



Inflammatory Bowel Disease

Lecture 6 - 7

430 Pathology Team

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Inflammatory Bowel Disease:

Definition:

Crohn disease and ulcerative colitis are chronic relapsing inflammatory disorders of unknown origin, collectively known as idiopathic inflammatory bowel disease (IBD), which share many common features. They result from an abnormal local immune response against the normal flora of the gut, and probably against some self-antigens, in genetically susceptible individuals. The tissue injury in IBD is likely to be initiated by diverse genetic and immunologic pathways that are modified by environmental influences, including microbes and their products.

Types:

1. Crohn's disease
2. ulcerative colitis.

Those two diseases differ in clinical features, signs and symptoms, prognosis

Cause: although their causes are still not clear, the two diseases probably have an immunologic hypersensitivity basis.

Theories:

1. Mutations in NOD2 → Abnormal recognition and response to intracellular pathogens → less effective at recognizing and combating luminal microbes' → **mucosal immune responses.**

N.B: mutations are seen in about 15% of Crohn's disease patients but are also seen in a smaller percentage of the general population. Therefore, mutations in NOD2 are neither necessary nor sufficient for the development of Crohn's disease

2. Abnormal intestinal epithelial tight junction barrier function → Transepithelial flux of luminal bacterial into the lamina propria components activates immune responses → **Mucosal immune responses.**

Usually Immunosuppression is the method of treatment of these diseases.

Pathophysiology:

It is an idiopathic disorder.

The pathophysiology of IBD is under active investigation.

Persons with IBD have a genetic predisposition for the disease such as HLA-DR1/DQw5 in Crohn's and HLA-DR2 in ulcerative colitis

Most investigators believe that the two diseases result from a combination of

1. Defects in host interactions with intestinal microbes
2. Intestinal epithelial dysfunction

3. Aberrant mucosal immune responses.
4. For unclear reasons, research suggests that smoking increases the risk of Crohn disease but reduces the likelihood of ulcerative colitis.

Clinical manifestations:

The manifestations of IBD generally depend on the area of the intestinal tract involved.

1. Colon
 - Bloody diarrhea
 - Tenesmus (Pain during defecation)
2. Small intestine
 - Abdominal pain
 - Intestinal obstruction
Semi or total obstruction of the intestinal wall is a result from edema, inflammation, fibrosis, and hypertrophy of the muscularis propria.
 - Steatorrhea because it is affecting the ileum which is the major site of absorption
3. Extraintestinal manifestations
 - Arthritis
 - Eye manifestation
 - Skin manifestation such as erythema nodosa

Occur mainly in ulcerative colitis

In Crohn's

Occur in both Crohn's and ulcerative colitis

Aside from intestinal damage, lymph node involvement may further complicate the malabsorption and steatorrhea.

Crohn's disease:

Is a chronic inflammatory disorder

Age group: any age but has its highest incidence in young adults (20-30 years old)

Sites of Involvement:

- Any part of the GIT from the mouth to the anus.
- Ileum (30%) colon (20%).
- most commonly terminal ileum

Clinical Features:

Extremely variable clinical feature.

- **Acute phase:** fever (lasting days to weeks), diarrhea, and right lower quadrant pain may mimic acute appendicitis.

Note: The active stage progresses insidiously, but the onset of the pain maybe so abrupt and the diarrhea so mild that abdominal examination is performed with a diagnosis of appendicitis.

- **Chronic disease** : remissions and relapses over a long period of time.

Note: These remissions may happen with or without therapy.

- Thickening of the intestine may produce an ill-defined mass in the abdomen.

Gross Appearance:

- Involvement is typically segmental, with skip areas of normal intestine between areas of involved bowel.
- Marked fibrosis causing luminal narrowing with intestinal obstruction.
- Fissures (deep and narrow ulcers that look like stabs with a knife that penetrate deeply into the wall of the affected intestine)

Note: These narrow fissures extend deep to the serosa. This may lead to adhesions with adjacent loops of bowel, and with further extension of fissures bridges may form, leading to **fistula or sinus tract formation**. These fistulas may be to adherent viscera like the outside skin, or into a blind cavity to form a localized abscess.

- Fistulas (communications with other viscera).

A fistula between the intestines and bladder may form, where a patient may present with fecal material in the urine which can be complicated to a UTI.

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



Picture (a): longitudinal serpiginous ulcers (U) separated by irregular islands of edematous mucosa (M). This results in the typical cobblestone effect.



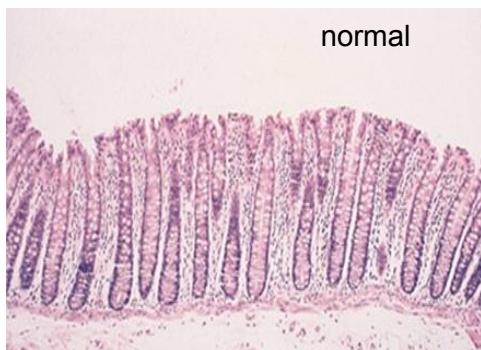
Picture (b): Section of opened intestine showing normal mucosa (N) and Crohn's segment (C), where there is clear stenosis in the Crohn's segment.

Fat : In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall **to prevent diffuse peritonitis** (creeping fat)

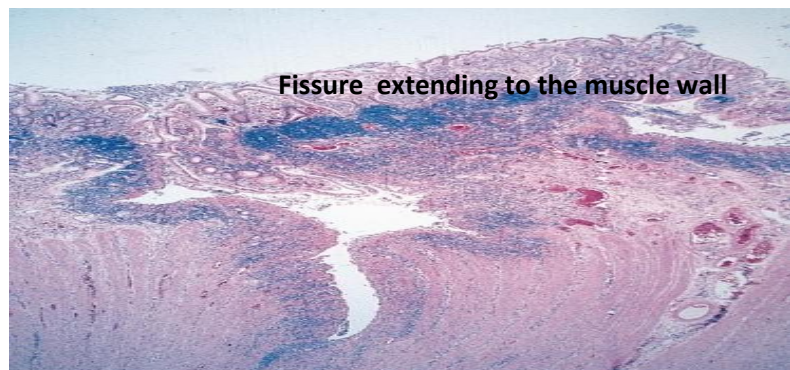
Microscopic Features

1. Distortion of mucosal crypt architecture **as a result of inflammation with accumulation of neutrophils in lumen** , this
2. Transmural inflammation.
3. Non-Caseating Epithelioid granulomas [60%].

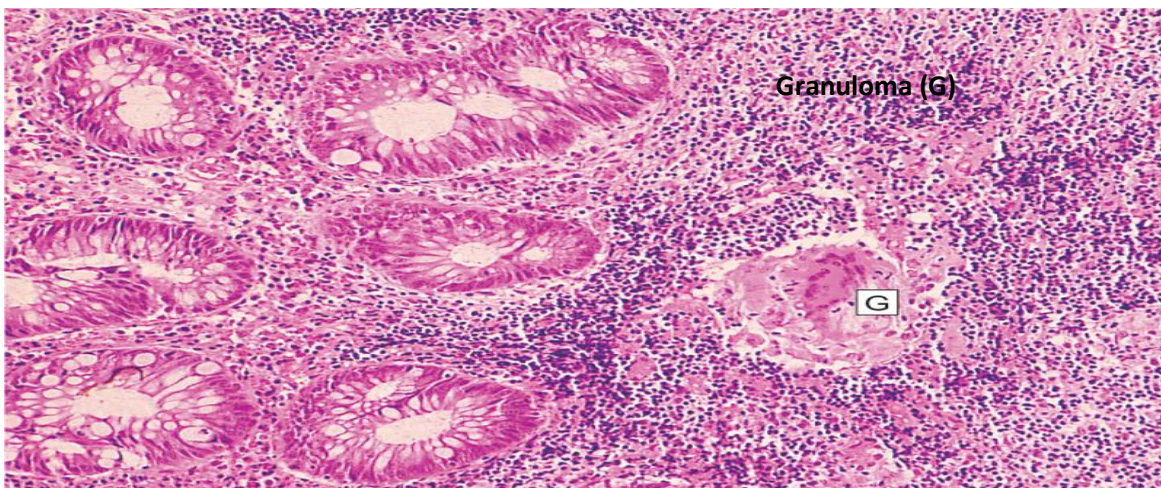
Fissure-ulcers and fistulas can be seen microscopically.



normal



Fissure extending to the muscle wall



Granuloma (G)

Stevens et al: Core Pathology, 3rd Edition.
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Complications

1. Intestinal obstruction
2. commonly (75%) have perianal lesions such as abscesses, fistulas, and skin tags.
Skin tags, also called fibroepithelial polyps, are benign skin tumors.
3. Fistula formation

- a) between the ileum and the colon result in malabsorption
 - b) Enterovesical fistulas lead to urinary infections and passage of gas and feces with urine.
 - c) Enterovaginal fistulas produce a fecal vaginal discharge.
4. Extraintestinal manifestations (arthritis and uveitis -is swelling and irritation of the uvea, the middle layer of the eye-)
 5. Slight increased risk of development of carcinoma of the colon—much less than in ulcerative colitis.

Summary

- Involvement of discontinuous segments of intestine (skip areas)
- Can involve any part of GIT.
- Noncaseating epithelioid cell granulomas
- Transmural (full-thickness) inflammation of the affected parts

Ulcerative Colitis:

Characteristics:

- is an inflammatory disease **which is limited to the mucosa**.
- It has a chronic course characterized by remissions and relapses.

Age group: 20- to 30-year but may occur at any age

Etiology :

- The cause is unknown
- Antibodies that cross-react with intestinal epithelial cells and certain serotypes of Escherichia coli have been demonstrated in the serum of some patients with ulcerative colitis.

Clinical Features

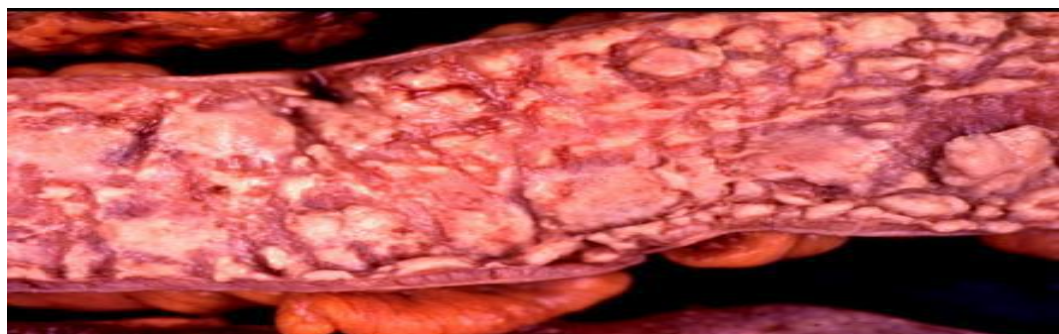
- In the acute phase and during relapse, the patient has fever, leukocytosis, lower abdominal pain, bloody diarrhea and mucus in the stool.
- The disease usually has a chronic course, with remissions and exacerbations.

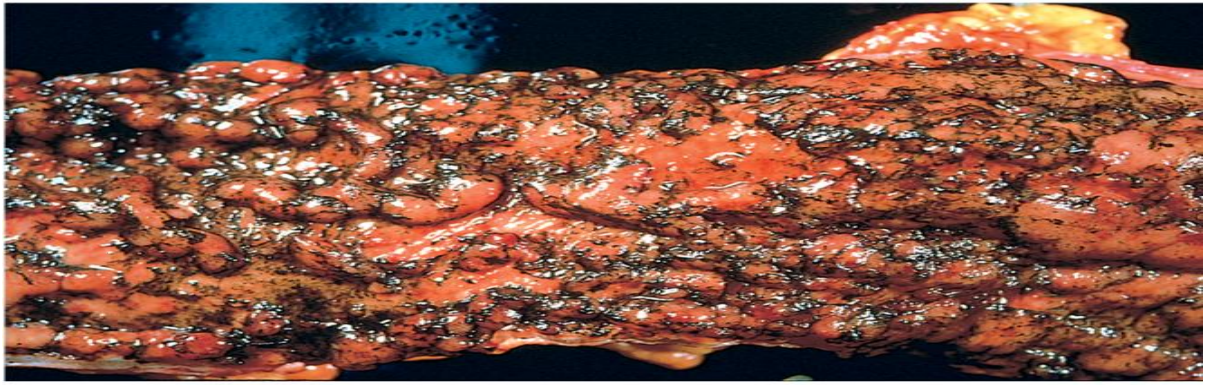
Sites of Involvement

- Ulcerative colitis is a disease of the rectum, and the colon.
- Rectum is involved in almost all cases
- The disease extends proximally from the rectum in a continuous manner without skip areas.
- The ileum is not involved as a rule

Gross Appearance

- Involves mainly the mucosa by diffuse hyperemia (**increase blood flow**) with numerous superficial ulcerations in the acute phase, with no skip lesions.
- The regenerated or nonulcerated mucosa may appear polypoid (inflammatory pseudopolyps) in contrast with the atrophic areas or ulcers.

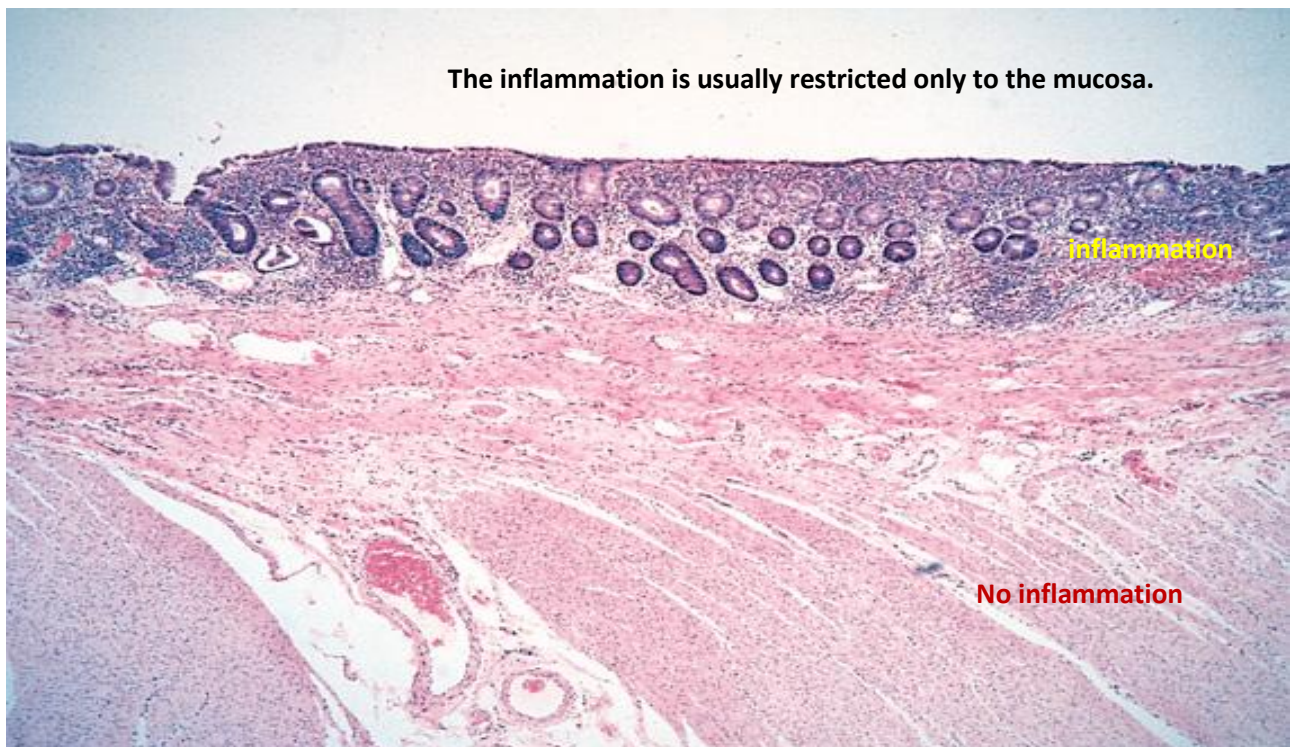


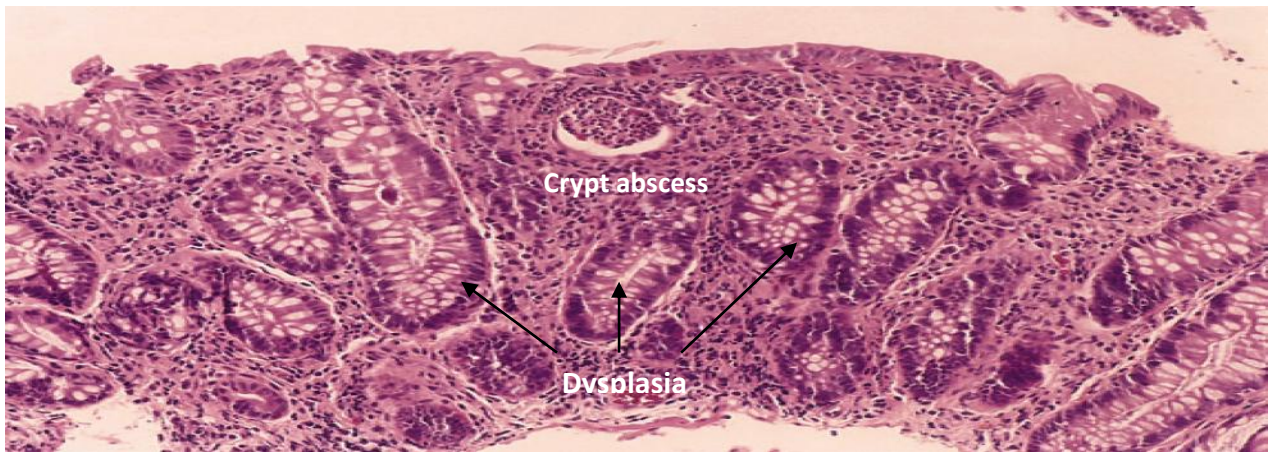
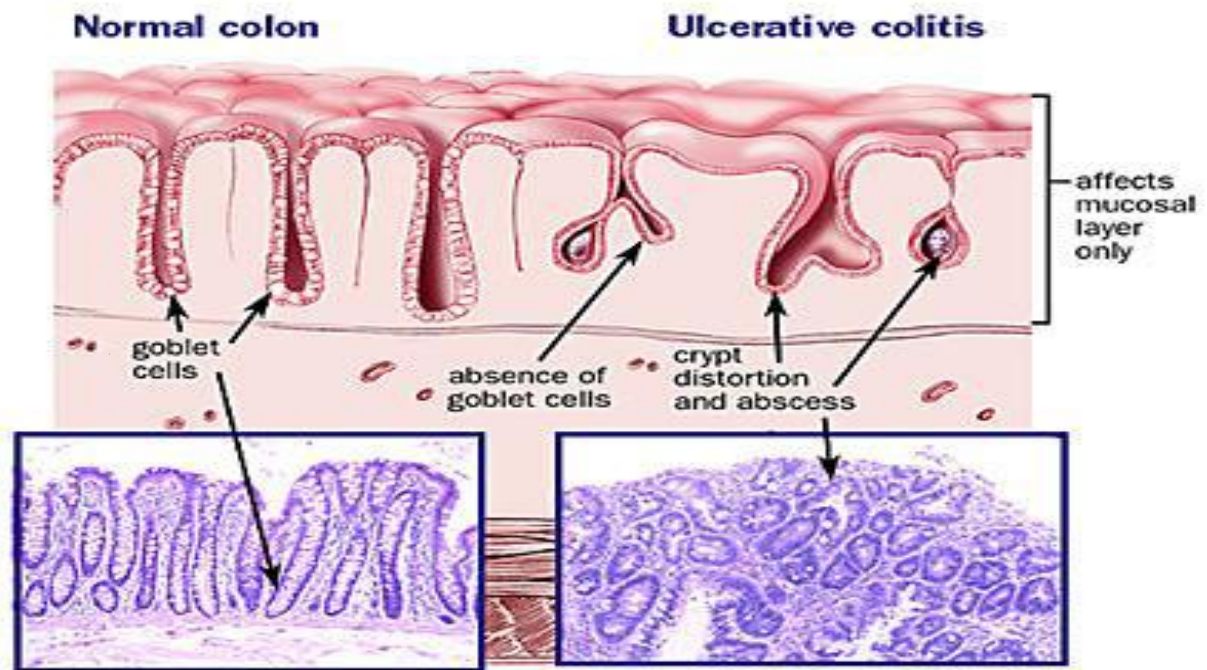


Inflammatory pseudopolyps

Microscopic Appearance:

- The inflammation is usually restricted to the mucosa.
- **In the active phase:** neutrophils (Cryptitis, crypt abscess)
 N.B: cryptitis happens when the neutrophils attack the epithelium
 Crypt abscess happens if the neutrophils are in the crypt lumen
- **In the chronic phase:** crypt atrophy and distortion
- In the regeneration phase patients may develop dysplasia → premalignant stage
- Active inflammation correlates well with the severity of symptoms.





Complications:

- **Acute phase:**

1. Severe bleeding
2. Toxic megacolon (dilation of the colon, with functional obstruction)

Exposure of the muscularis propria (muscular layer) and neural plexus to fecal material also may lead to complete shutdown of neuromuscular function. When this occurs, the colon progressively swells and dilates and becomes gangrenous (**toxic megacolon**). This is a life-threatening medical emergency and colonic resection has to be done.

- **Chronic ulcerative colitis:**

- Increase risk of developing colon carcinoma, **more than that of Chron's disease**
- The presence of high-grade dysplasia in a mucosal biopsy imposes a high risk of cancer and is an indication for colectomy.

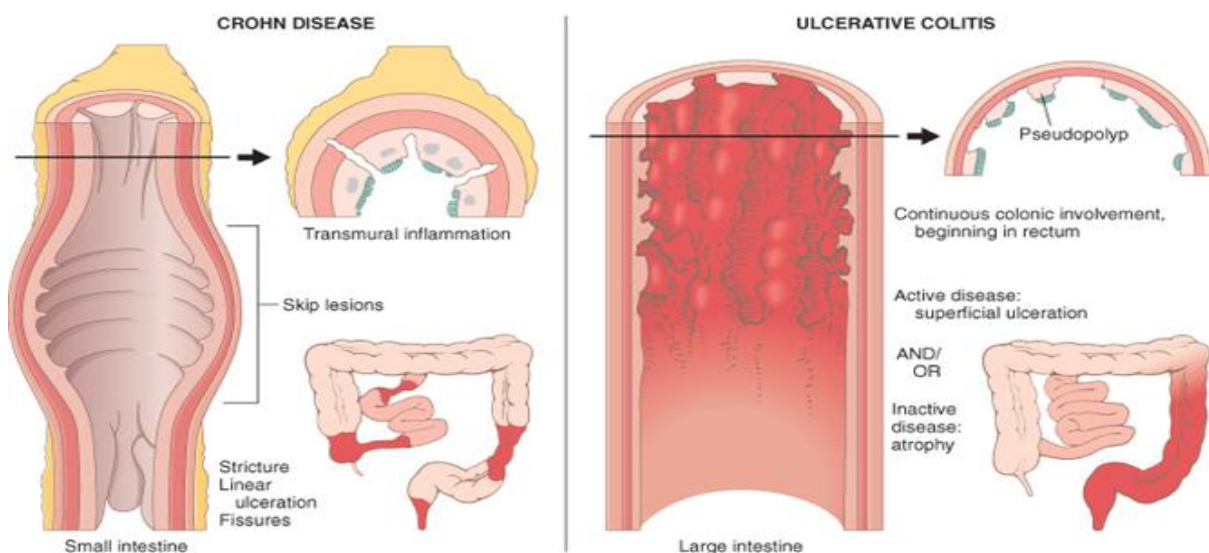
- **Extraintestinal manifestations**

Occur more commonly in ulcerative colitis than in Crohn's disease.

1. Arthritis
2. Uveitis (**Uveitis** is swelling and irritation of the uvea, the middle layer of the eye.)
3. skin lesions (pyoderma gangrenosum),
4. sclerosing pericholangitis (fibrosis around bile ducts), leading to obstructive jaundice.

Summary :

	Crohn's disease	Ulcerative Colitis
Site	Any part of the GIT	Colon only
Pattern	Skip areas of normal mucosa	Diffuse involvement of mucosa
Depth of the ulcer	Deep ulcers (fissure)	Superficial ulcers
Extent of inflammation	Transmural inflammation	Mucosal inflammation only
Fistula formation	Yes	No
Creeping mesenteric fat	Yes	No
Fibrous thickening of wall	Yes	No
Granulomas	Yes	No
Dysplasia	rare	Common
Carcinoma	rare	more common (10%)
Mucosal appearances	Cobblestone	Pseudopolyps
Bowel wall	Thickened wall Narrow lumen	Thin wall Dilated lumen
MHC Class II	HLA-DR1/DQw5	HLA-DR2
Complications	Short gut syndrome Fistula formation Bowel perforation Stricture formation	Haemorrhage Electrolyte loss Toxic megacolon Systemic effects



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Comparison of the distribution patterns of Crohn disease and ulcerative colitis, and the different conformations of the ulcers and wall thickenings.