

INFLAMMATORY BOWEL DISEASE

General considerations

Epidemiology:

IBD includes ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis. The incidence is higher in Western countries than in Asia. Both Ulcerative colitis and Crohn's disease have bimodal peaks which is during the third decade of life and again in the seventh decade of life for UC while in CD, most cases occurring between ages 15 to 30 and ages 55 to 60 years.

Etiology:

Multiple etiologies have been proposed but none are proven.

In summary these are

- Environmental factors as diet and infection,
- Smoking, alcohol, and oral contraceptives have been implicated
- Family history may play a role as 10 to 30% of patients with IBD report a family member with the same disease
- Autoimmune mechanism and/or defect in the intestinal immune system and there is a general agreement that interaction among the immune system, the mucosal barrier of the gut and a variety of infectious agents is involved in the pathogenesis of IBD.
- Bacteria such as Mycobacterium paratuberculosis and Listeria monocytogenes and viruses such as paramyxovirus and measles have been suggested as etiological agents in Crohn's disease.

Regardless of the underlying cause of either ulcerative colitis or Crohn, disease, both disorders are characterized by intestinal inflammation and medical therapy is largely based upon reducing inflammation.

Pathology and clinical features

Although ulcerative colitis and Crohn's disease share many pathological features these two conditions may be differentiated in 85% of patients.

Ulcerative colitis is a mucosal process in which the colonic mucosa and submucosa are infiltrated with inflammatory cells. The mucosa may be atrophic and crypt abscesses are common (Fig. 1)

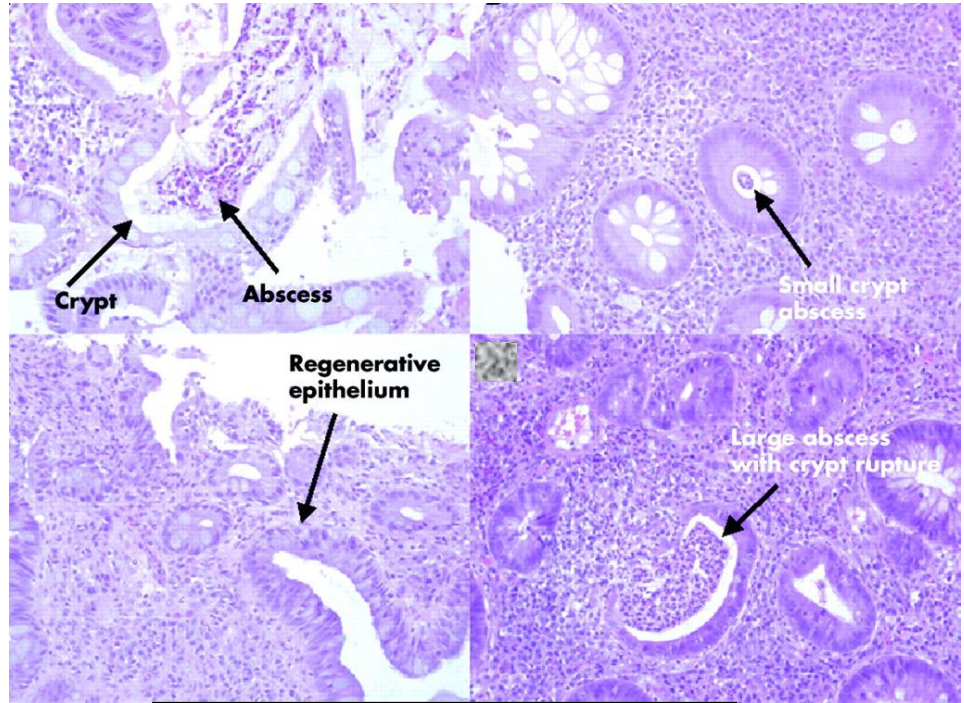


Figure 1. Histopathology of ulcerative colitis

Endoscopically, the mucosa is frequently friable and may possess multiple inflammatory pseudopolyposis. (Fig. 2)

In long standing ulcerative colitis, the colon may be foreshortened and the mucosa replaced by scar. In quiescent ulcerative colitis, the colonic mucosa may appear normal endoscopically and microscopically.



Figure 2. Pseudopolyposis

Ulcerative colitis may affect the rectum (proctitis), rectum and sigmoid colon (proctosigmoiditis), rectum and left colon (left sided or distal colitis) or the rectum and entire colon (pancolitis). (Fig. 3)

Ulcerative colitis doesn't involve the small intestine, but the terminal ileum but may demonstrate inflammatory changes (backwash ileitis).

A key feature of ulcerative colitis is the continuous involvement of the rectum and colon; rectal sparing or skip lesions suggest a diagnosis of Crohn's disease.

Symptoms are related to the degree of mucosal inflammation and the extent of colitis.

Patients typically complain of bloody diarrhea and crampy abdominal pain.

Proctitis may produce tenesmus. Severe abdominal pain and fever raises the concern of **fulminant colitis** or **toxic megacolon**.

Physical findings are non-nonspecific and range from minimal abdominal tenderness and distension to frank peritonitis. In contrast to ulcerative colitis; Crohn's disease is a transmural inflammatory process that can affect any part of the GI tract from mouth to anus. Mucosal ulcerations, an inflammatory cell infiltrate, and noncaseating granuloma are characteristic pathological findings. (Fig. 4). Chronic inflammation can ultimately result in fibrosis, stricture, and fistulas in either the colon or small intestine.

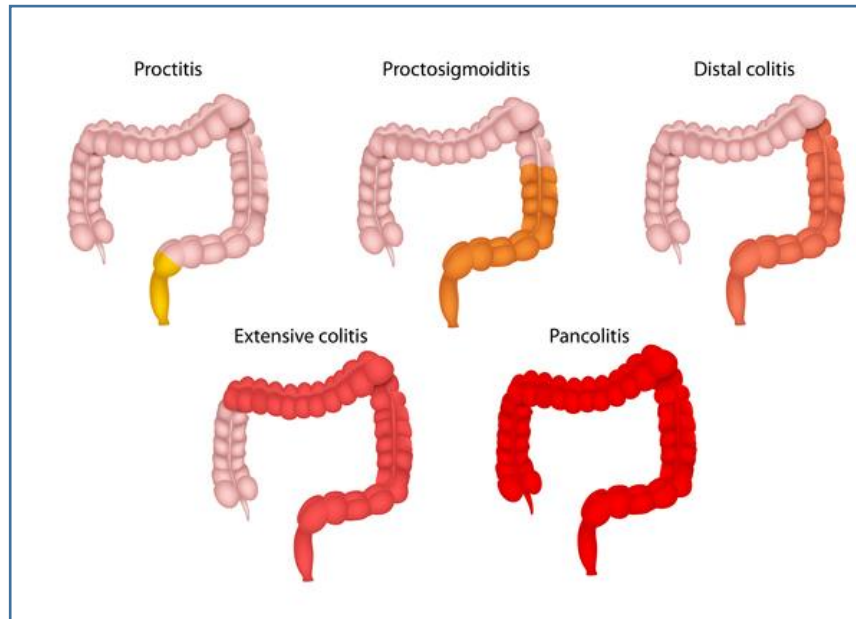


Figure 3. Types of ulcerative colitis

The endoscopic appearance of Crohn's colitis is characterized by deep serpiginous ulcers and a cobblestone appearance. (Fig. 5)

Skip lesions and rectal sparing are common.

Symptoms of Crohn's disease depend upon the severity of inflammation and/or fibrosis and the location of inflammation in GI tract.

Acute inflammation may produce diarrhea, crampy abdominal pain, and fever.

Strictures may produce symptoms of obstruction. Weight loss is common because of obstruction and from protein loss.

Perineal Crohn's disease may present with pain, swelling, and drainage from fistulas and abscesses.

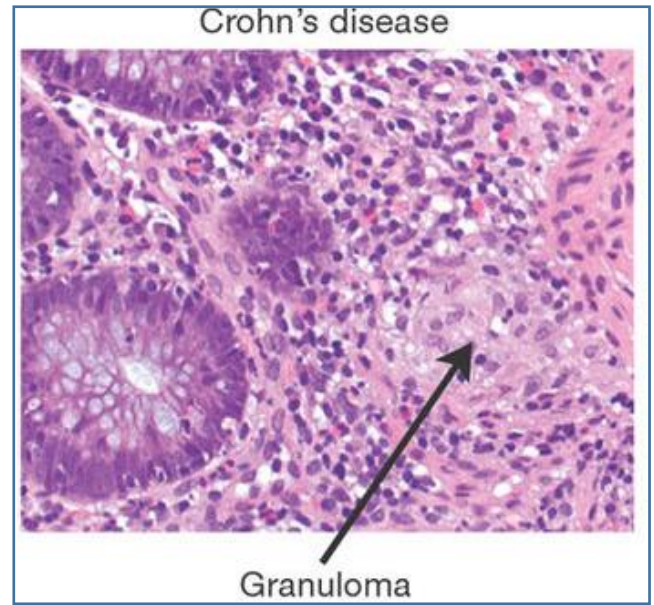


Figure 4 Histopathology of Crohn's disease

Mucosa: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa. This results in the typical **cobblestone effect**.



Figure 5. Cobblestone appearance in Crohn's disease

Differential diagnosis;

- Indeterminate colitis
- Infectious colitis as Entamoeba histolytica, C. difficile, Salmonella and Shigella

Extra intestinal manifestations

- Liver is common site of extra colonic manifestation
 - Fatty infiltration(reversible with medical treatment)
 - Cirrhosis
 - Primary sclerosing cholangitis
 - Pericholangitis
 - Bile duct carcinoma
- Arthritis, sacroiliitis and ankylosing spondylitis
- Erythema nodosum, pyoderma gangrenosum
- Ocular lesion such as uveitis, iritis and conjunctivitis

Principles of Nonoperative management

Medical therapy of bowel disease focus on decreasing inflammation and alleviating symptoms and many of the agents used are the same for both ulcerative colitis and Crohn's disease.

Mild and moderate cases can be treated in the outpatient setting while more severe cases mandate hospitalization.

Salicylates

Sulfasalazine (Azulfidine). 5-ASA are first line agents in the medical treatment of mild to moderate inflammatory bowel disease. These compounds decrease inflammation by inhibition of cyclooxygenase and 5-lipoxygenase in the gut mucosa. They require direct contact with affected mucosa.

Antibiotics

Metronidazole has been reported to improve Crohn's colitis and perianal disease. In the absence of fulminant colitis or toxic megacolon, antibiotics are not to treat ulcerative colitis.

Corticosteroids

Corticosteroids (oral or parenteral) are a key component of treatment for acute exacerbation of either ulcerative colitis or Crohn's disease. Corticosteroids are nonspecific inhibitors of the immune system and 75 to 90% of patients will improve with the administration of these drugs. However, corticosteroids have a number of serious side effects and use of these drugs should be for shortest possible course.

Corticosteroid enemas provide local therapy for proctitis and proctosigmoiditis and have fewer side effects.

Immunosuppressive Agents

- Azathioprine and 6-mercaptopurine are antimetabolite drugs that interfere with nucleic acid synthesis and thus decrease proliferation of inflammatory cells. These agents are useful for treating ulcerative colitis and Crohn's disease who have failed salicylate therapy or who are dependent upon or refractory to corticosteroids. These agents require 6 - 12 weeks to start action.
- Cyclosporine is an immunosuppressive that interferes with T-cells function. It needs 2 weeks to start action and long term use cause significant toxicity.
- Methotrexate is a folate antagonist that also has been used for treatment of IBD.
- Infliximab is a monoclonal antibody against tumor necrosis factor alpha. IV infusion of this agent decreases inflammation systemically and more than 50% of patients with moderate to severe Crohn's disease will improve with infliximab. This drug has not been used as extensively for treatment of ulcerative colitis
- Newer agents of monoclonal antibodies as vedolizumab and ustekinumab
- Nutrition. Nutritional status of the patient should be considered and parameters such as serum albumin, Prealbumin and transferrin should be assessed especially before any surgical intervention.

ULCERATIVE COLITIS

Ulcerative colitis is characterized by remissions and exacerbations. The clinical spectrum ranges from an inactive or quiescent phase to low grade active disease to fulminant disease. The onset of UC may be insidious with minimal bloody stool or the onset can be abrupt with severe diarrhea and bleeding, tenesmus, abdominal pain and fever.

Investigations:

- **Endoscopy**
Diagnosis of UC almost always is made endoscopically. Because the rectum is invariably involved, proctoscopy may be adequate to establish the diagnosis. The earliest manifestation is mucosal edema, which results in a loss of the normal vascular pattern. While mucus friability ulceration are seen in more advanced cases. Mucosal biopsy is diagnostic in chronic phase.
- **Barium enema**
In long standing UC, the colon is foreshortened and lacks haustral marking (lead pipe colon). Any stricture must be presumed to be malignant until proven otherwise.

Indications for surgery

- Emergency surgery required for patients with:
 - Massive life threatening haemorrhage
 - Toxic megacolon
 - Fulminant colitis who fail to respond rapidly to medical therapy which is bowel rest, hydration, broad spectrum antibiotics and parenteral corticosteroids and antidiarrheal agents should be avoided.
- Elective surgery indicated in
 - Intractability despite maximal medical therapy
 - High risk development of major complication of medical therapy such as aseptic necrosis of joints secondary to chronic steroid use.
 - Patients at significant risk of developing colorectal carcinoma
Risk of malignancy increases with pancolonial disease and the duration of symptoms is approximately 2% after 10 years and 8% after 20 years.

In Emergency the operations are

- Total abdominal colectomy with end ileostomy (Fig.6)
- Rarely loop ileostomy and decompressing colostomy when the patient can't withstand colectomy

In Elective situation the operations are

- Abdominal colectomy with ileorectal anastomosis, but there is a risk of ongoing inflammation and the risk of malignancy so
- Total proctocolectomy with continent ileostomy was developed to improve quality of life but morbidity is significant
- Restorative proctocolectomy with ileal pouch-anal anastomosis.

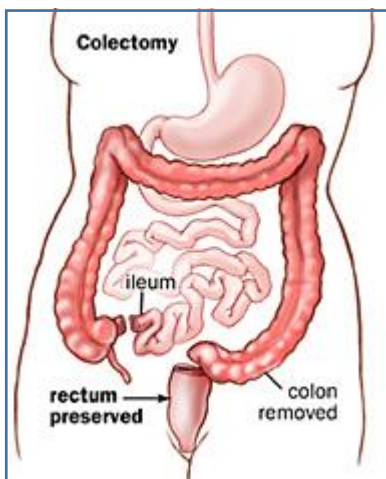


Figure 6. Total abdominal colectomy with end ileostomy

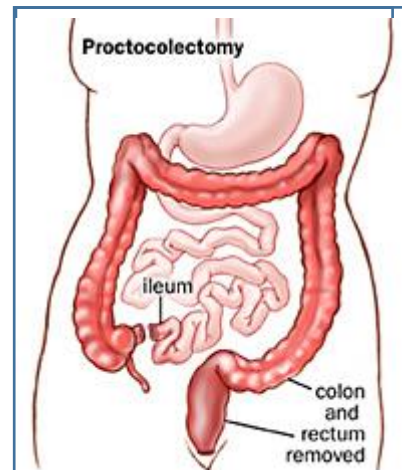


Figure 7. Total proctocolectomy with end ileostomy is the gold standard

CROHN'S DISEASE

Crohn's disease like ulcerative colitis is characterized by exacerbation and remission. It may affect any part of the intestinal tract from mouth to anus.

Diagnosis may be made by colonoscopy or esophagogastroduodenoscopy, or by barium small bowel study or enema, depending upon which part of the intestine is most affected.

Skip lesions are key in differentiating Crohn's colitis from ulcerative colitis and rectal sparing occurs in approximately 40% of patients. The most common site of involvement in Crohn's disease is the terminal ileum and caecum (ileocolic Crohn's disease), followed by the small bowel, and then by the colon and rectum. Perianal and anal Crohn's disease manifest by complex anal fistulas and/or abscesses, anal ulcers, and large skin tags may be the initial site of presentation in up to 4% of cases.

Indications for surgery

Because Crohn's disease can affect any part of the GI tract, the therapeutic rationale is fundamentally different from that of the ulcerative colitis. Ulcerative colitis may be cured by removal of the affected intestinal segment (the colon and rectum). In Crohn's disease it is impossible to remove all of the at risk intestine, therefore surgical therapy is reserved for consequences of the disease that cannot be well managed medically or to reduce the need for high risk medications, particularly steroids.

Typical surgical indications include *fibrotic obstruction, abscesses, perforation, fistulas, anorectal disease, cancer, and the rare instance of life threatening bleeding.*

INDETERMINATE COLITIS

Approximately 15% of patients with inflammatory bowel disease manifest clinical and pathologic characteristics of both ulcerative colitis and Crohn's disease.

Endoscopy, barium enema, and biopsy may be unable to differentiate ulcerative colitis from Crohn's colitis in this setting. The indications for surgery are the same as those for ulcerative colitis: intractability, complications of medical therapy, and

risk of or development of malignancy. In the setting of indeterminate colitis in a patient who prefers a sphincter-sparing operation, a total abdominal colectomy with end ileostomy may be the best initial procedure. Pathological examination of the entire colon may then allow a more accurate diagnosis. If the diagnosis suggests ulcerative colitis, an ileal pouch-anal anastomosis procedure can be performed. If the diagnosis remains in question, the safest surgical option is complete proctectomy with end ileostomy.