

Gastrointestinal Block

Pathology lecture

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Inflammatory bowel disease

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Learning Objectives

1. Know the two forms of idiopathic inflammatory bowel disease (IBD).
2. Compare and contrast Crohn's disease and Ulcerative Colitis with respect to:
 - a. clinical features and extraintestinal manifestations
 - b. pathogenesis
 - c. pathology (gross and microscopic features)
 - d. complications (especially adenocarcinoma preceded by dysplasia)

Inflammatory Bowel Diseases

Inflammatory bowel disease (IBD) is a chronic condition resulting from inappropriate mucosal immune activation

- ❑ Crohn's disease (CD) and ulcerative colitis (UC)
- ❑ Ulcerative colitis is the common inflammatory bowel disease
- ❑ Although their causes are still not clear, the two diseases probably have an immunologic hypersensitivity basis.

Epidemiology

- Both Crohn's disease (CD) and ulcerative colitis (UC) are more common in females and in young adults

Ulcerative colitis

More common in whites than blacks

Occurs between 14 and 38 years of age

Lower incidence in smokers and other nicotine users

Lower incidence if previous appendectomy <20 years

Crohn's disease

More common in whites than blacks, in Jews than non-Jews. More common in children than adults.

Smoking is a risk factor

Majority (>75%) of cases occur between 11 and 35 years of age

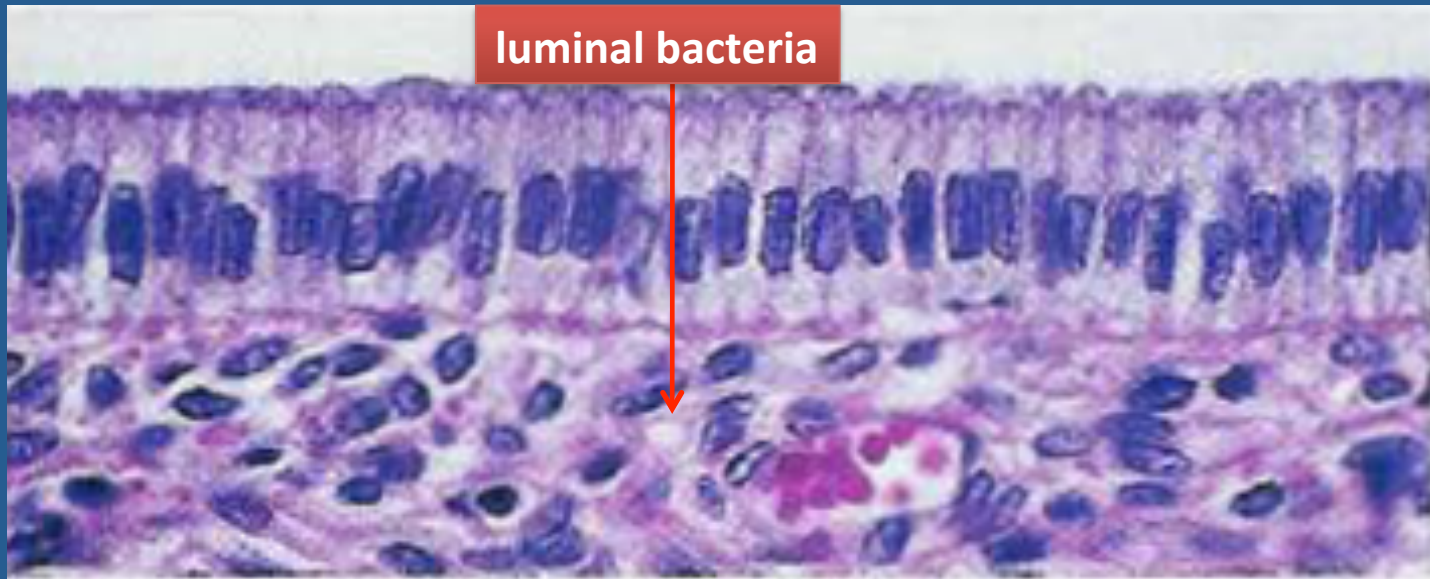
Epidemiology

- The geographic distribution of IBD is highly variable, but it is most prevalent in North America, northern Europe, and Australia.
- IBD incidence worldwide is on the rise and is becoming more common in regions in which the prevalence was historically low.

Epidemiology

- The *hygiene hypothesis* suggests that these changes in incidence are related to:
 - improved food storage conditions and decreased food contamination.
 - improved hygiene has resulted in inadequate development of regulatory processes that limit mucosal immune responses early in life.
 - As a result, exposure of susceptible individuals to normally innocuous microbes later in life triggers inappropriate immune responses due to loss of intestinal epithelial barrier function.

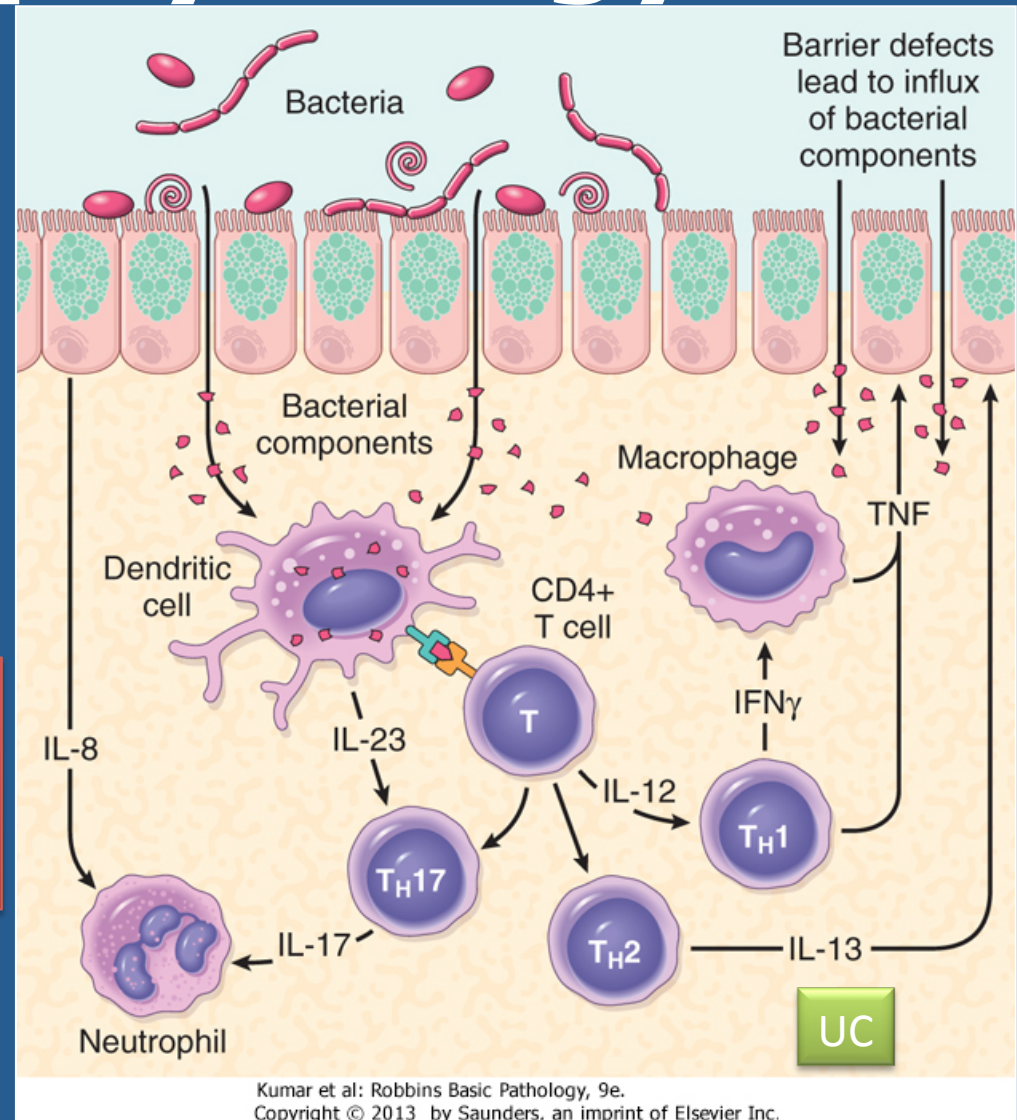
Pathophysiology



Pathophysiology

1. Defects in host interactions with intestinal microbes
2. Intestinal epithelial dysfunction
3. Aberrant mucosal immune responses.

For unclear reasons, research suggests that smoking increases the risk of Crohn's disease but reduces the likelihood of ulcerative colitis.



Pathophysiology

Genetics: mutation in **Nucleotide-binding oligomerization domain-containing protein 1** (encodes a protein that binds to intracellular bacterial peptidoglycans) **NOD2**..... susceptibility gene in Crohn disease
..... **Abnormal recognition and response to pathogens**

THEORY

Abnormal in
epithelial tight
barrier function

Leak

Immune responses.

Transepithelial flux of luminal
bacterial components activates
immune responses

Immunosuppression is the
mainstay of IBD therapy.

Inflammation

Clinical

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

Colon

Bloody diarrhea,
Tenesmus

Small intestine

Abdominal pain
Intestinal obstruction.
Steatorrhea

Extraintestinal manifestations

Arthritis
Eye manifestation
Skin manifestation

Crohn's disease

- is a chronic inflammatory disorder that most commonly affects the **ileum** and colon but has the potential to involve **any part** of the gastrointestinal tract from the mouth to the anus.

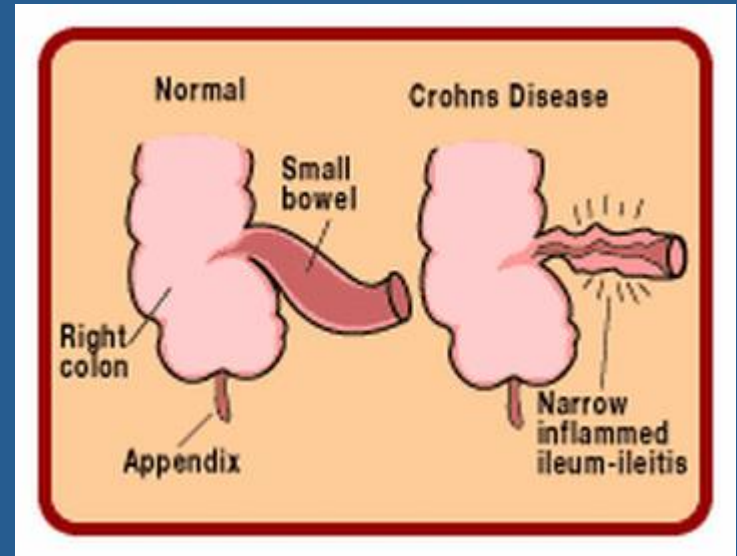
Crohn's disease

Clinical Features

- ❑ Any age but has its highest incidence in young adults
- ❑ Extremely variable clinical feature.
- **Acute phase:** fever, diarrhea, and right lower quadrant pain may mimic acute appendicitis.
- **Chronic disease:** remissions and relapses over a long period of time.
- Thickening of the intestine may produce an ill-defined mass in the abdomen.

Crohn's disease

- **Sites of Involvement:**
 - ✓ Any part of the GIT from the mouth to the anus.
 - ✓ ileum (30%) colon (20%).
 - ✓ most commonly terminal ileum
 - ✓ Commonly (75%) have perianal lesions such as abscesses, fistulas, and skin tags.

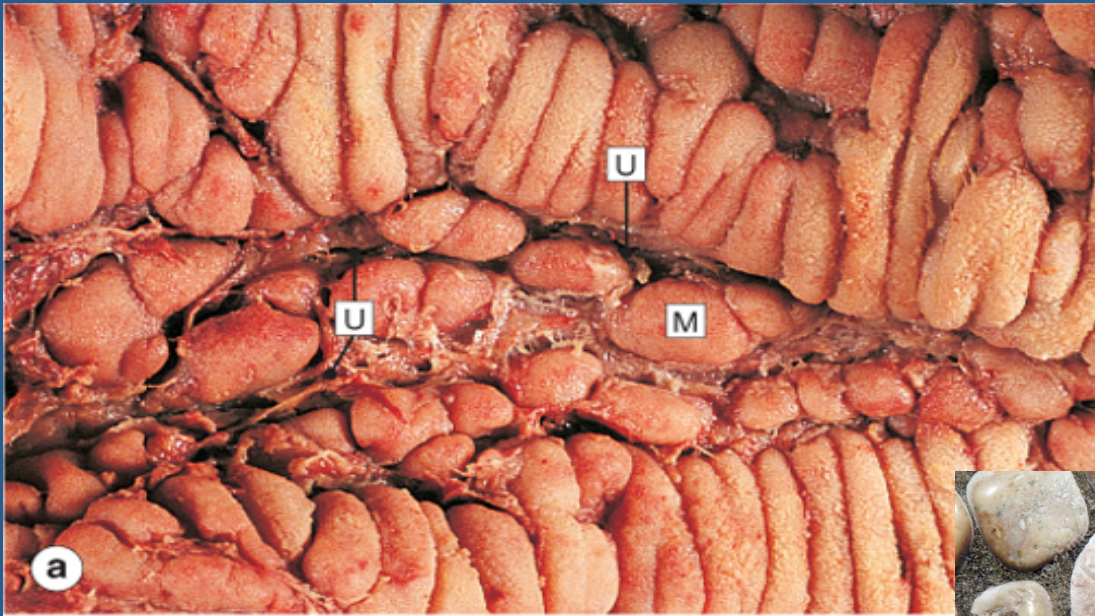


Crohn's disease

- **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)
- **fistulas** (communications with other viscera).



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



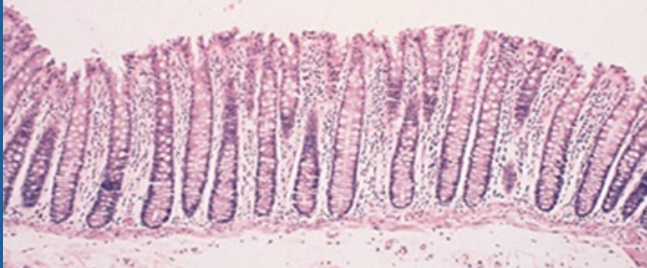
FAT : In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (**creeping fat**)



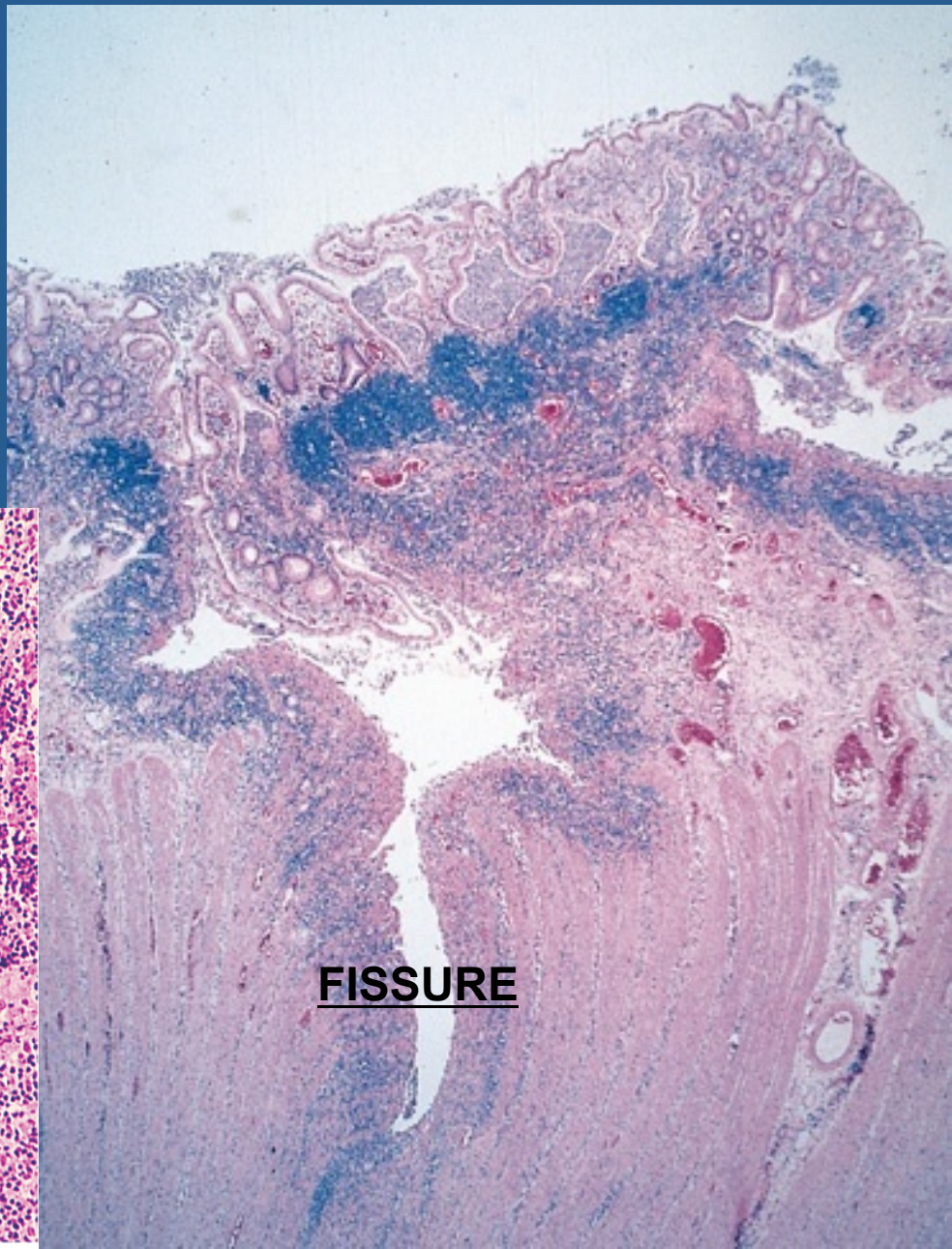
Crohn's disease

- **Microscopic Features**
 1. Distortion of mucosal crypt architecture with mucosal inflammation
 2. Transmural inflammation
 3. Epithelioid granulomas [60%]
- Fissure-ulcers and fistulas can be seen microscopically

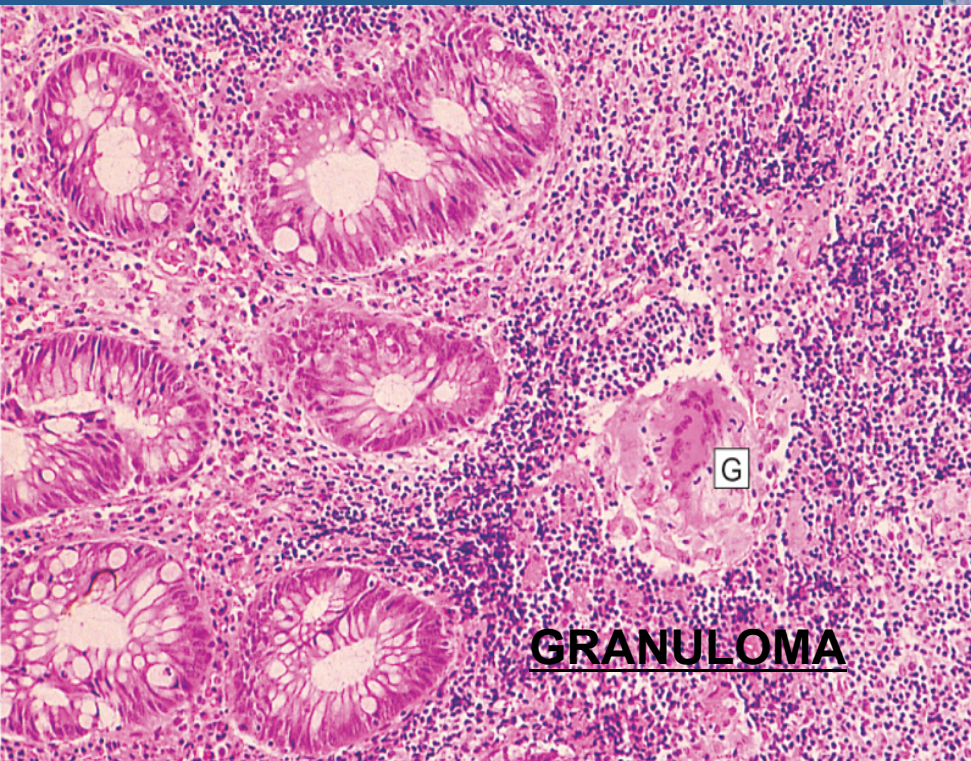
Normal



Crohn's Disease



FISSURE



G

GRANULOMA

Crohn's disease

Clinical findings

- Recurrent right lower quadrant colicky pain (obstruction) with diarrhea and weight loss
- Bleeding occurs only with colon or anal involvement (fistulas; abscesses)
- Aphthous ulcers in mouth
- Extragastrintestinal: erythema nodosum, sacroiliitis (HLA-B27 association), pyoderma gangrenosum, iritis (CD > UC), primary sclerosing cholangitis (UC > CD)

Crohn's disease

Complications

1. Intestinal obstruction
2. 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.
3. Extraintestinal manifestations (arthritis and uveitis)
4. Slight increased risk of development of carcinoma of the colon—much less than in ulcerative colitis.

Crohn's disease

- **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

CROHN'S DISEASE

- Familial Tendencies
- Peaks Ages 15-40 Yrs
- ? Autoimmune Factors
- Nausea & Vomiting

- Abdominal Pain and Distention
- Tenderness in RLQ

* Later S & S's *

- Dehydration
- Electrolyte Imbalance
- Anemia

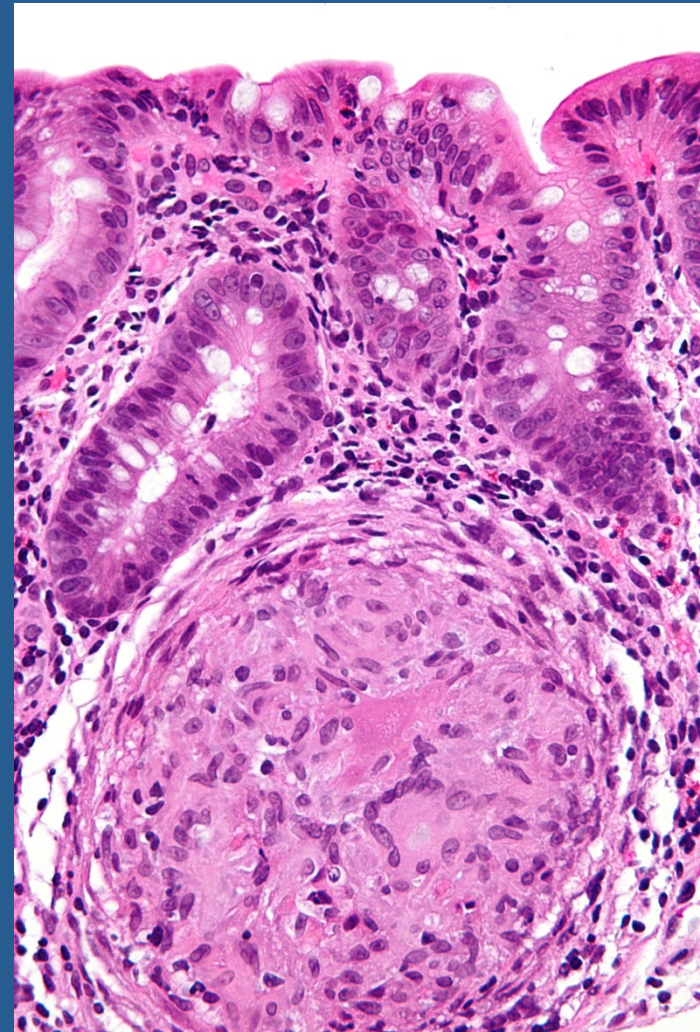
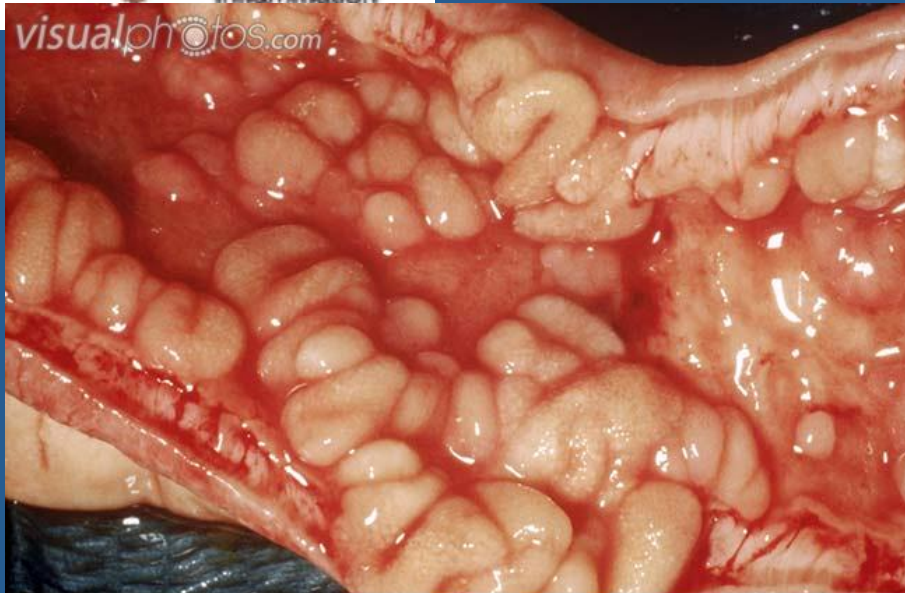
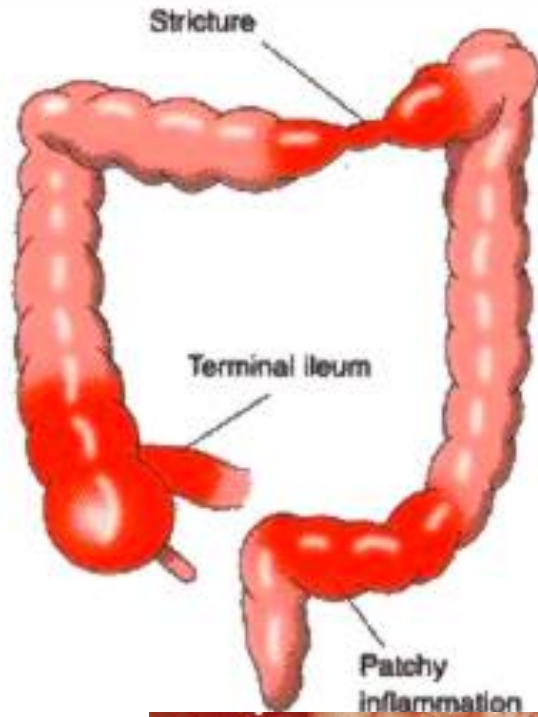


- Severe Diarrhea
- Low Grade Fever
- Bloody Stools
- Weight Loss
- Severe Malabsorption

* Complications *

- Intra-abdominal Abscesses
- Intestinal Fistulas
- Peritonitis
- Development of Fistulas

Crohn's colitis



Complications of Crohn's disease

Normal



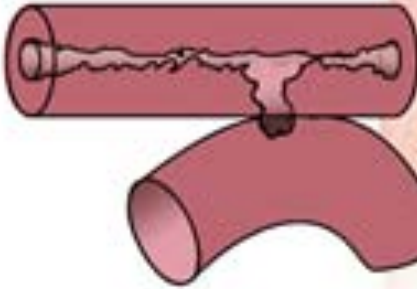
Inflammation



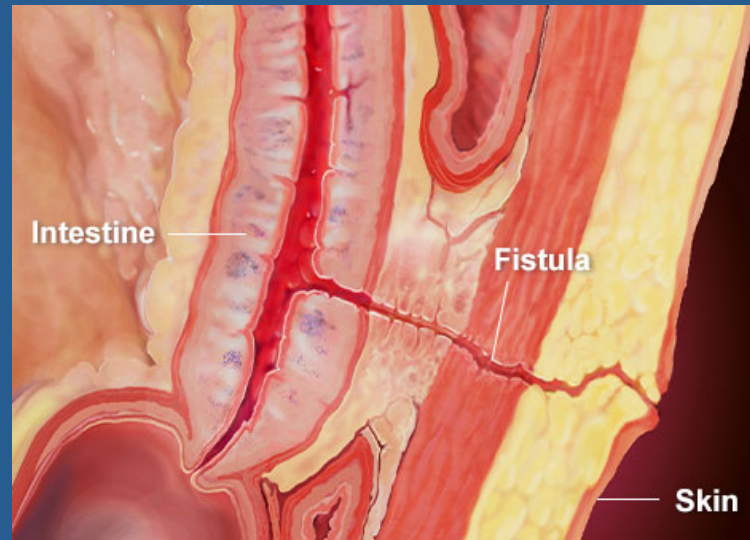
Stricture



Fistula



small intestine



Intestine

Fistula

Skin

Ulcerative Colitis

- Definition—chronic relapsing ulceroinflammatory disease of undetermined etiology
- 20- to 30-year age group but may occur at any age
- Most common inflammatory bowel disease
- Ulcerations are in continuity

Ulcerative Colitis

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.

Ulcerative Colitis

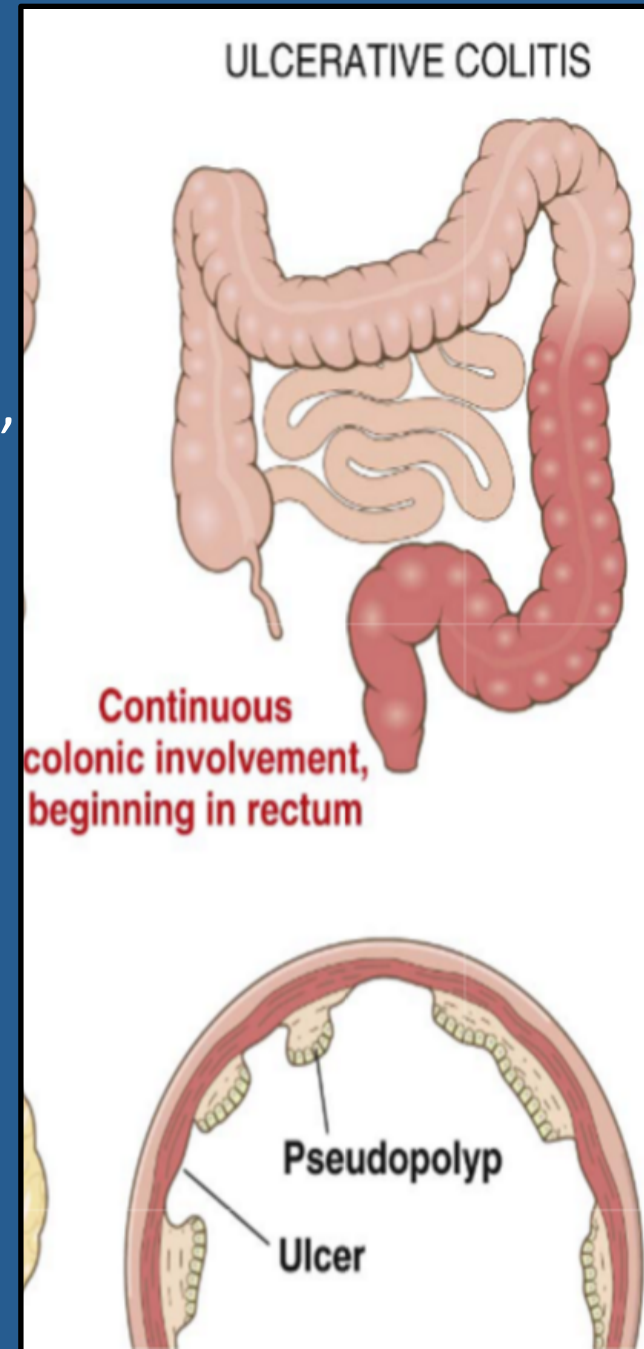
Clinical Features

- 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.

Ulcerative Colitis

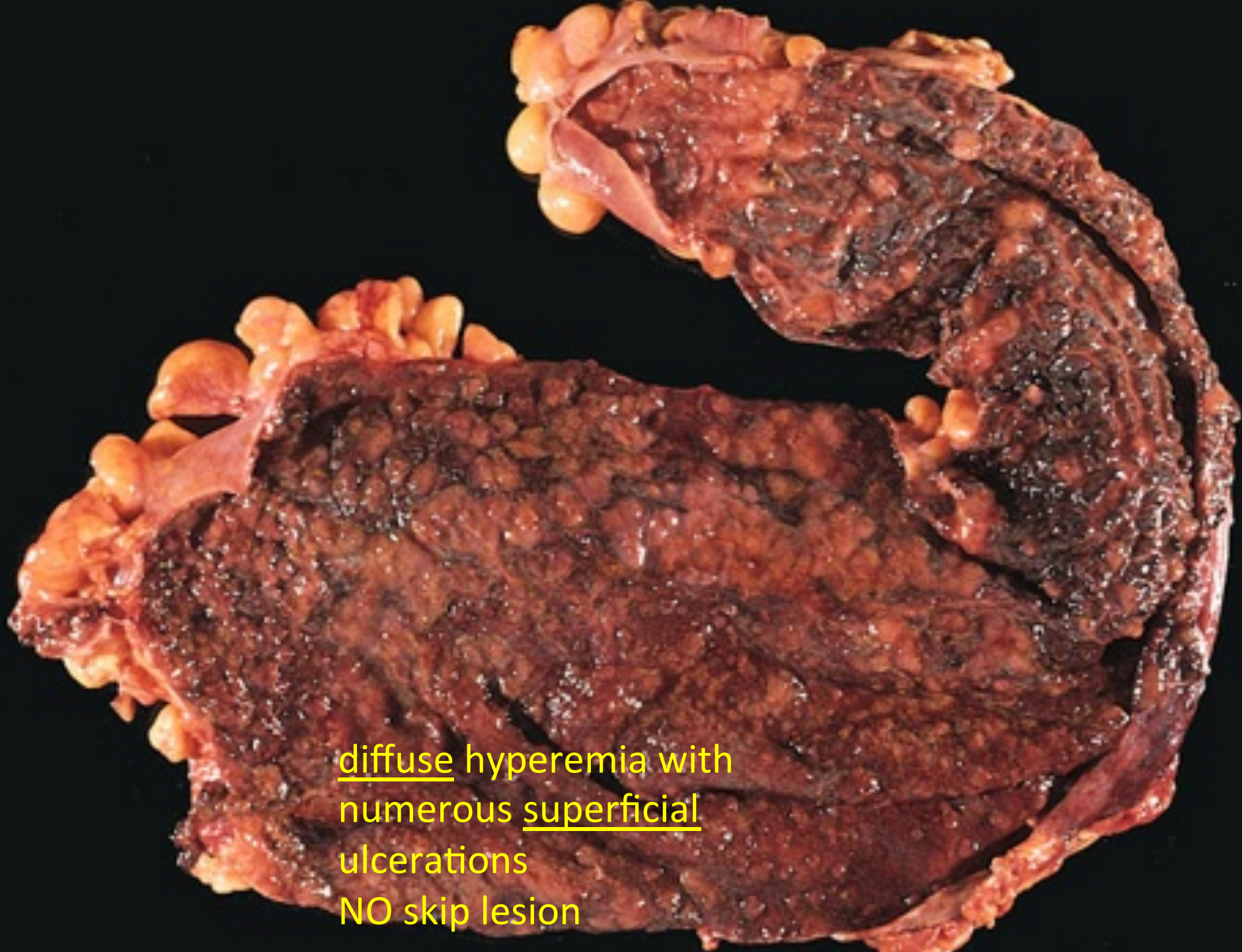
Sites of Involvement

- 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



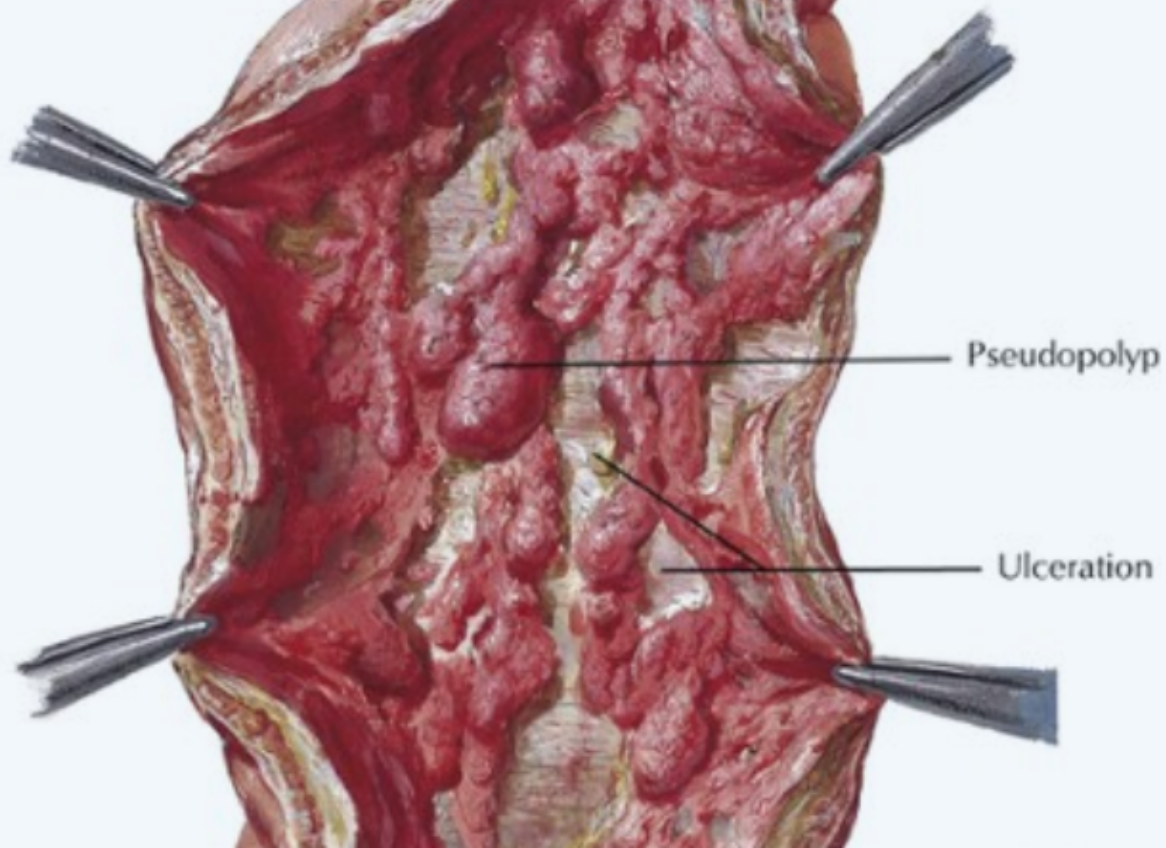
Ulcerative Colitis

- **Gross Appearance**
- Involves mainly the mucosa (diffuse hyperemia with numerous superficial ulcerations in the acute phase.
- The regenerated or nonulcerated mucosa may appear polypoid (inflammatory pseudopolyps) in contrast with the atrophic areas or ulcers.



diffuse hyperemia with
numerous superficial
ulcerations
NO skip lesion

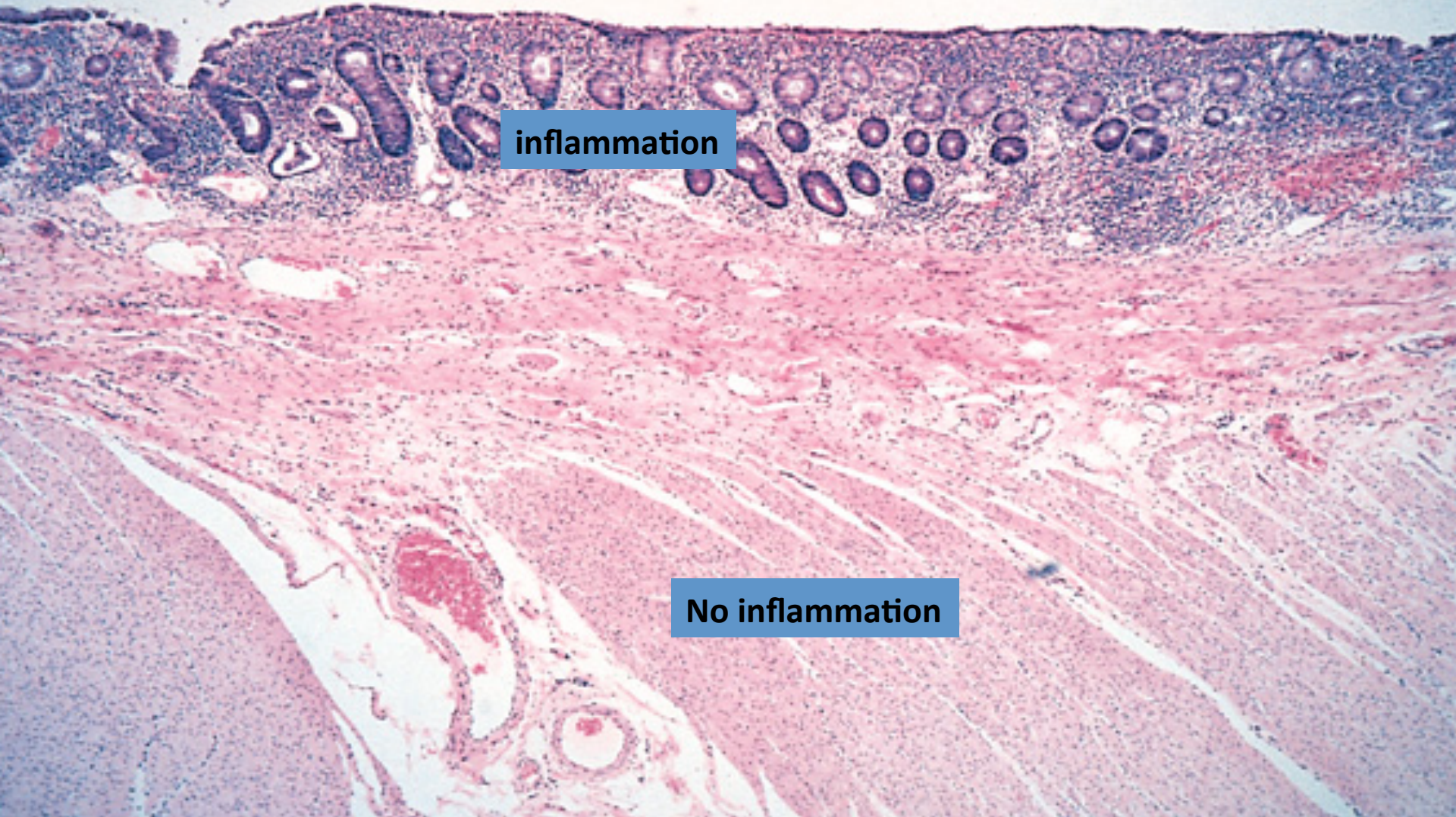
**Advanced colitis with
ulceration and pseudopolyps**



Ulcerative Colitis

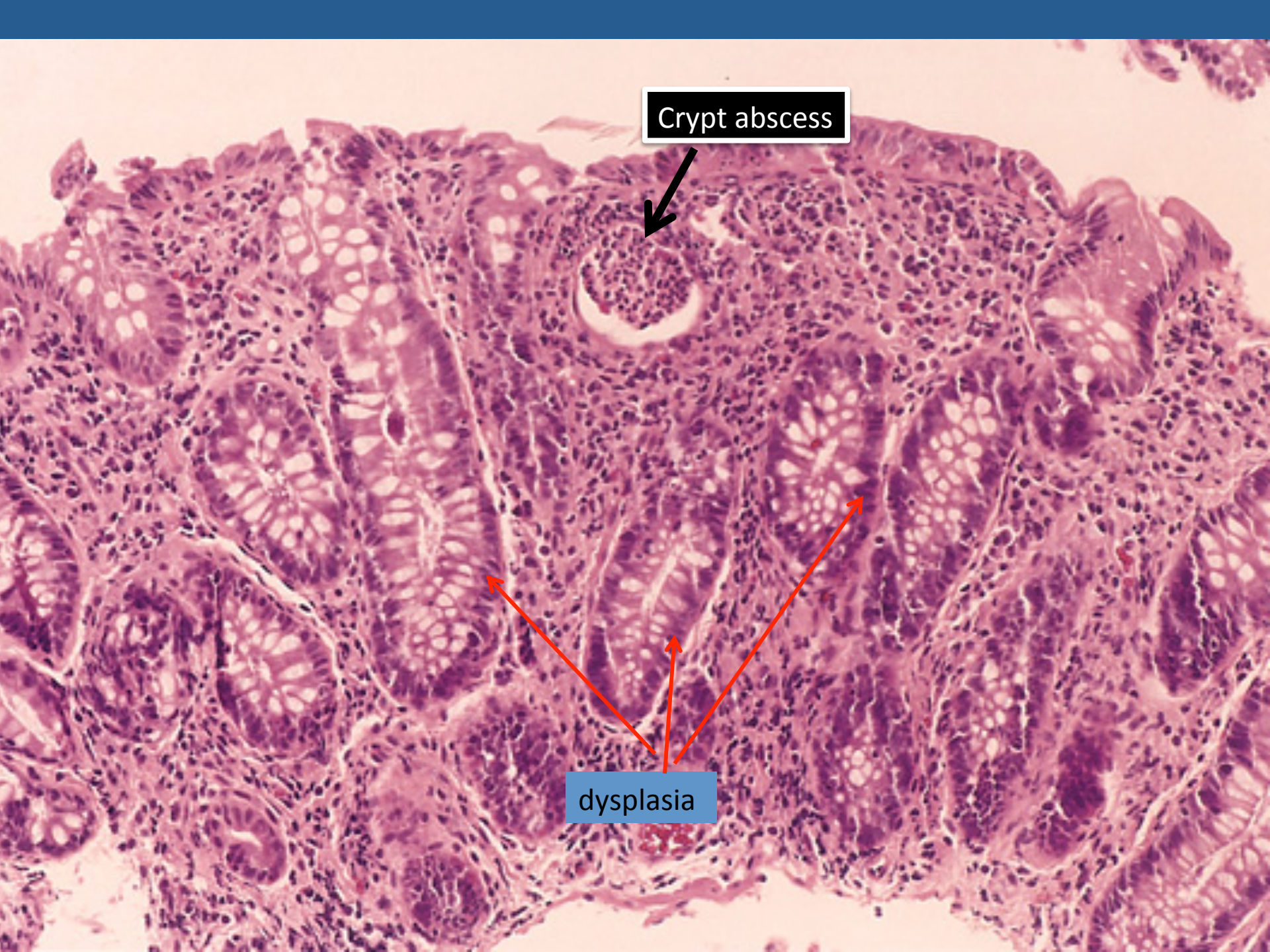
- **Microscopic Appearance**
- The inflammation is usually restricted to the mucosa.
- In the active phase....neutrophils (Cryptitis, crypt abscess)
- In the chronic phase.....crypt atrophy and distortion
- Active inflammation correlates well with the severity of symptoms.

The inflammation is usually restricted only to the mucosa.



inflammation

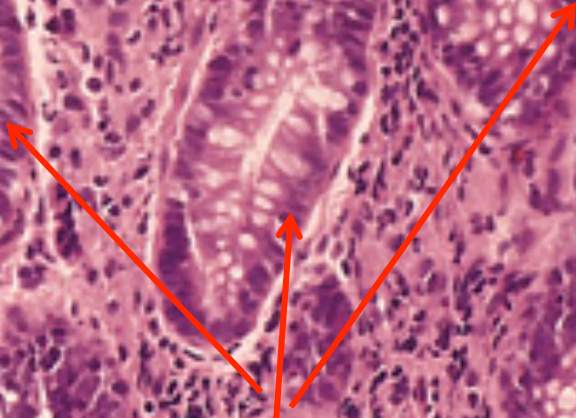
No inflammation



Crypt abscess



dysplasia



Ulcerative Colitis

Clinical findings

- Recurrent left-sided abdominal cramping with bloody diarrhea and mucus
- Fever, tenesmus, weight loss
- Toxic megacolon (up to 10% of patients). Mortality rate 50%.
- Extra-gastrointestinal: primary sclerosing cholangitis (UC > CD), erythema nodosum, iritis/uveitis (CD > UC), pyoderma gangrenosum, HLA-B27 positive arthritis.
- p-ANCA antibodies >45% of cases

Ulcerative Colitis

- Extraintestinal manifestations
 1. Arthritis
 2. Uveitis
 3. Skin lesions (pyoderma gangrenosum),
 4. Sclerosing cholangitis (fibrosis around bile ducts), leading to obstructive jaundice.

Ulcerative Colitis

- **Complications**

- Acute phase

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

- Chronic ulcerative colitis

- ✓ Increase risk of developing colon carcinoma.
- ✓ The presence of high-grade dysplasia in a mucosal biopsy imposes a high risk of cancer and is an indication for colectomy.

	Crohn's disease	Ulcerative Colitis
Site		
Pattern		
Depth of the ulcer		
Extent of inflammation		
Fistula formation		
Creeping mesenteric fat		
Fibrous thickening of wall		
Granulomas		
Dysplasia		
Carcinoma		
Mucosal appearances		
Bowel wall		
Lymphoid reaction		
Complications		

	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
Lymphoid reaction	Marked	Moderate
Complications	Short gut syndrome Fistula formation Bowel perforation Stricture formation	Haemorrhage Electrolyte loss Toxic megacolon Systemic effects
Recurrence after surgery	Common	No

CROHN DISEASE

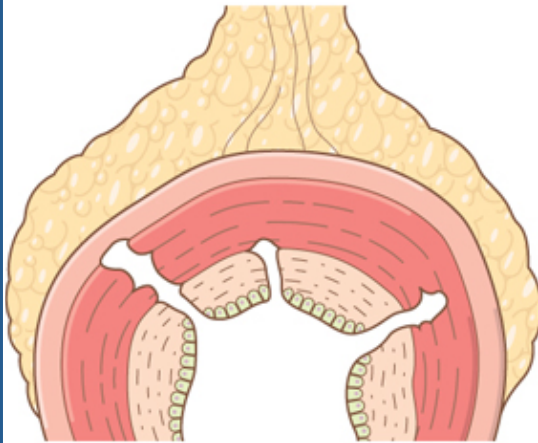


Skip lesions

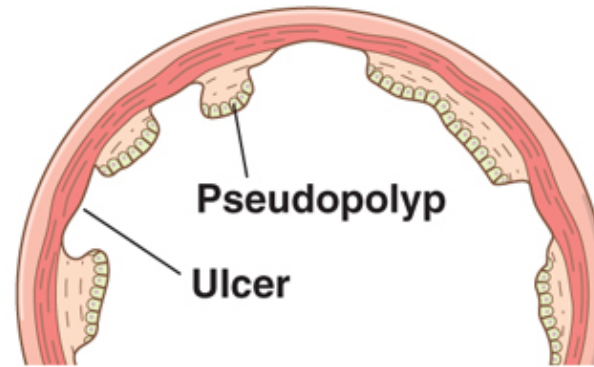
ULCERATIVE COLITIS



Continuous colonic involvement, beginning in rectum



**Transmural inflammation
Ulcerations
Fissures**



**Pseudopolyp
Ulcer**

Inflammatory bowel diseases

MATCH

1. Colon only
2. Diffuse involvement of mucosa
3. Superficial ulcers
4. Any part of the GIT
5. Skip areas of normal mucosa
6. Mucosal inflammation only
7. Fistula formation
8. Transmural inflammation
9. Granulomas
10. Deep ulcers (fissure)
11. Dysplasia is common
12. Carcinoma is more common (10%)

A. Crohn's disease

B. Ulcerative Colitis