colon have a 9 percent chance of progression to

pancolitis. Patients with left-sided ulcerative colitis and a cecal patch have a similar disease course as those with isolated left-sided ulcerative colitis [51].

Smoking — Cigarette smoking may influence the course of ulcerative colitis [52,53]. Patients who develop ulcerative colitis following smoking cessation may be more difficult to treat, and symptoms may decrease or even resolve with resumption of cigarette smoking. (See "Definitions, epidemiology, and risk factors for inflammatory bowel disease", section on 'Smoking'.)

Colectomy risk — Approximately 20 to 30 percent of patients with ulcerative colitis will require colectomy for acute complications or for medically intractable disease. The likelihood and timing of colectomy depends on the extent of the disease and severity at presentation [41,42,54]. As an example, for patients with pancolitis, the rate of colectomy is approximately 19 percent after 10 years [41]. In contrast, 5 percent of patients who present with proctitis alone have undergone colectomy after 10 years.

Appendectomy at a younger age and prior to the diagnosis of ulcerative colitis is associated with a lower risk of both colectomy and hospitalizations related to UC, although whether this is due to genetic or immunologic factors is unclear [55,56]. In a nationwide cohort study of over 63,000 patients with ulcerative colitis, patients who had appendicitis requiring appendectomy before the age of 20 years and prior to their diagnosis of ulcerative colitis were less likely to undergo colectomy and less likely to be hospitalized for ulcerative colitis compared with UC patients with an intact appendix (HR 0.44, 95% CI 0.27-0.72 and incidence rate ratio [IRR] 0.68, 95% CI 0.64-0.73, respectively [56]. (See "Acute appendicitis in children: Management".)

Chronic complications — Long-term complications of ulcerative colitis include strictures, dysplasia, and colorectal cancer (CRC).

Stricture — Benign strictures can occur due to repeated episodes of inflammation and muscle hypertrophy in approximately 10 percent of cases with ulcerative colitis [57]. Strictures are most frequently seen in the rectosigmoid colon and may cause symptoms of obstruction. Strictures in ulcerative colitis should be considered malignant until proven otherwise by endoscopic evaluation with biopsy. Surgery is indicated for strictures that cause continued symptoms of obstruction or that cannot be fully evaluated to exclude malignancy. (See "Surgical management of ulcerative colitis", section on 'Surgical options'.)

Dysplasia or colorectal cancer — Patients with ulcerative colitis are at increased risk for CRC (image 5). The extent of colitis and duration of disease are the two most important risk factors for CRC [58].

The risk of CRC appears to be highest in patients with pancolitis, while those with proctitis and proctosigmoiditis are probably not at increased risk of CRC, regardless of the duration of disease [59]. The CRC risk begins to increase 8 to 10 years following the onset of symptoms in patients with pancolitis [60-62]. In one prospective study, the cumulative incidence of CRC was 2.5 percent after 20 years and 7.6 percent after 30 years of disease [63]. Patients with left-sided colitis have almost the same risk of CRC and dysplasia as those with pancolitis, but the risk of CRC increases only after 15 to 20 years [64,65]. (See "Surveillance and management of dysplasia in patients with inflammatory bowel disease".)

Other factors that are associated with an increased risk of CRC include endoscopic and histological severity of inflammation, positive family history of sporadic colorectal cancer (twofold increased risk), postinflammatory pseudopolyps (twofold increased risk), and the presence of primary sclerosing cholangitis (fourfold increased risk) [19,66-70]. (See "Primary sclerosing cholangitis: Inflammatory bowel disease and colorectal cancer", section on 'Epidemiology'.)

Impact on survival

Overall mortality — Patients with ulcerative colitis may have a slightly higher overall mortality compared with the general population (hazard ratio [HR] 1.2, 95% CI 1.22-1.28) [71-73]. The overall mortality appears to be highest in the first year after ulcerative colitis diagnosis (HR 2.4, 95% CI 2.3-2.6). Long-term, cause-specific mortality may also be increased in patients with ulcerative colitis (infectious disease HR 1.6, 95% CI 1.2-2.2; gastrointestinal disorders other than ulcerative colitis HR 1.3, 95% CI 1.1-1.5; and colorectal cancer HR 1.5, 95% CI 1.2-1.8). However, mortality rates appear to have decreased over time [72].

Severe colitis — Some patients with UC develop severe colitis during the course of their disease. While severe UC can be a life-threatening condition, death is uncommon [74,75]. Historically, mortality rates were high for patients with acute severe disease (eg, up to 30 percent) [76]; however, medical management and early colectomy for nonresponders have contributed to a sharp decline in mortality. In a 2019 meta-analysis of six studies including over 2000 patients with acute severe UC, the pooled mortality rates at 3 and 12 months were 0.8 and 1.0 percent, respectively [75]. Management of acute severe UC is discussed separately. (See "Management of the hospitalized adult patient with severe ulcerative colitis" and "Surgical management of ulcerative colitis".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Ulcerative colitis in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Ulcerative colitis in adults (The Basics)")
- Beyond the Basics topics (see "Patient education: Ulcerative colitis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical features** – Ulcerative colitis is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. It commonly involves the rectum and may extend in a proximal and continuous fashion to involve other parts of the colon. (See 'Clinical manifestations' above.)

  Patients with ulcerative colitis usually present with diarrhea, which is frequently associated with blood. Associated symptoms include colicky abdominal pain, urgency, and tenesmus. Patients with mainly distal disease may have constipation accompanied by frequent discharge of blood and mucus.

  Patients may also have fever, fatigue, and weight loss. Ulcerative colitis primarily involves the intestine but may be associated with several extraintestinal manifestations (table 1).

- **When to suspect ulcerative colitis** – Ulcerative colitis should be suspected in patients with chronic diarrhea for more than four weeks. The clinical presentation, including laboratory features, endoscopic appearance, and radiology findings, is not specific for ulcerative colitis, and may be seen in a number of other causes of colitis including Crohn disease, radiation colitis, ischemic colitis, infectious colitis, and colitis related to medications (table 3). (See 'Differential diagnosis' above.)

- **Establishing the diagnosis** – The diagnosis of ulcerative colitis is based on the presence of diarrhea for more than four weeks and evidence of chronic colitis on endoscopy and biopsy. Since these features are not specific for ulcerative colitis, establishing the diagnosis also requires the exclusion of other causes of colitis by history, laboratory studies, and by biopsies of the colon. (See 'Diagnosis' above.)

- **Disease course** – Patients with ulcerative colitis usually present with attacks of bloody diarrhea that lasts for weeks to months. The course of ulcerative colitis typically consists of intermittent exacerbations alternating with periods of complete symptomatic remission. However, a small percentage of patients have continuing symptoms and are unable to achieve remission. Overall, patients who present initially with proctitis have a more benign disease course and frequently respond to topical therapy, whereas those who present with more extensive disease require systemic therapy and have a higher risk of colectomy. (See 'Disease severity' above and 'Factors affecting disease course' above.)

  Extension of colonic disease is seen in up to 20 percent of patients within five years. Approximately 67 percent of patients have at least one relapse within 10 years following the diagnosis. The risk of relapse depends on the age at initial diagnosis. The likelihood and timing of colectomy depends on the extent of the disease and severity at presentation. Mucosal healing in response to treatment is an important predictor of long-term clinical outcomes. (See 'Natural history' above.)

- **Complications** – Complications associated with ulcerative colitis include severe bleeding, toxic megacolon, perforation, strictures, and the development of dysplasia and colorectal cancer. Patients with ulcerative colitis may have a slightly higher mortality as compared with the general population. (See 'Chronic complications' above.)

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Topic 4067 Version 44.0

GRAPHICS

Extraintestinal manifestations of inflammatory bowel disease

Common extraintestinal manifestations
Musculoskeletal
Arthritis – Colitic type, ankylosing spondylitis, isolated joint involvement such as sacroiliitis.
Hypertrophic osteoarthropathy – Clubbing, periostitis, metastatic Crohn disease.
Miscellaneous – Osteoporosis, aseptic necrosis, polymyositis, osteomalacia.
Skin and mouth
Reactive lesions – Erythema nodosum, pyoderma gangrenosum, aphthous ulcers, vesiculopustular eruption, cutaneous vasculitis, neutrophilic dermatosis, metastatic Crohn disease, epidermolysis bullosa acquisita.
Specific lesions – Fissures and fistulas, oral Crohn disease, drug rashes.
Nutritional deficiency – Acrodermatitis enteropathica (zinc), purpura (vitamins C and K), glossitis (vitamin B), hair loss and brittle nail (protein).
Associated diseases – Vitiligo, psoriasis, amyloidosis, epidermolysis bullosa acquisita.
Hepatobiliary
Specific complications – Sclerosing cholangitis (large-duct or small-duct), bile duct carcinoma, cholelithiasis.
Associated inflammation – Autoimmune chronic active hepatitis, pericholangitis, portal fibrosis and cirrhosis, granuloma in Crohn disease.
Metabolic – Fatty liver, gallstones associated with ileal Crohn disease.
Ocular
Uveitis iritis, episcleritis, scleromalacia, corneal ulcers, retinal vascular disease, retrobulbar neuritis, Crohn keratopathy.
Metabolic
Growth retardation in children and adolescents, delayed sexual maturation.
Less common extraintestinal manifestations
Blood and vascular
Anemia due to iron, folate, or vitamin B12 deficiency or autoimmune hemolytic anemia, anemia of chronic disease, thrombocytopenic purpura; leukocytosis and thrombocytosis; thrombophlebitis and thromboembolism, arteritis and arterial occlusion, polyarteritis nodosa, Takayasu arteritis, cutaneous vasculitis, anticardiolipin antibody, hyposplenism.

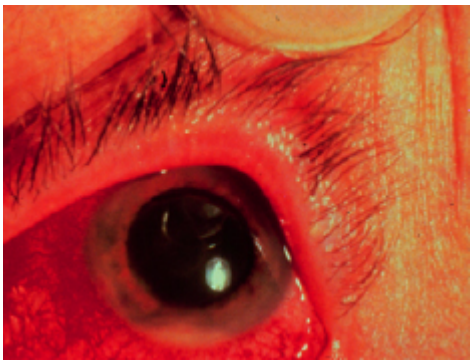
Renal and genitourinary tract
Urinary calculi (oxalate stones in ileal disease), local extension of Crohn disease involving ureter or bladder, amyloidosis, drug-related nephrotoxicity.
Renal tubular damage with increased urinary excretion of various enzymes (eg, beta N-acetyl-D-glucosaminidase).
Neurologic
Up to 3% of patients may have non-iatrogenic neurologic involvement, including peripheral neuropathy, myelopathy, vestibular dysfunction, pseudotumor cerebri, myasthenia gravis, and cerebrovascular disorders. Incidence equal in ulcerative colitis and Crohn disease. These disorders usually appear 5 to 6 years after the onset of inflammatory bowel disease and are frequently associated with other extraintestinal manifestations.
Airway and parenchymal lung disease
Pulmonary fibrosis, vasculitis, bronchitis, necrobiotic nodules, acute laryngotracheitis, interstitial lung disease, sarcoidosis. Abnormal pulmonary function tests without clinical symptoms are common (up to 50% of cases).
Cardiac
Pericarditis, myocarditis, endocarditis, and heart block – More common in ulcerative colitis than in Crohn disease; cardiomyopathy, cardiac failure due to anti-TNF therapy.
Pericarditis may also occur from sulfasalazine/5-aminosalicylates.
Pancreas
Acute pancreatitis – More common in Crohn disease than in ulcerative colitis. Risk factors include 6-mercaptopurine and 5-aminosalicylate therapy, duodenal Crohn disease.
Autoimmune
Drug-induced lupus and autoimmune diseases secondary to anti-TNF-alpha therapy.
Positive ANA, anti-double-stranded DNA, cutaneous and systemic manifestations of lupus.

TNF: tumor necrosis factor; ANA: antinuclear antibody; DNA: deoxyribonucleic acid.

Modified from: Das KM. Relationship of extraintestinal involvements in inflammatory bowel disease: New insights into autoimmune pathogenesis. Dig Dis Sci 1999; 44:1.

Graphic 81867 Version 12.0

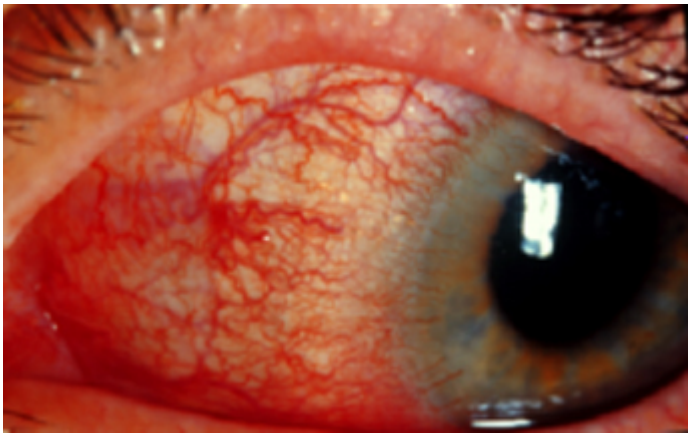
Anterior uveitis in a patient with inflammatory bowel disease



Anterior uveitis in a patient with inflammatory bowel disease is characterized by injection of the conjunctiva and opacity in the anterior chamber.

Graphic 75384 Version 5.0

Diffuse episcleritis

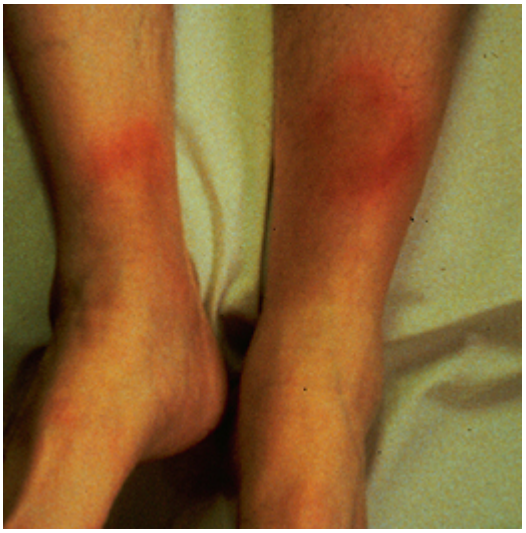


Monocular attack of diffuse episcleritis in a patient with relapsing polychondritis. There is diffuse injection of the episcleral vessels, but the underlying sclera is normal.

Courtesy of Reza Dana, MD, MSc, MPH.

Graphic 76962 Version 2.0

Erythema nodosum

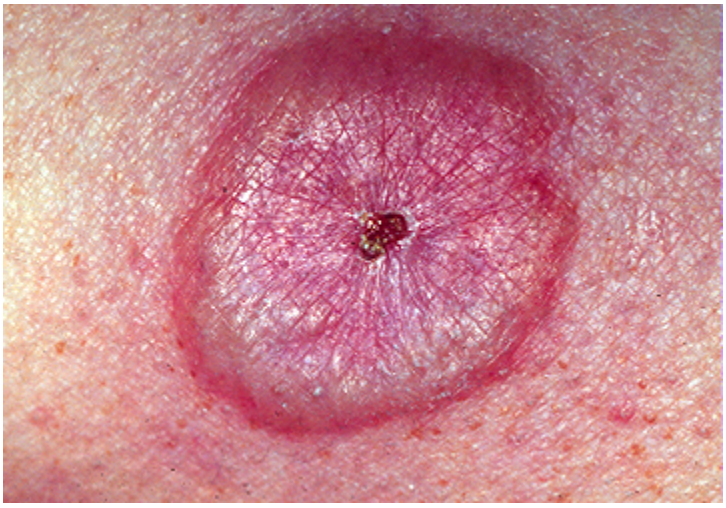


Patient with inflammatory bowel disease with red nodular areas on the shins which are characteristic of erythema nodosum.

Courtesy of the American Gastroenterological Association©. This slide cannot be downloaded but may be purchased as part of a set from the AGA.

Graphic 71344 Version 3.0

Pyoderma gangrenosum

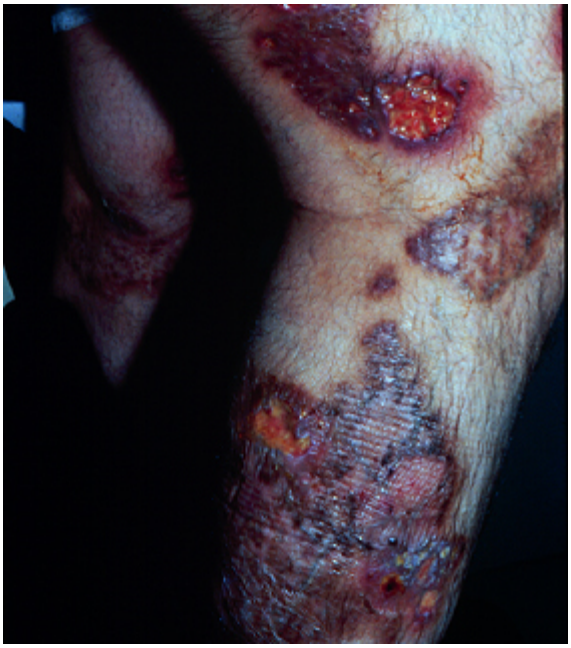


Early lesion in pyoderma gangrenosum presenting as a pustular and violaceous plaque with incipient breakdown.

Courtesy of Cynthia Magro, MD.

Graphic 53733 Version 1.0

Pyoderma gangrenosum



Multiple active and healing lesions of pyoderma gangrenosum with cribriform scarring in patient with inflammatory bowel disease.

Courtesy of Samuel Moschella, MD.

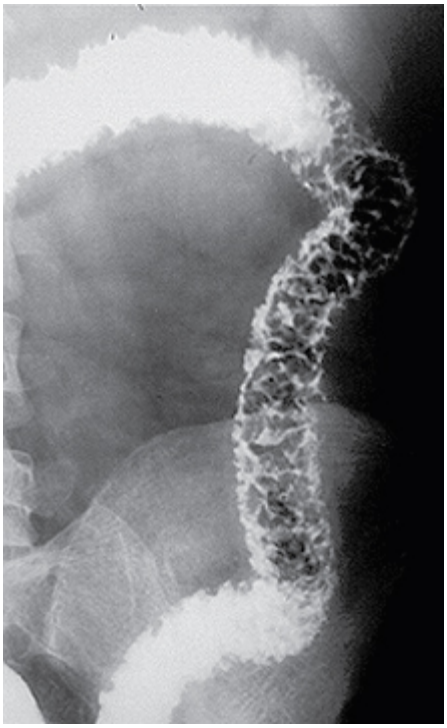
Graphic 52528 Version 1.0

Hypercoagulability in inflammatory bowel disease

Clinical characteristics
Unusual sites
Associated with active disease and better when disease controlled
Associated with use of steroids (possibly indicating active disease)
Recurrent
Serious
Younger age
Abnormalities described
Abnormal fibrinolysis
Abnormal platelet aggregation
Activated protein C increased
Circulating immune complexes
Decreased antithrombin III
Factor V Leiden mutation
Increased cytokines (interleukin-6, thrombopoietin)
Increased factors V and VIII
Increased plasminogen activator inhibitor
Increased sedimentation rate, fibrinogen
Lupus anticoagulant
Thrombocytosis and leukocytosis (uniformly present in most studies)

Graphic 68675 Version 1.0

Acute ulcerative colitis

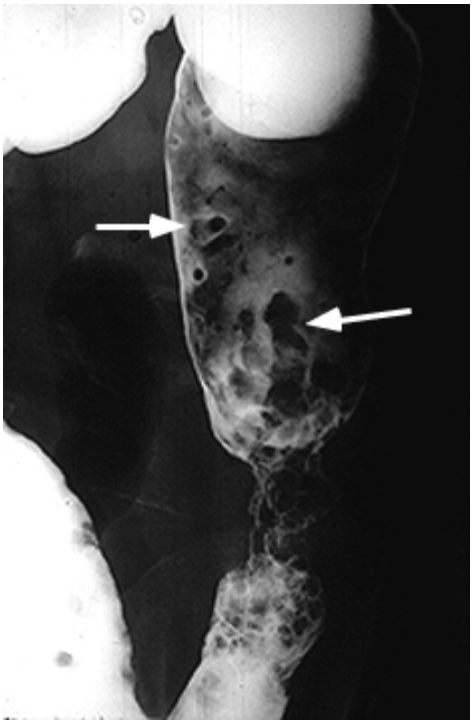


Double contrast barium enema demonstrates extensive mucosal ulceration and inflammation throughout the colon.

Courtesy of Jonathan Kruskal, MD

Graphic 60508 Version 2.0

Pseudopolyps in ulcerative colitis

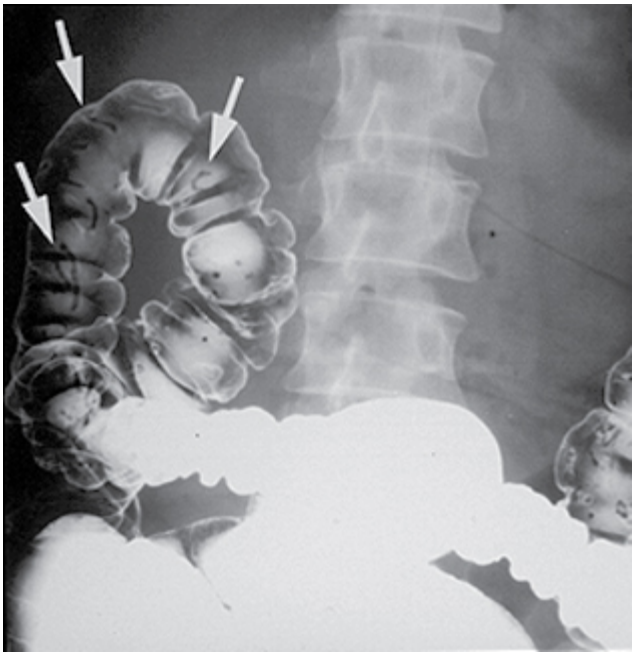


Double contrast barium enema demonstrates mucosal pseudopolyps (arrows) and a stricture arising in the descending colon.

Courtesy of Norman Joffe, MD.

Graphic 56793 Version 2.0

Filiform polyps in chronic ulcerative colitis

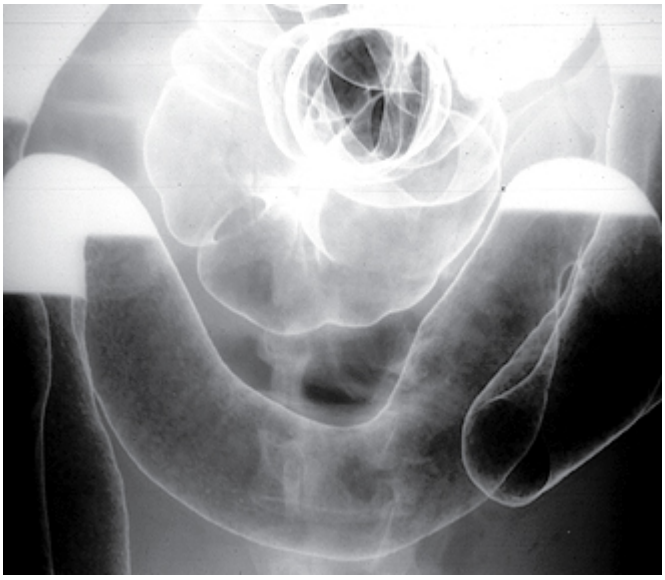


Double contrast barium enema shows fine linear polyps arising from the colon wall (arrows). These polyps are typically seen in chronic ulcerative colitis.

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 63353 Version 2.0

Chronic ulcerative colitis

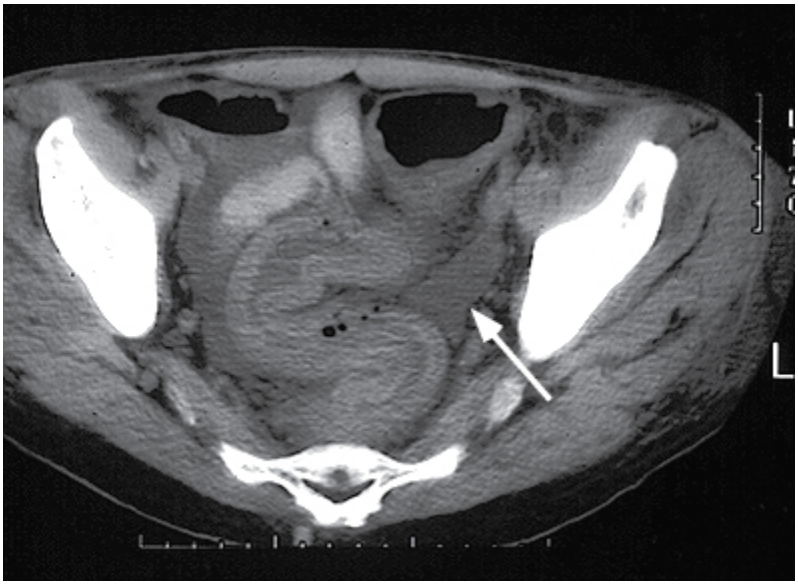


Double contrast barium enema in a patient with chronic ulcerative colitis shows a featureless colon with complete loss of folds in the sigmoid colon.

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 65953 Version 2.0

CT scan of ulcerative colitis

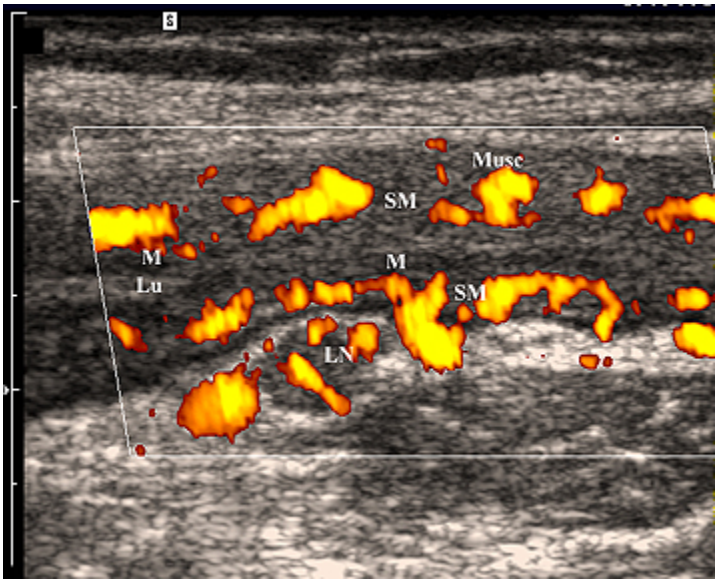


Axial CT scan through the pelvis shows marked thickening of the wall of the rectum and sigmoid colon with some free fluid in the pelvis (arrow). These features are not specific and may be seen in any form of colitis.

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 70898 Version 2.0

Ulcerative colitis on ultrasound

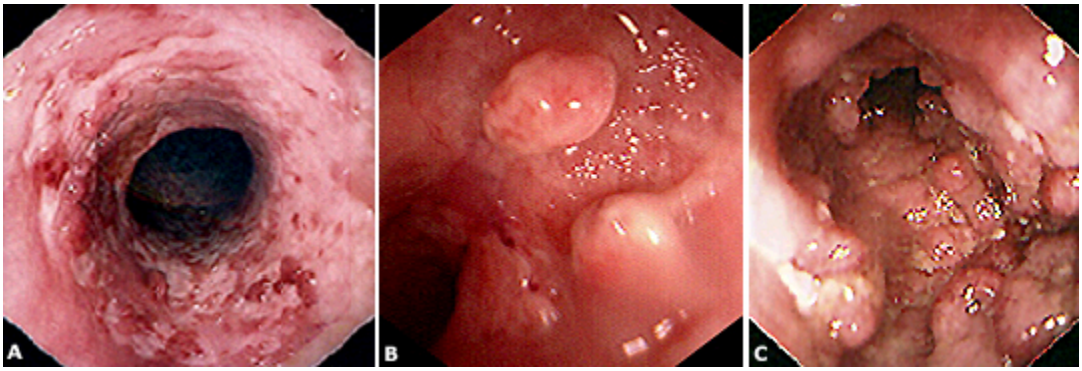


Transabdominal ultrasound of chronic active ulcerative colitis of the sigmoid colon showing a symmetric mural inflammatory reaction by color Doppler imaging. Bowel wall thickening of the mucosa (M), echorich and hypervascular submucosa (SM) and echopoor muscularis propria (Musc) is indicated. The lumen is not seen due to mucosal swelling. A small (6 mm) periintestinal lymph node (LN) is indicated as well.

Courtesy of Christoph F Dietrich, MD.

Graphic 59627 Version 3.0

Ulcerative colitis

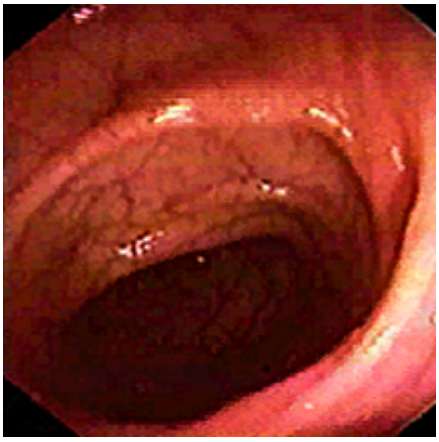


Endoscopic appearance of ulcerative colitis. Extensive ulceration of the mucosa is the most common endoscopic finding (panel A). The surface is irregular, friable, and erythematous, with loss of the normal vascular markings. Pseudopolyps may form as a reaction to inflammation (panel B); these can become quite extensive (panel C).

Courtesy of James B McGee, MD.

Graphic 81755 Version 2.0

Normal sigmoid colon

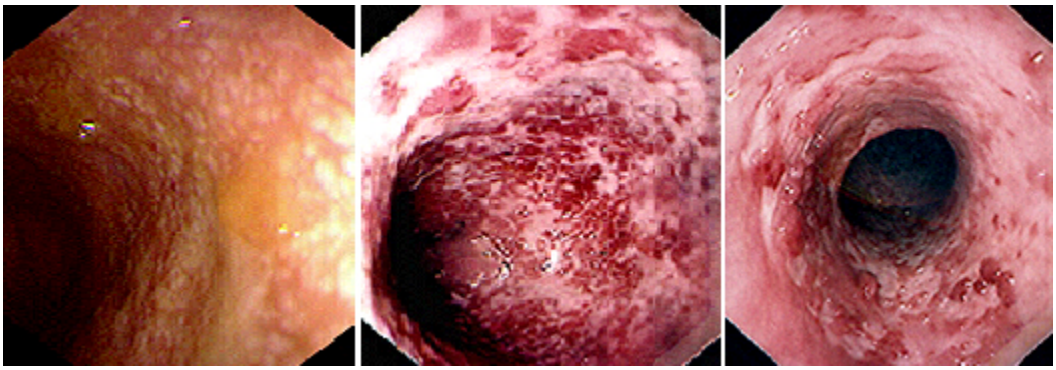


Endoscopic appearance of the normal sigmoid colonic mucosa. The fine vasculature is easily visible, and the surface is shiny and smooth. The folds are of normal thickness.

Courtesy of James B McGee, MD.

Graphic 55563 Version 1.0

Continuous involvement of colonic lesions in ulcerative colitis



In contrast with Crohn disease, lower endoscopy in ulcerative colitis shows continuous and circumferential involvement, with no normal areas of mucosa.

Courtesy of James B McGee, MD.

Graphic 76332 Version 4.0

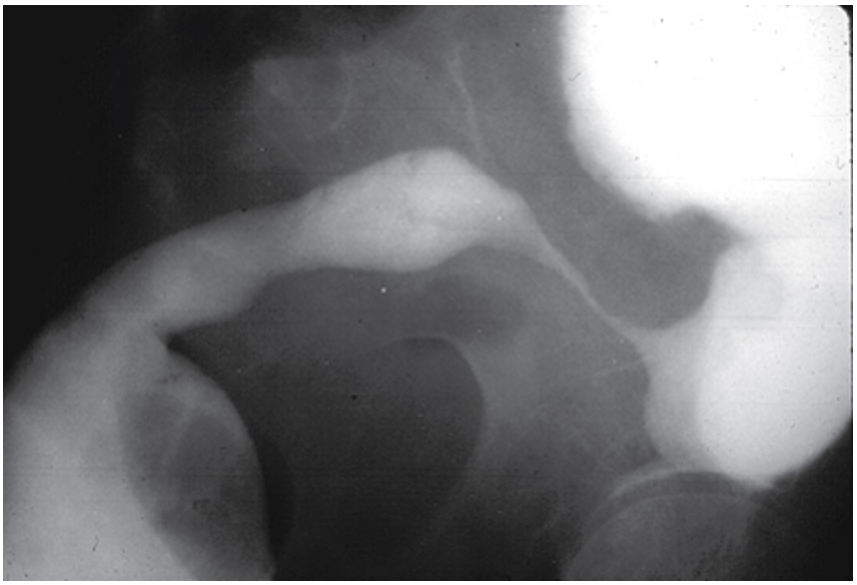
Infectious mimics of inflammatory bowel disease

Infectious agents causing colitis and/or ileitis
Bacteria
Shigella species
Enterohemorrhagic *Escherichia coli*
Enteroinvasive *E. coli*
Campylobacter jejuni
Salmonella species (gastroenteritis and typhoid fever)
Yersinia enterocolitica
Mycobacterium tuberculosis
Clostridioides (formerly *Clostridium*) *difficile*
Vibrio parahaemolyticus
Chlamydia trachomatis (lymphogranuloma venereum serotypes)
Parasites
Entamoeba histolytica
Schistosoma species
Balantidium coli
Trichinella spiralis
Viruses
Cytomegalovirus
Infectious agents causing proctitis
Neisseria gonorrhoeae
Herpes simplex virus
C. trachomatis
Treponema pallidum
Cytomegalovirus

Adapted from: Guerrant RL, Lima AA. Inflammtory enteritides. In: Principles and Practice of Infectious Diseases, 5th ed, Mandell GL, Bennett JE, Dolin R (Eds), Churchill Livingstone, Philadelphia 2000. p.1127.

Graphic 67648 Version 4.0

Sigmoid cancer developing in ulcerative colitis, as seen on barium enema



Barium enema study demonstrates a focal stricture in the sigmoid colon caused by an infiltrating cancer. The adjacent bowel is featureless and folds are absent, findings characteristic of chronic ulcerative colitis.

Courtesy of Norman Joffe, MD.

Graphic 63411 Version 3.0

Contributor Disclosures

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