

# 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

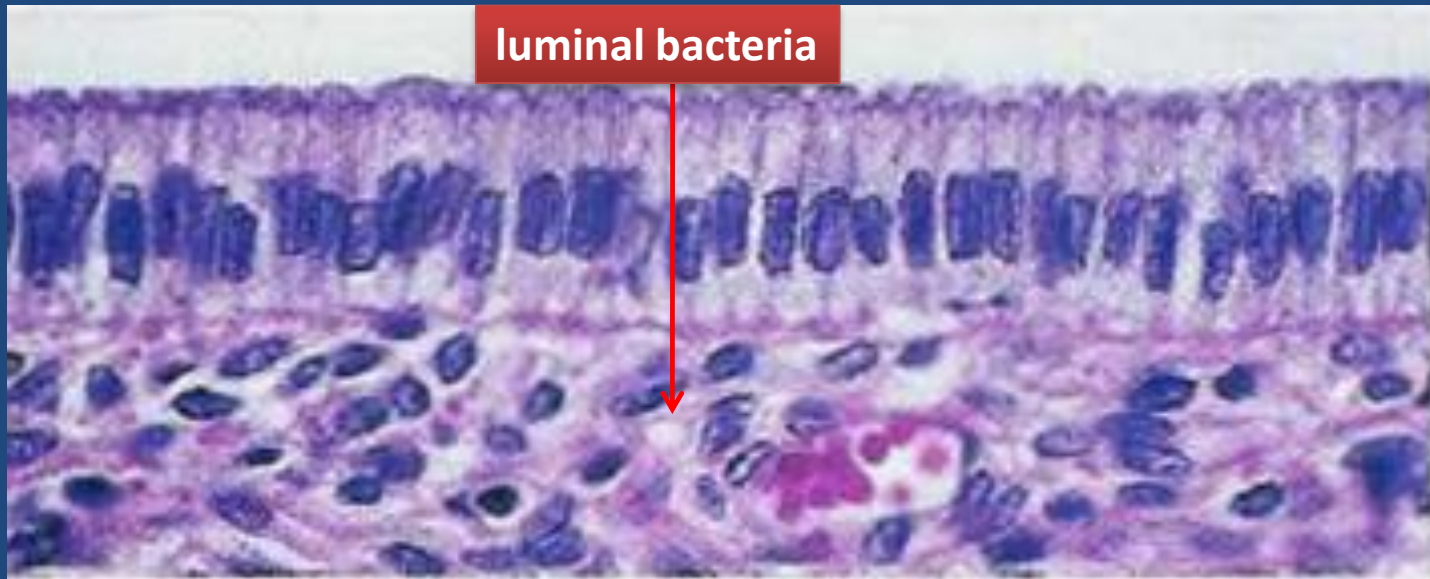
# *Epidemiology*

- 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.

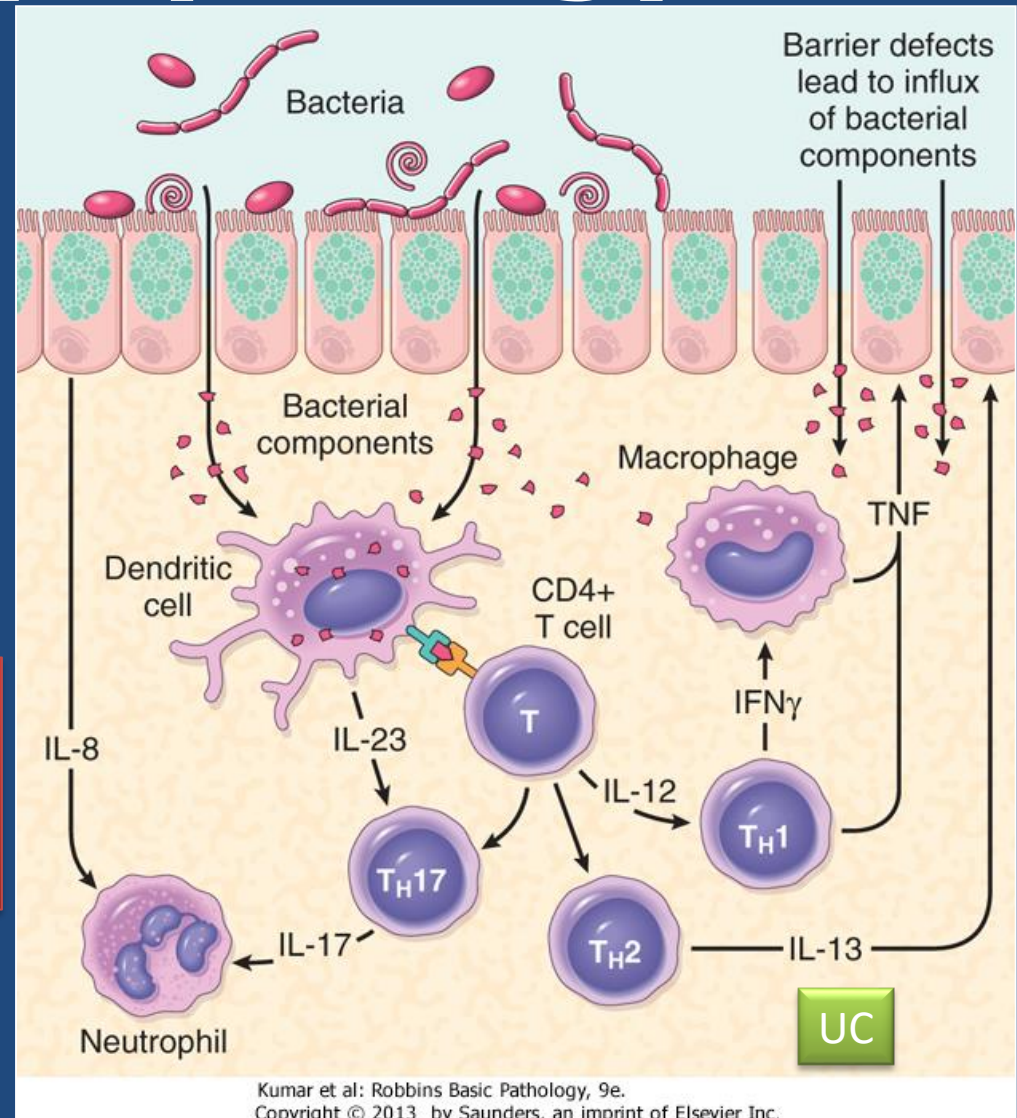
# Pathophysiology



# 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

Less

Immune responses.

Abnormal in  
epithelial tight  
barrier function

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.

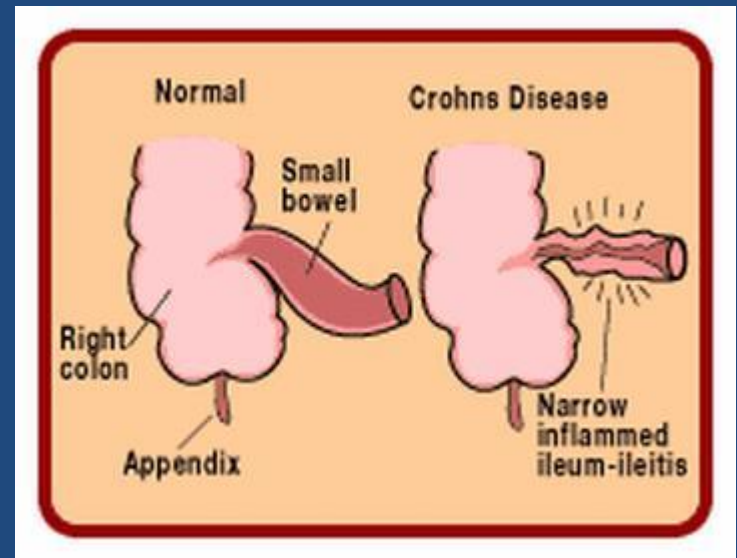
# Crohn's disease

## 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.

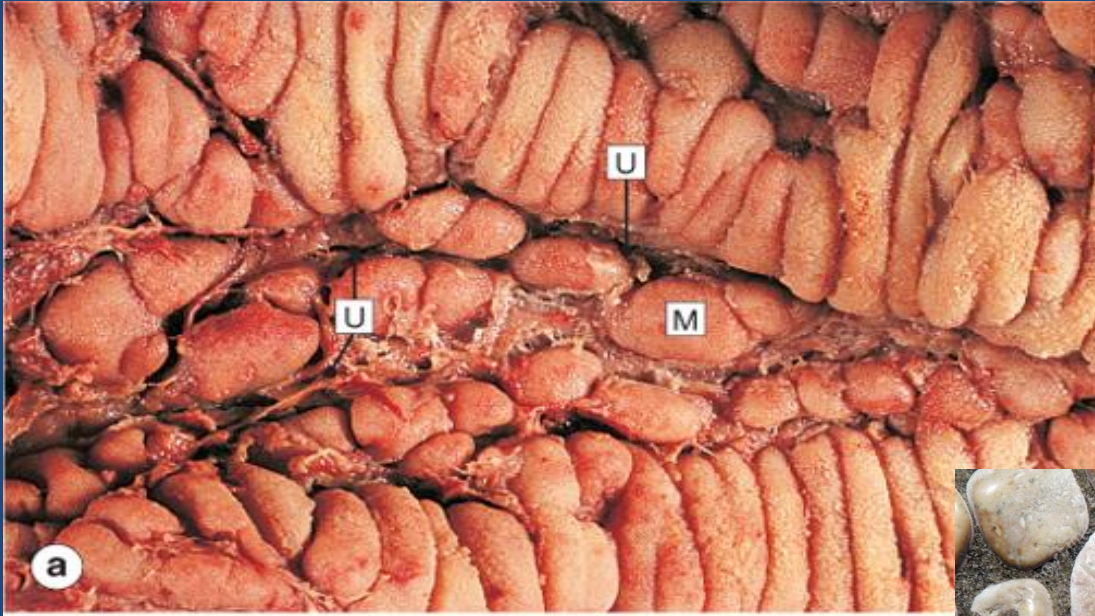


# Crohn's disease

- **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).

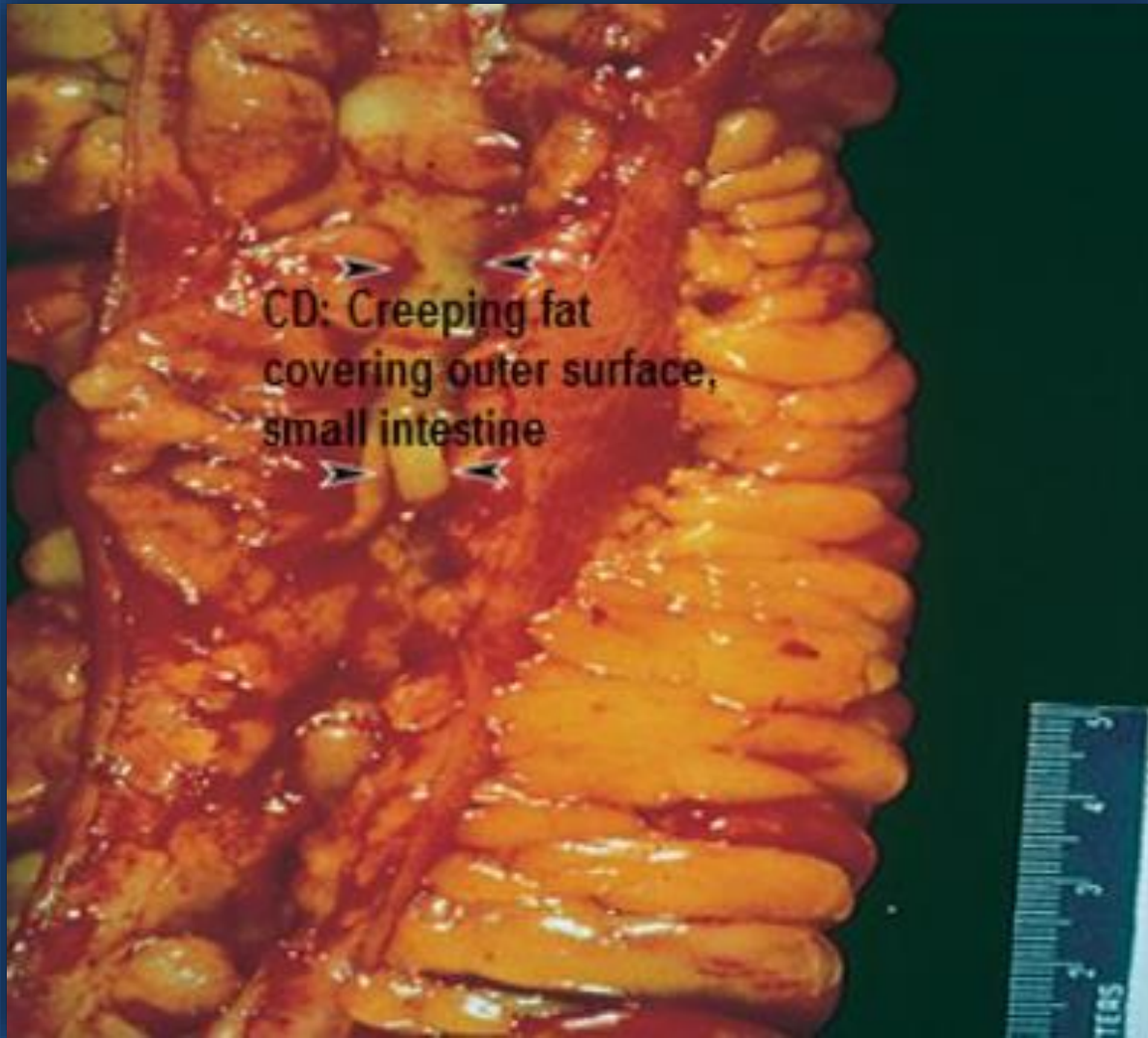


**Mucosa**: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa. This results in the typical **cobblestone effect**.





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



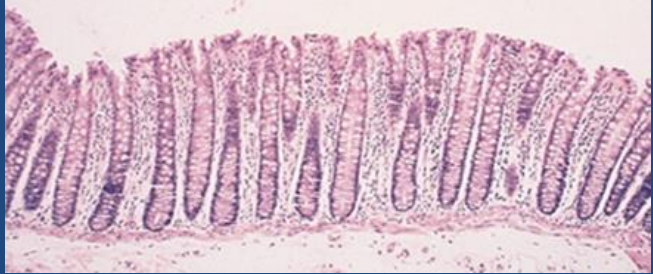


# Crohn's disease

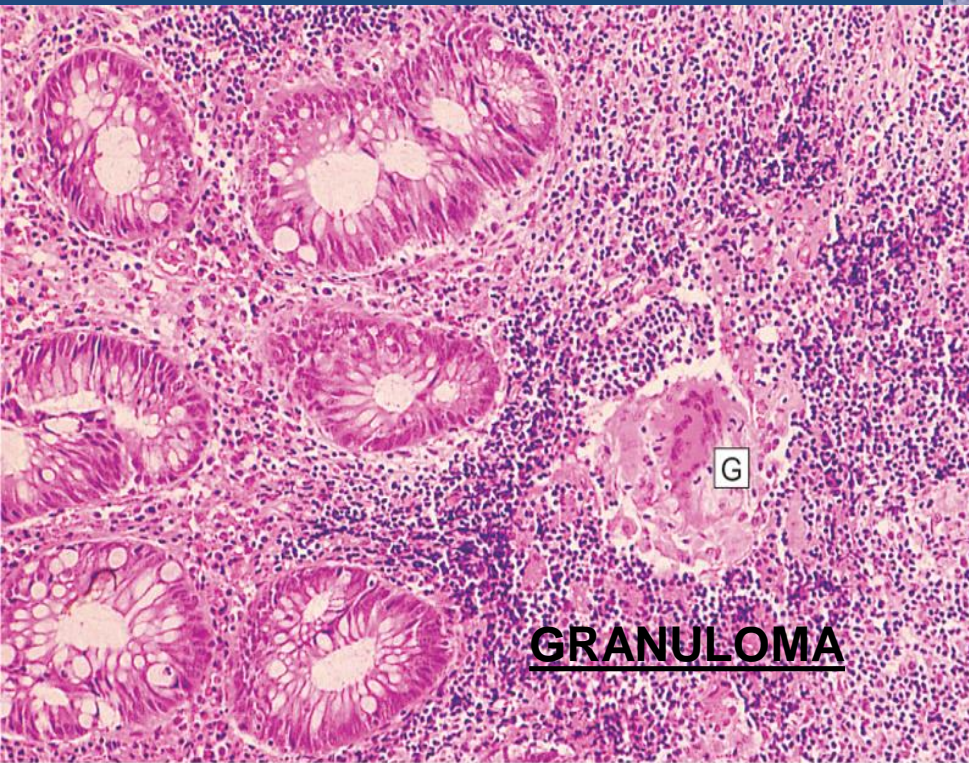
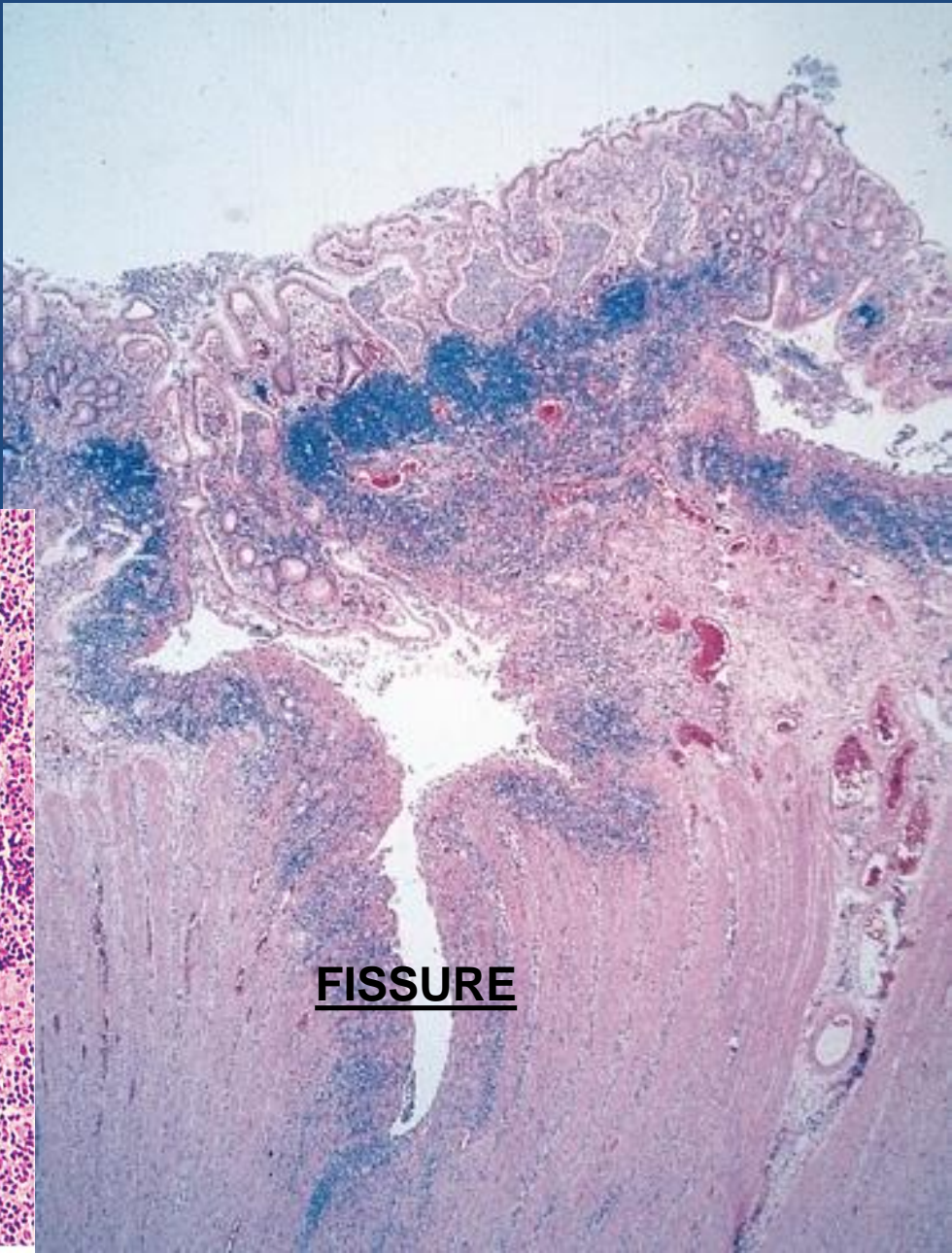
- **Microscopic Features**

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

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

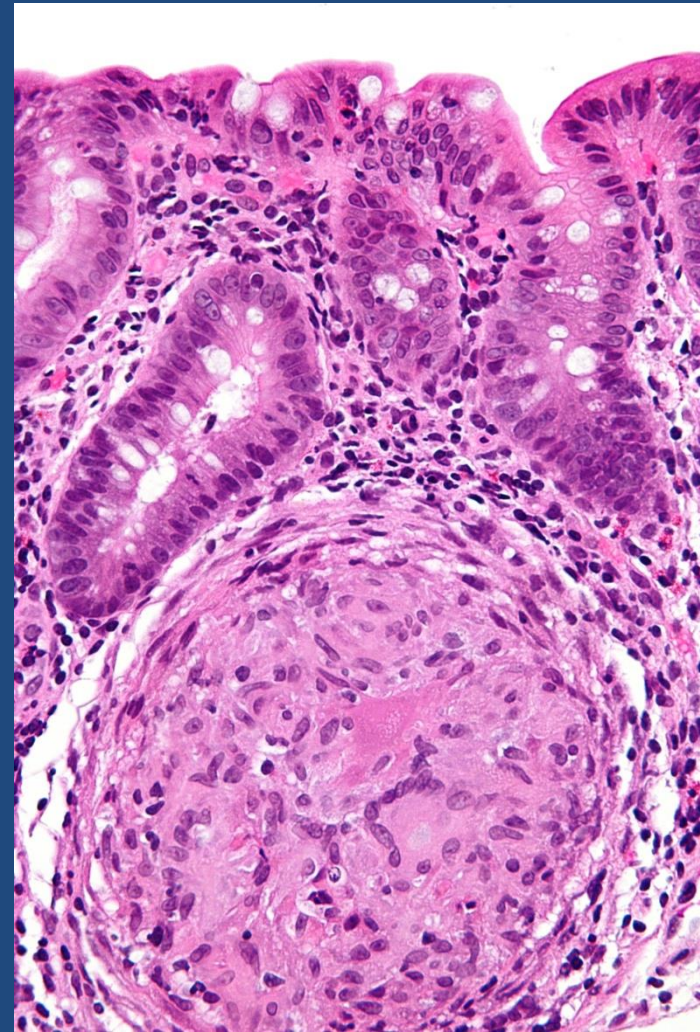
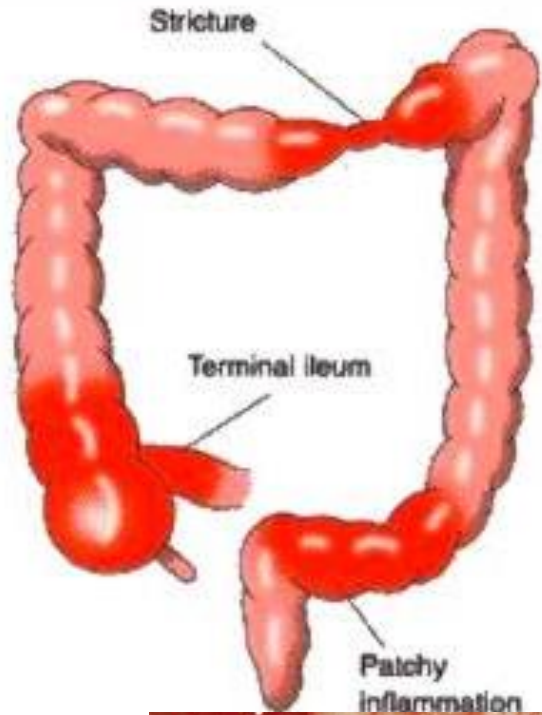


- Severe Diarrhea
- Low Grade Fever
- Bloody Stools
- Weight Loss
- Severe Malabsorption

## \* Complications \*

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

# Crohn's colitis





# Complications of Crohn's disease

Normal



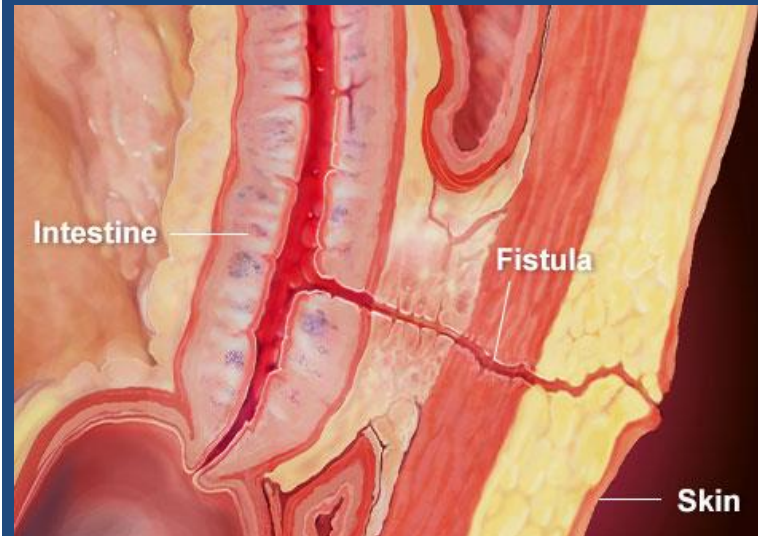
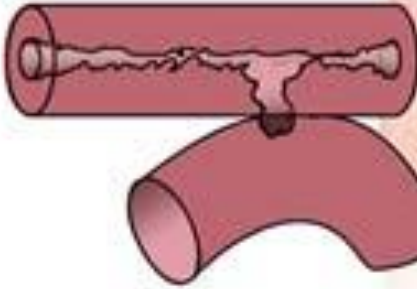
Inflammation



Stricture



Fistula





# 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

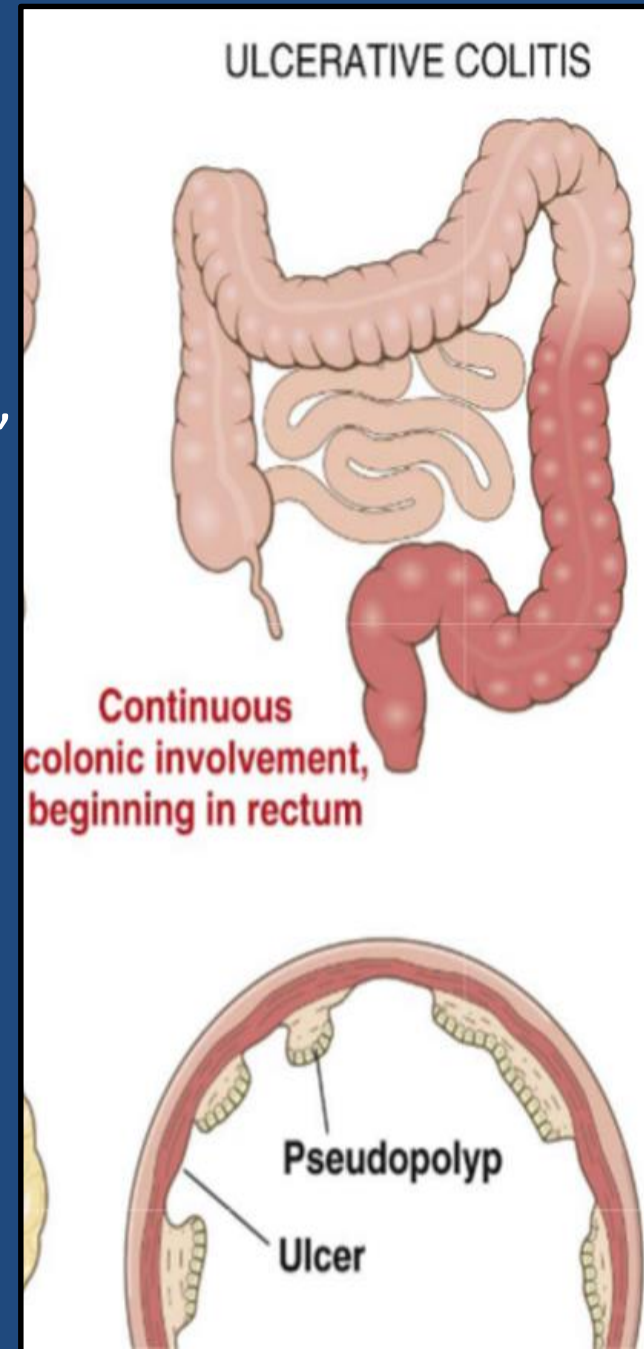
## Clinical Features

- 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.



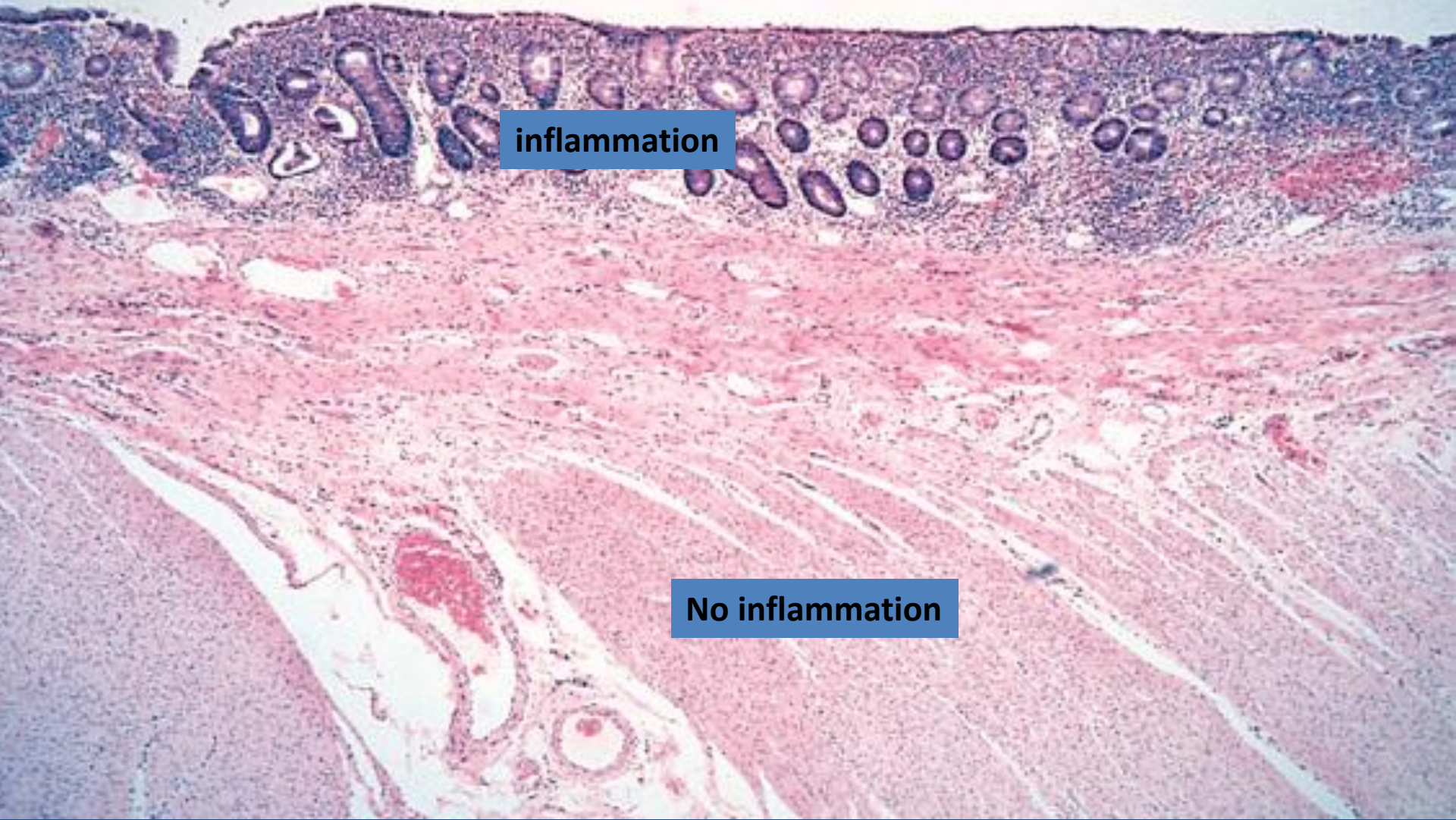
diffuse hyperemia with  
numerous superficial  
ulcerations  
NO skip lesion

# 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.



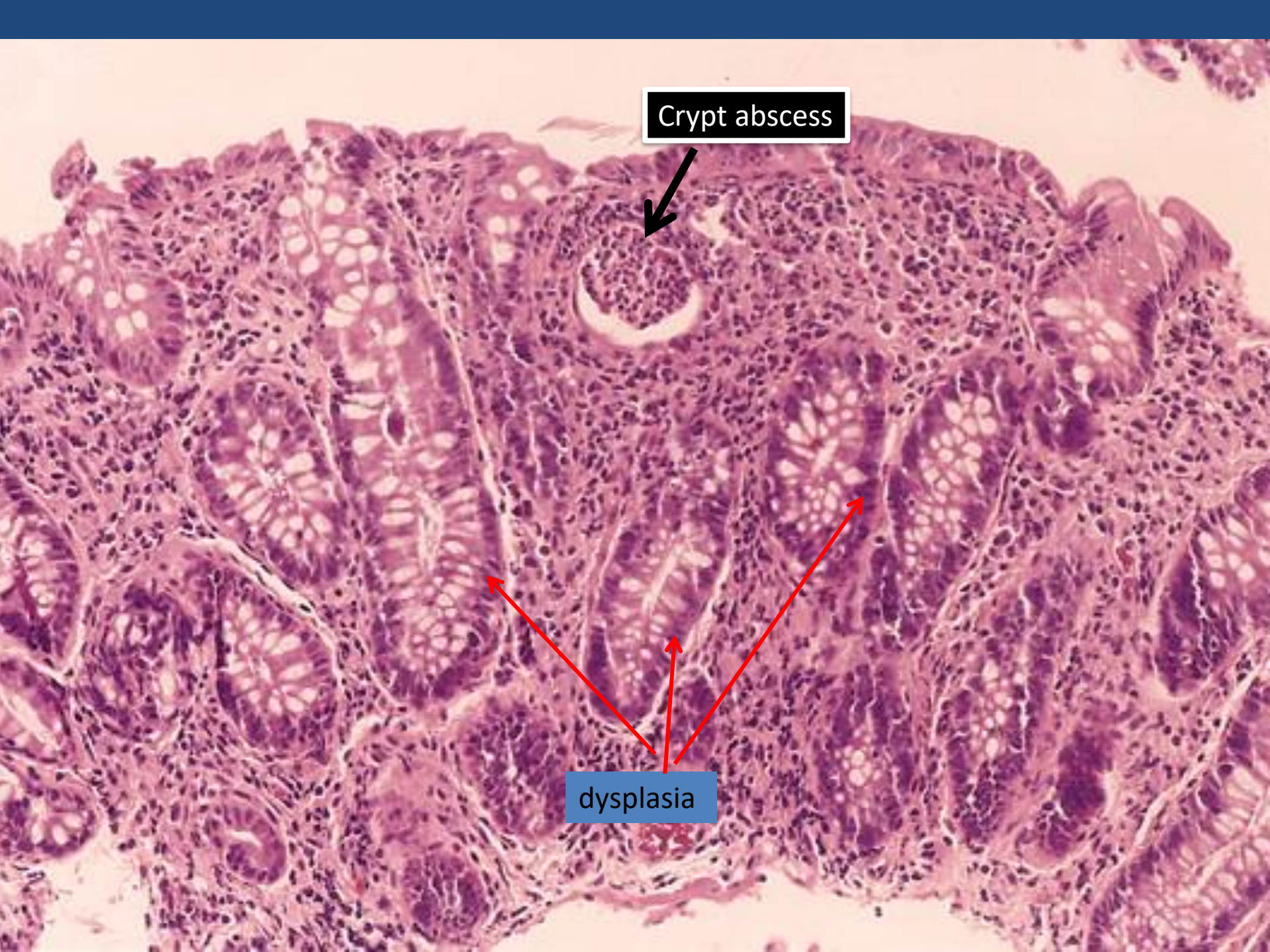
The inflammation is usually restricted only to the mucosa.



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		



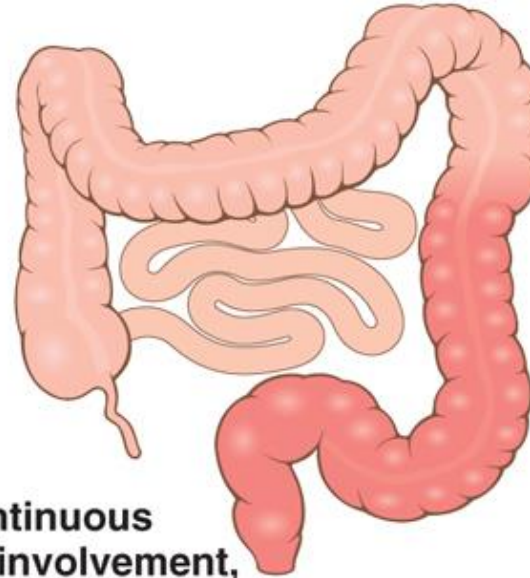
	<b>Crohn's disease</b>	<b>Ulcerative Colitis</b>
Site	Any part of the GIT	Colon only
Pattern	Skip areas of normal mucosa	Diffuse involvement of mucosa
Depth of the ulcer	Deep ulcers ( fissure )	Superficial ulcers
Extent of inflammation	Transmural inflammation	Mucosal inflammation only
Fistula formation	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

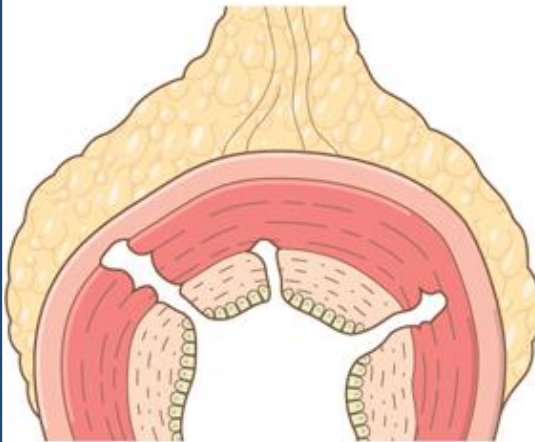


**Skip lesions**

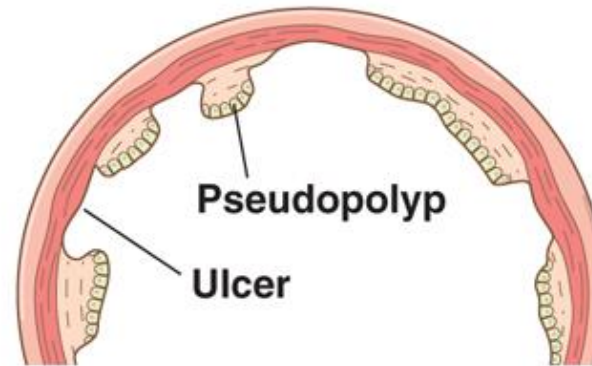
## ULCERATIVE COLITIS



**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**

# What factors are believed to underlie the pathogenesis of inflammatory bowel disease?

The etiology of IBD (ulcerative colitis and Crohn disease) is unknown.

Familial aggregation suggests a genetic predisposition, but no definite genetic markers have been identified except for the uniform presence of HLA-B27 in patients with IBD and ankylosing spondylitis.

Current opinion favors abnormal host immunoreactivity to luminal or mucosal antigens. The occurrence of IBD in mice lacking selected cytokines (IL-2, IL-10) or with disruption of T-cell receptors favors this concept.

The beneficial effects of immunosuppressive therapy also point to the role of an aberrant immune response in the pathogenesis of IBD.



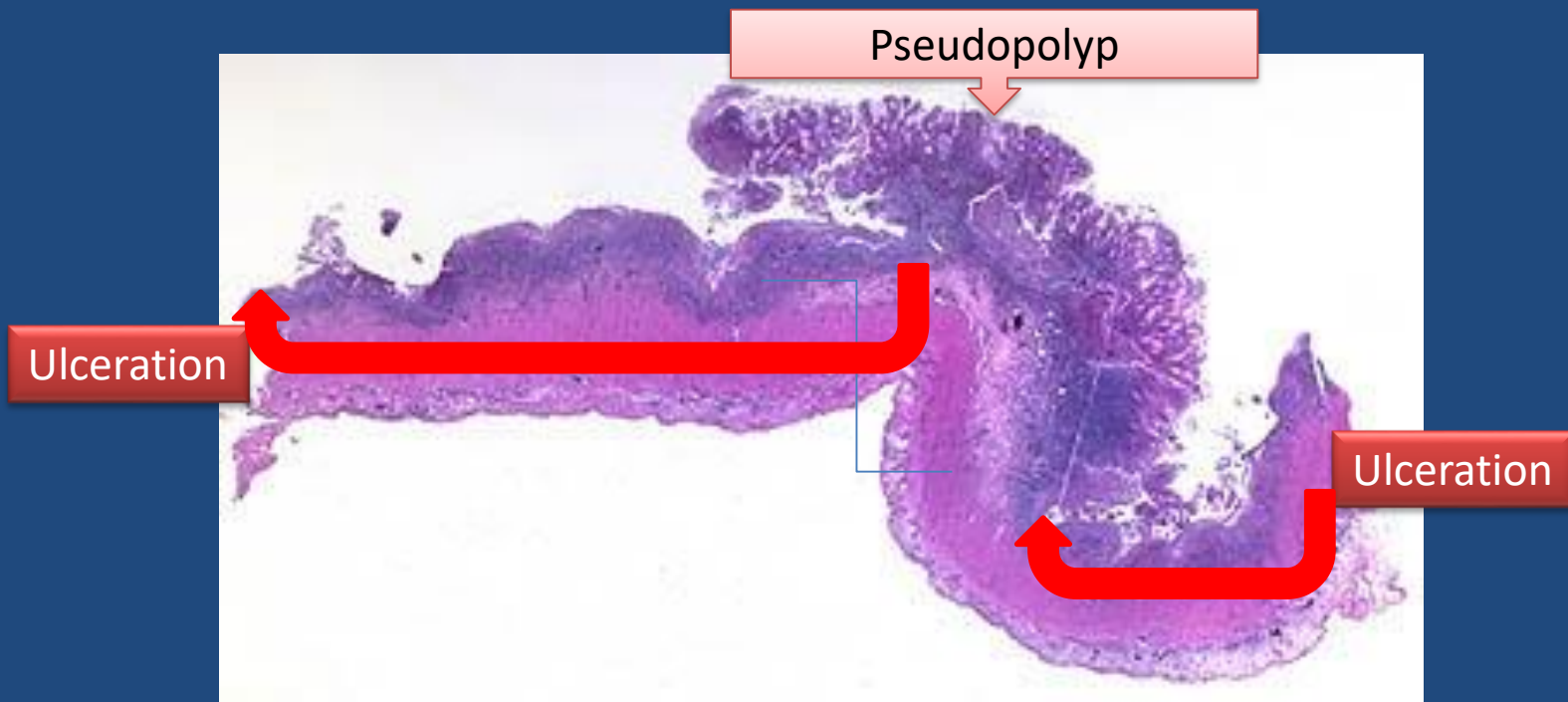


Is the picture consistent with Crohn disease?

No, this is not consistent with Crohn disease because of the uninterrupted involvement of the mucosa. Although Crohn disease may involve the colon, affected areas are sharply delimited by intervening unaffected areas.

What is the definition of a polyp?

- The term *polyp* is used to describe any nodule or mass that projects above the level of surrounding mucosa; it may be hyperplastic or neoplastic.



- Why are the lesions in ulcerative colitis called pseudopolyps?  
These lesions are not really the result of mucosal proliferation, but rather are the result of mucosal ulceration. Focal areas that are unaffected by ulceration appear to project above the denuded mucosa surrounding them.

- How is the extent of disease in ulcerative colitis different from that seen in Crohn disease?

Crohn disease causes transmural inflammation that ultimately results in fibrosis and thickening of the bowel wall.



- What histologic feature is seen in Crohn disease that is not seen in ulcerative colitis? Granulomas and transmural inflammation in the resected specimen are seen in Crohn disease.



- What are the complications of ulcerative colitis?  
The most serious complication is the development of carcinoma. Cancers are preceded by dysplasia, which tends to arise in multiple sites. The risk of cancer is highest in patients with pancolitis of 10 or more years' duration, in whom it is 20-fold to 30-fold higher than in a control population.
- Other life-threatening complications include severe diarrhea and electrolyte disturbances, severe colonic dilation (toxic megacolon) with potential for perforation and peritonitis, and massive hemorrhage.

- What is the risk of colon carcinoma in Crohn disease?

Although the risk of colon carcinoma is increased, it is less so than in ulcerative colitis. There is a five-fold to six-fold increased risk over age-matched populations.

- What are the complications of Crohn disease? Fissures in the mucosa can extend through the wall and form sinus tracts, resulting in fistula formation to other loops of bowel, urinary bladder, or vagina; there may be localized peritonitis and abdominal abscesses; fibrosis of the gut wall may lead to strictures and obstruction.
- Extensive involvement of the small bowel may cause marked loss of albumin (protein-losing enteropathy) or malabsorption.