

# Inflammatory Bowel Disease

- Define inflammatory bowel disease (IBD)
- Know the two forms of idiopathic IBD
- 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)

Black: original content

Red: Important

Green: only found in males slides

Orange: Doctor notes

Grey: Extra/Robbins

Purple: Only found in females slides



# Inflammatory Bowel Diseases

- **Chronic** (remission and relapse) condition resulting from complex interactions between intestinal microbiota and host immunity in **genetically predisposed individuals** resulting an inappropriate **mucosal immune activation**.
- **Types** based on the distribution of affected sites and the morphologic expression:
  - **Crohn's disease (CD)** and **Ulcerative colitis (UC)** which is more common.
  - Although their causes are still not clear, the two diseases probably have an **immunologic hypersensitivity basis**.

## ► Epidemiology (Female's slides)

- The geographic distribution of IBD is **variable**
- It is most prevalent in North America, northern Europe, and Australia.
- Crohn's disease (CD) and ulcerative colitis (UC) are more common in **females and in young adults**.

Ulcerative colitis	Crohn's disease
<ul style="list-style-type: none"><li>- More common in whites than blacks</li><li>- Occurs between <b>14 and 38</b> years of age</li><li>- <b>Lower incidence in smokers</b> and other nicotine users</li><li>- Lower incidence if previous <b>appendectomy</b> &lt;20 years.</li><li>- The Concordance rate<sup>1</sup> of monozygotic twins is only 16%.</li></ul>	<ul style="list-style-type: none"><li>- More common in whites than blacks, in Jews than non-Jews.</li><li>- More common in <b>children</b> than adults.</li><li>- <b>Smoking is a risk factor</b></li><li>- Majority &gt;75% of cases occur between 11 and 35 years of age</li><li>- The concordance rate for monozygotic twins is approximately 50%.</li></ul>

- IBD incidence worldwide is rising and becoming more common in regions in which the prevalence was **historically low**.
- The hygiene hypothesis suggests that 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**. (children don't get exposed to enough microbes, so they don't have immunity against them)
  - 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.

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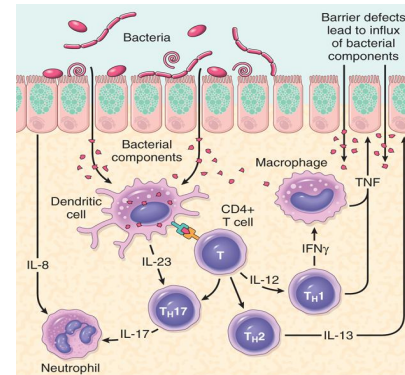
(1) The presence of the same trait in both members of a pair of twins.

# Inflammatory Bowel Diseases

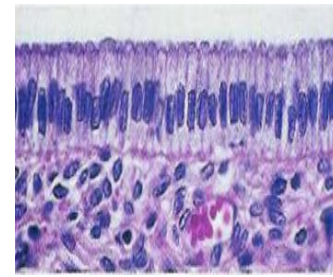
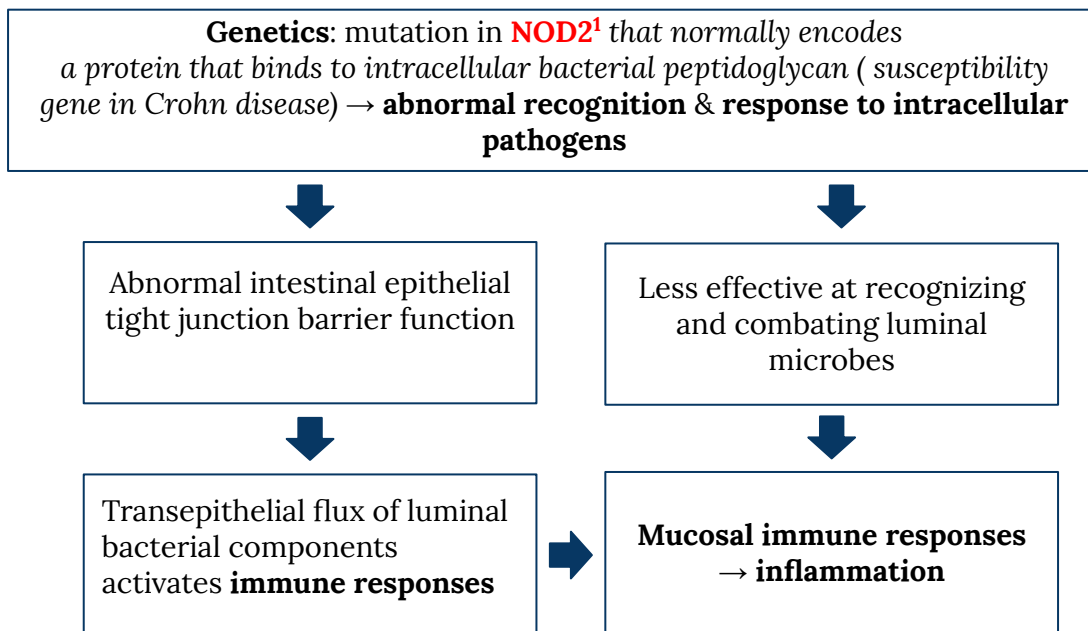
## ► Pathophysiology idiopathic

- Defects in host interactions** with intestinal microbes.
- Intestinal **epithelial dysfunction**.
- Aberrant **mucosal immune responses**.
- Altered composition** of the gut microbiome.

**Result:** activates innate and adaptive immune responses. In a genetically susceptible host, the subsequent release of **TNF** and other immune signals directs epithelia to **increase tight junction permeability**, which further **increases the flux of luminal material** resulting in IBD.



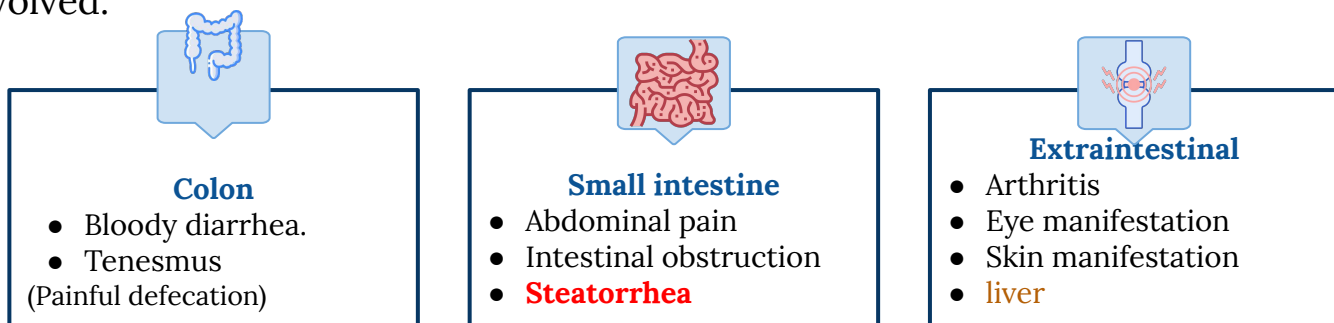
## ► Pathophysiology (based on theories)



- **Immunosuppression** is the mainstay of IBD therapy.
- **NOD2 mutations are not sufficient for the development of Crohn's disease** because it is seen in 15% of patients but are also seen in a smaller percentage of the general population.

## ► Clinical manifestations

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



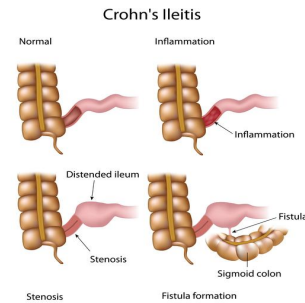
(1) (Nucleotide-binding oligomerization domain)

# Crohn's disease

- 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.

## ► 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.



## ► Clinical findings (Female's slides)

- Recurrent **right lower quadrant colicky pain** (obstruction) with diarrhea and weight loss.
- Bleeding occurs with colon or anal involvement → fistulas, abscesses.
- Aphthous ulcers in mouth.
- Extragastrointestinal: erythema nodosum<sup>1</sup>, sacroiliitis<sup>2</sup> (HLA-B27 association), pyoderma gangrenosum<sup>3</sup>, iritis (CD > UC), primary sclerosing cholangitis<sup>4</sup> (UC > CD).

## ► 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.

(1) Inflammation of the fat cells under the skin, resulting in tender red nodules.

(2) Inflammation of joint between sacrum and ilium.

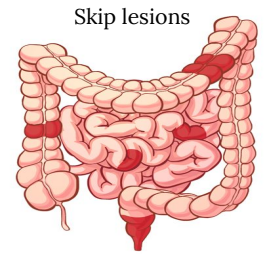
(3) Is a condition that causes tissue to become necrotic, causing deep ulcers usually occur on the legs.

(4) Fibrosis around bile ducts leading to obstructive jaundice.

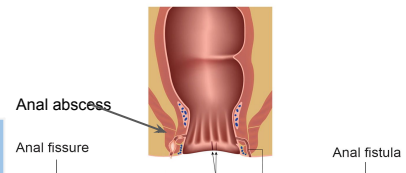
# Crohn's disease

## Gross appearance

- **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.

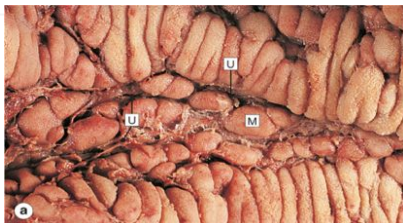


An anal fissure is a tear of the skin near the anus. An anal fistula is an infected tunnel between the skin and the anus.



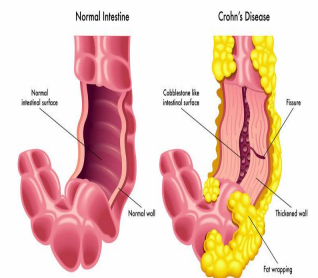
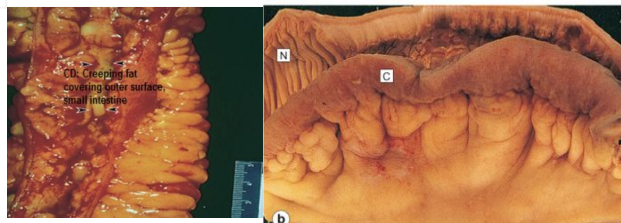
### Mucosa

**Cobblestone effect**: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa.



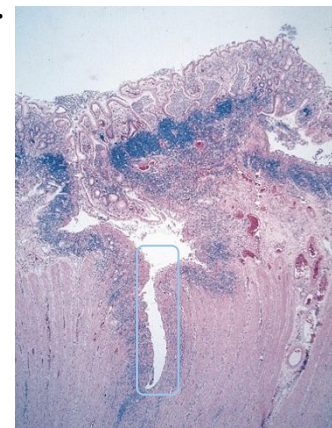
### Fat

**Creeping fat**: In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall.



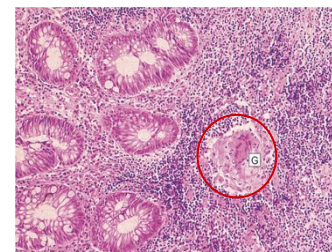
## Microscopic appearance

- Distortion of mucosal crypt architecture with mucosal inflammation.
- **Transmural** (involves all the layers from mucosa to serosa) inflammation.
- Epithelioid noncaseating **granulomas** [60%]
- **Fissure** ulcers and fistulas can be seen microscopically.



## Complications

- **Intestinal obstruction** due to fibrosis
- **Fistula formation**
  - Between the ileum and the colon → malabsorption
  - Enterovesical fistulas → urinary infection and passage of gas and feces with urine
  - Enterovaginal fistulas → fecal vaginal discharge
  - Peritonitis
- **Extraintestinal manifestations**: arthritis and uveitis.
- Slight increased risk of development of **carcinoma** of the colon - much less than in ulcerative colitis.



# Ulcerative Colitis

- Chronic **relapsing** ulcero inflammatory disease of undetermined etiology.
- **Most common inflammatory bowel disease.**

## ► Incidence

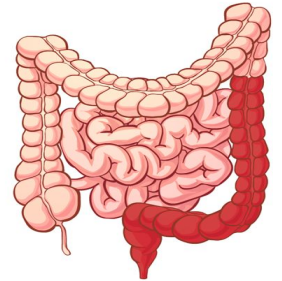
- 20 - 30 year age group but may occur at any age.

## ► 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. most commonly terminal ileum.
- Smoking reduces the risk of ulcerative colitis.

## ► Site of involvement

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



## ► Clinical findings

- **Toxic megacolon<sup>1</sup>**: up to 10% of patients, mortality rate 50%.
- **Extra-gastrointestinal** more seen in UC than in CD:
  - Primary sclerosing cholangitis (**pericholangitis**) (UC > CD): fibrosis around bile ducts leading to obstructive jaundice.
  - Skin lesions: erythema nodosum and pyoderma gangrenosum.
  - Iritis or uveitis (CD > UC).
  - **HLA-B27 positive** arthritis.
- **p-ANCA antibodies > 45% of cases.**

### Acute

Fever, tenesmus, weight loss, leukocytosis, **lower abdominal pain**, bloody diarrhea and mucus in the stool.

### Chronic

Remissions and exacerbations.

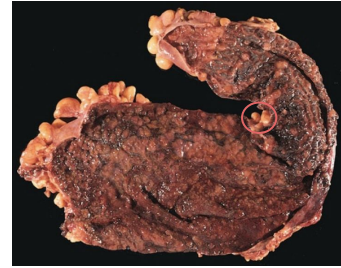
(1) Dilation of the colon, with functional obstruction → decreased motility.

# Ulcerative Colitis



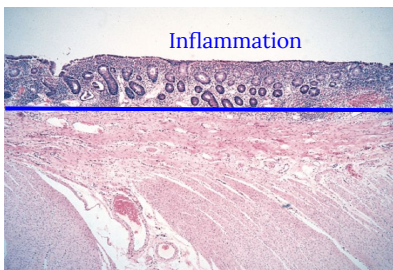
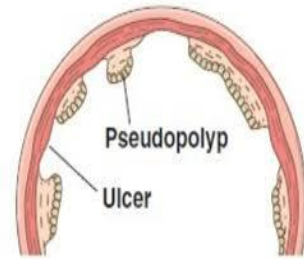
## Gross appearance

- Involves mainly the **mucosa**:
  - **Diffuse** hyperemia.
  - **Superficial** ulcerations in the acute phase.
- The regenerated or non ulcerated mucosa may appear **polypoid (inflammatory pseudopolyps)** in contrast with the atrophic areas or ulcers.



## 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 (dysplasia).
- Active inflammation correlates well with the severity of Symptoms.



## Complications

- **Acute phase:**
  - Severe bleeding
  - **Toxic megacolon** (dilation of the colon, with functional **obstruction**.)

Obstruction here is due to dilation while in crohn's is due to fibrosis.

- **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.





# Summary



Crohn's disease	Ulcerative Colitis
<b>Any part of the GIT</b>	Colon only
<b>Skip areas</b> of normal mucosa	Diffuse involvement of mucosa
Deep ulcers ( <b>fissure</b> )	Superficial ulcers
Transmural inflammation	Mucosal inflammation only
<b>Fistula formation</b>	-
Creeping mesenteric fat	-
Fibrous thickening of wall	-
Granulomas	-
Dysplasia is Rare	Dysplasia is Common
Carcinoma is rare	Carcinoma is more common (10%)
Cobblestone appearances	Pseudopolyps appearances
Thickened wall Narrow lumen	Thin wall Dilated lumen
Marked Lymphoid reaction	Moderate Lymphoid reaction
<b>Complications:</b> <ul style="list-style-type: none"><li>• Short gut syndrome</li><li>• Fistula formation</li><li>• Bowel perforation</li><li>• Stricture formation</li></ul>	<b>Complications:</b> <ul style="list-style-type: none"><li>• Haemorrhage</li><li>• Electrolyte loss</li><li>• Toxic megacolon</li><li>• Systemic effects</li></ul>



# Quiz

**Q1: A complication of ulcerative colitis?**

- A) Enterovesical fistulas.
- B) Intestinal obstruction due to thickened wall and narrow lumen
- C) Entervaginal fistula
- D) Pyoderma gangrenosum

**Q2: One of the manifestation of IBD involving colon is:**

- A) Intestinal obstruction
- B) Steatorrhea
- C) Tenesmus
- D) Uveitis

**Q3: A patient diagnosed with ulcerative colitis is at increased risk of developing which of the following complications?**

- A) Adenocarcinoma
- B) Fistula
- C) Granulomatous lymphadenitis
- D) Transmural inflammation

**Q4: A 24-year-old man is brought to the emergency room with symptoms of acute intestinal obstruction. His temperature is 38°C. Physical examination reveals a mass in the right lower abdominal quadrant. At laparoscopy, there are numerous small bowel strictures and a fistula extending into a loop of small bowel. Which of the following is the most likely diagnosis?**

- A) Adenocarcinoma
- B) Crohn disease
- C) Pseudomembranous colitis
- D) Ulcerative colitis

**Q5: A 25-year-old woman is brought to the emergency room with symptoms of acute intestinal obstruction. The patient has an 8-month history of blood-tinged diarrhea and cramping abdominal pain. There is abdominal tenderness to palpation. A CT scan of the abdomen shows massive distention of the transverse colon. Which of the following is the most likely diagnosis?**

- A) Adenocarcinoma
- B) Crohn disease
- C) Pseudomembranous colitis
- D) Ulcerative colitis

**Q6: On histological examination of the bowel, granulomas are highly suggestive of?**

- A) Crohn's disease
- B) Ulcerative colitis
- C) Both
- D) Neither

**Q7: Enterovesical fistula result in?**

- A) malabsorption
- B) A fecal vaginal discharge
- C) passage of gas and feces with urine
- D) Obstruction

**Q8: Crohn's disease:**

- A) Always affects the colon
- B) May lead to intestinal obstruction
- C) Is best treated surgically
- D) Requires a gluten free diet

**Q9: Toxic megacolon is a complication of:**

- A) Chronic ulcerative colitis
- B) Chronic crohn's disease
- C) Acute phase of ulcerative colitis
- D) Acute phase of crohn's disease

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THANK YOU