Lecture 8 & 9
Inflammatory Bowel Disease

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

Revised by
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Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes

Objectives:

- Know the two forms of idiopathic inflammatory bowel disease (IBD).
  - Crohn's disease and ulcerative colitis
- Describe the pathogenesis of IBD.
  - Theories
  - Autoimmunity
- Compare and contrast Crohn disease and ulcerative colitis with respect to:
  - Clinical features and extraintestinal manifestations
  - Pathology (gross and microscopic features) of IBD.
  - Complications of IBD (especially adenocarcinoma preceded by dysplasia)

References: Lecture Slides & Robbins

Inflammatory Bowel Disease:

Also called (idiopathic IBD) because it has unknown etiology

A chronic condition resulting from inappropriate mucosal immune activation.

- 2 major entities: 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.

Overstimulation of immune system

There will be an increase in immunologic reaction, so there will be more infiltration in bowel inflammatory cell which lead to inflammation in mucosa

Genes:

Mutations in *NOD2* are seen in about 15% of Crohn's disease patients but are also seen in a smaller percentage of the general population, so mutations in *NOD2* are neither necessary nor sufficient for the development of Crohn's disease

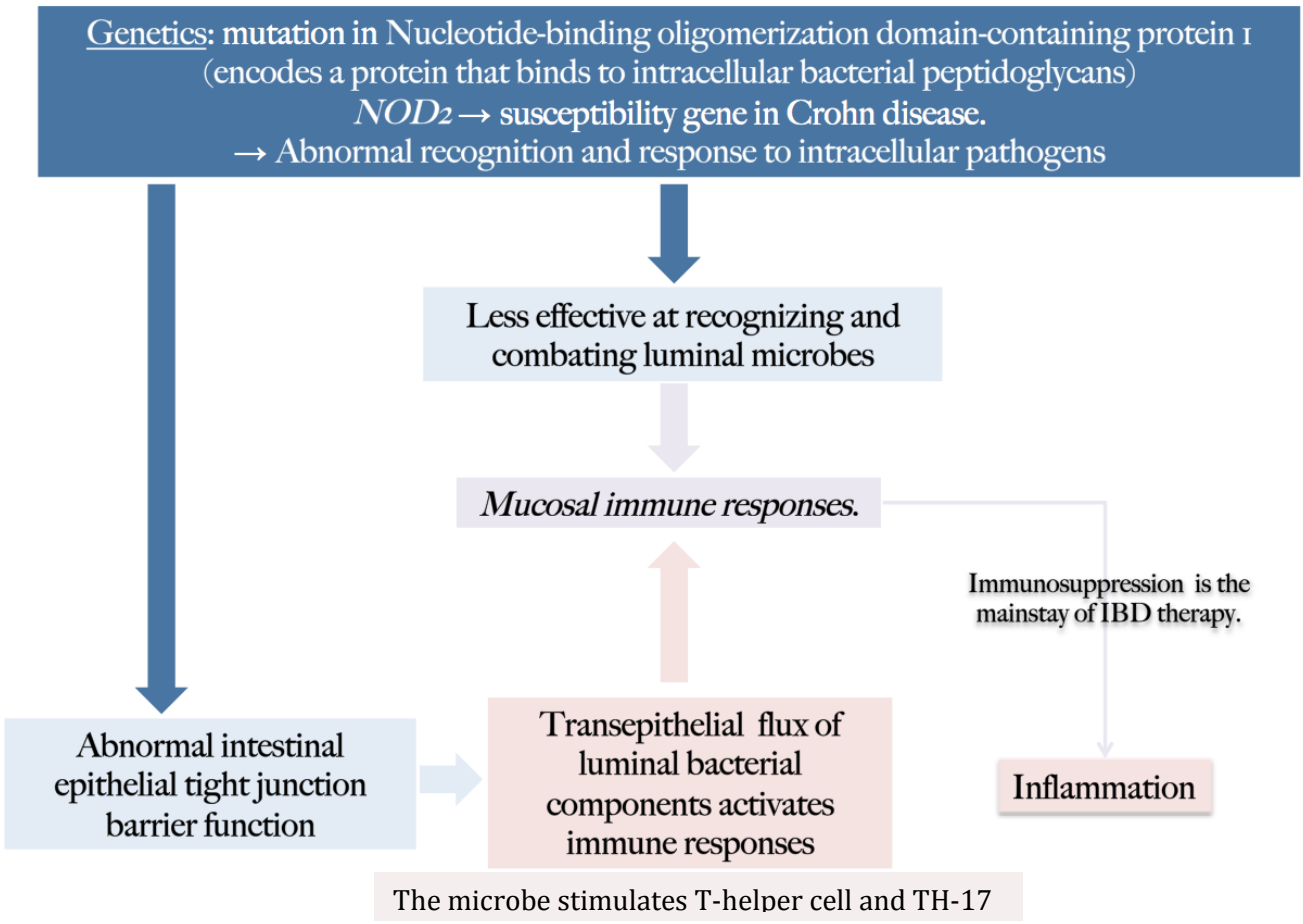
Pathophysiology: (Not Important)

That's why when we give them immunosuppression the patient will improve

- An idiopathic Disorder **(Mainly Immune-Response)**
- The pathophysiology of IBD is under active investigation.
- Persons with IBD have a genetic predisposition for the disease.
- Most investigators believe that the two diseases result from a combination of
  - Defects in host interactions with intestinal microbes
  - Intestinal epithelial dysfunction
  - Aberrant mucosal immune responses.
- For unclear reasons, research suggests that smoking increases the risk of Crohn disease but reduces the likelihood of ulcerative colitis.

Smoking is a risk factor in Crohn's disease, but in ulcerative colitis it's protective.

Theory:



Clinical manifestations:

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

- **Colon:** Bloody diarrhea, Tenesmus

Tenesmus means colicky abdominal pain during defecation

- **Small intestine:** Abdominal pain, Intestinal obstruction & Steatorrhea.
- **Extraintestinal manifestations:** Arthritis, Eye manifestation & Skin manifestation.

Extraintestinal means it affects other organs in the body, for example:
- Affects the joint → Arthritis | - Affects liver → Sclerosing cholangitis
- Affects the eye → Uveitis | - Affects skin → Erythema in the skin

Crohn's disease:

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.

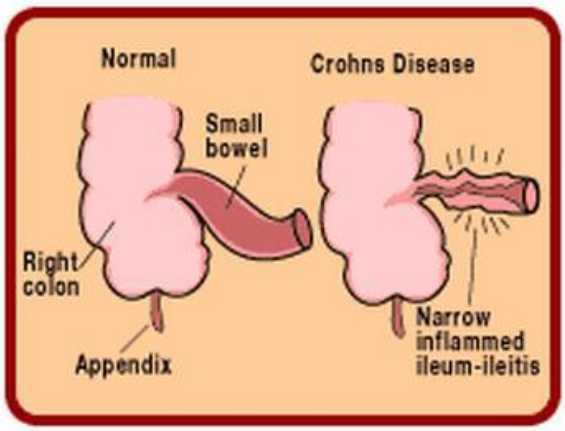
If it involves the colon → bloody diarrhea or tenesmus. If it involve the small intestine → abdominal pain, obstruction, malabsorption or steatorrhea.

Clinical Features:

- Occurs at any age but has its highest incidence in young adults.
- Extremely variable clinical features
  - **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.

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.



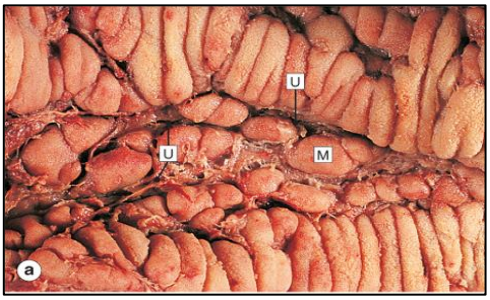
Gross Appearance: (Very Important)

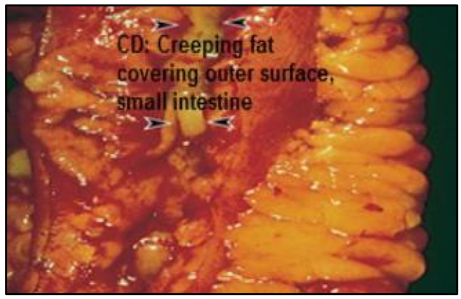
- Involvement is typically segmental (discontinuous or skip lessions) , with skip areas of normal intestine between areas of involved bowel.
- **Marked fibrosis** causing luminal narrowing with intestinal obstruction.
- **Fissures** (deep and narrow ulcers that look like stabs with a knife that penetrate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

Fissures and Fistulas are only seen in Crohn's not in UC

Fissures could be between a part of small intestine and another part of the small intestine or between the urinary bladder and the small intestine leading to inflammation in the urinary bladder.

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





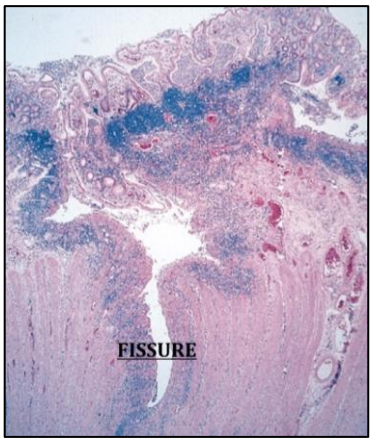
FAT : In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (creeping fat)

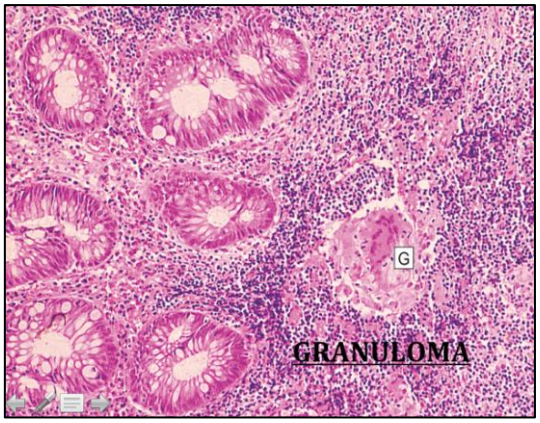
Microscopic Features:

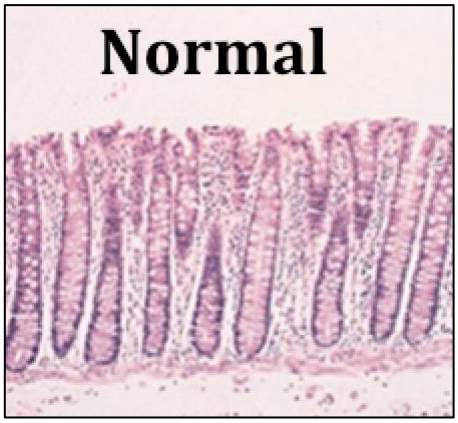
It involves the full thickness

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

Distortion of Mucosal crypt is seen in both Crohn's and UC. (indicates a chronic injury)







Complications:

- **Intestinal obstruction.**

Obstruction mainly occurs in the ileum, because of the fibrosis

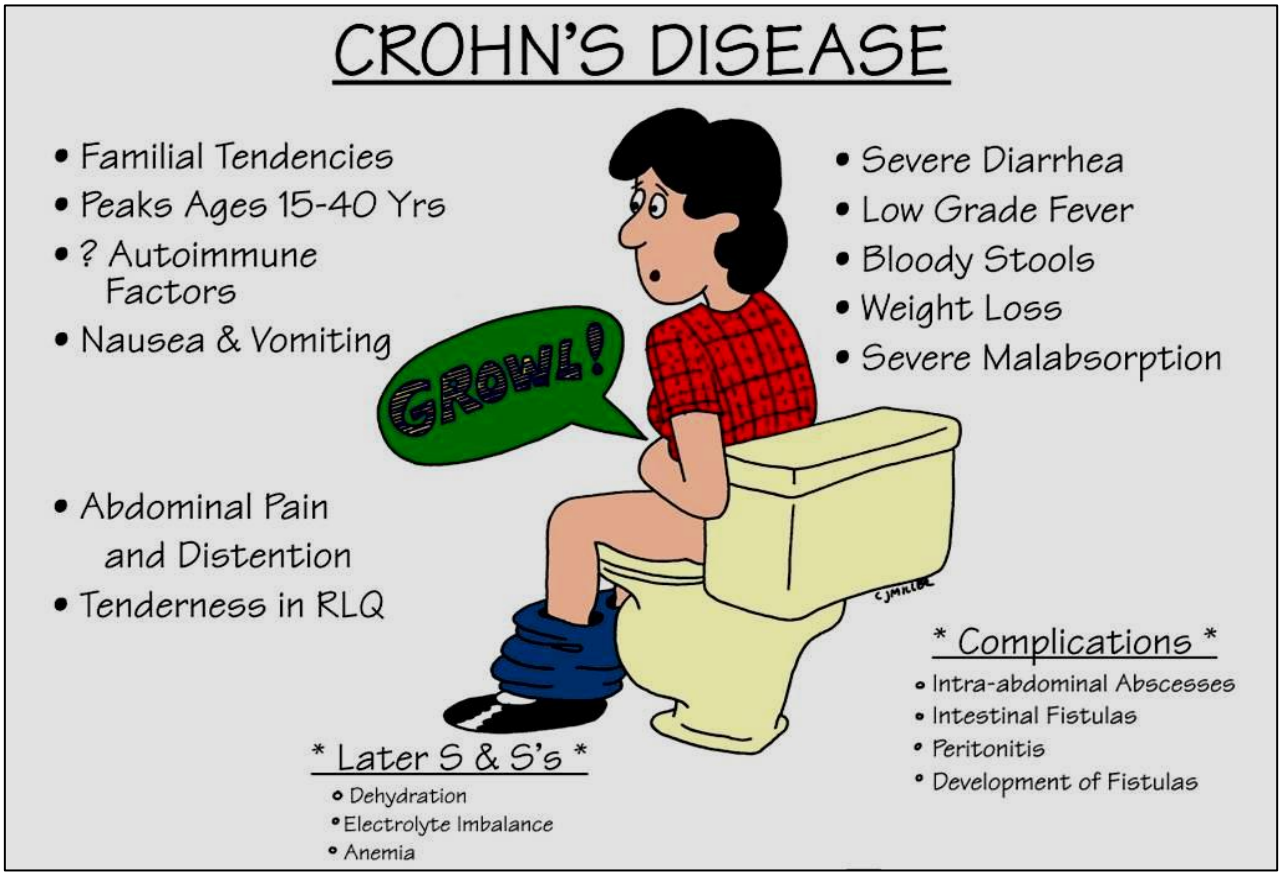
- **Fistula formation:**
  - Between the ileum and the colon result in **malabsorption**
  - **Enterovesical** fistulas lead to urinary infections and **passage of gas and feces with urine.**
  - **Enterovaginal** fistulas produce a **fecal vaginal discharge**.
- **Extraintestinal manifestations (arthritis and uveitis)**
  - Slight increased risk of development of carcinoma of the colon—much less than in ulcerative colitis.

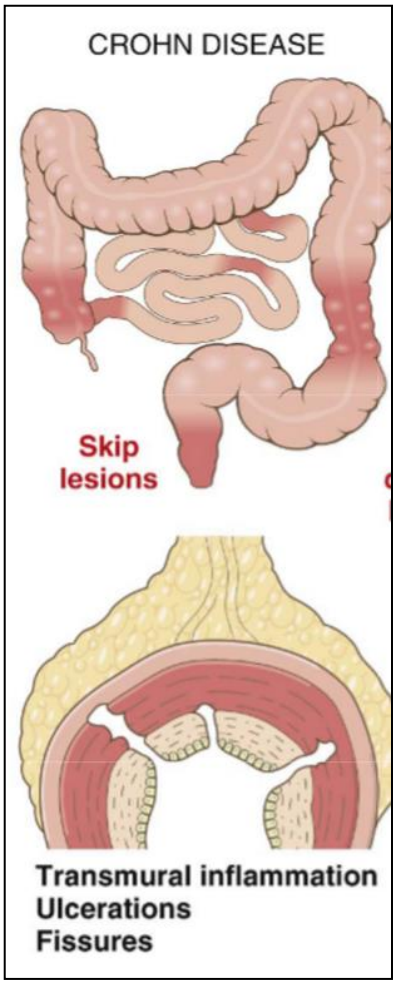
Both of them (crohn's and ulcerative colitis) could have extraintestinal manifestations.

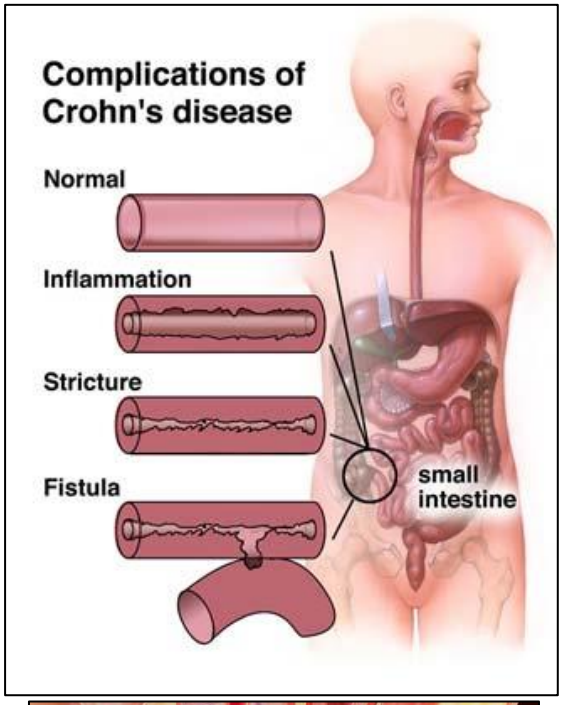
[1] Involves all the layers of GIT wall

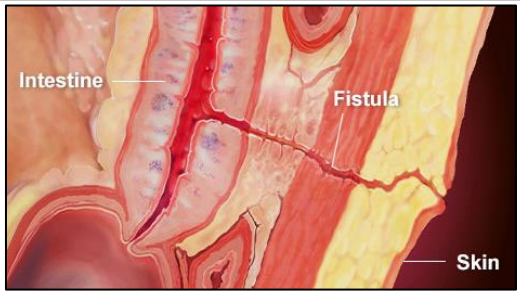
Summary

- 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:

Relapsing means يجي المريض أحيانًا تعبان جدًا وأحيانًا بيتحسن

- 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.

Continuity means there is no skip lesiosn as in Crohn's disease

Etiology: (Not important)

- 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 (relieved by defecation), bloody diarrhea and mucus in the stool.
- The disease usually has a chronic course, with remissions and exacerbations.
- Smoking may partially relieve symptoms.

Sites of Involvement:

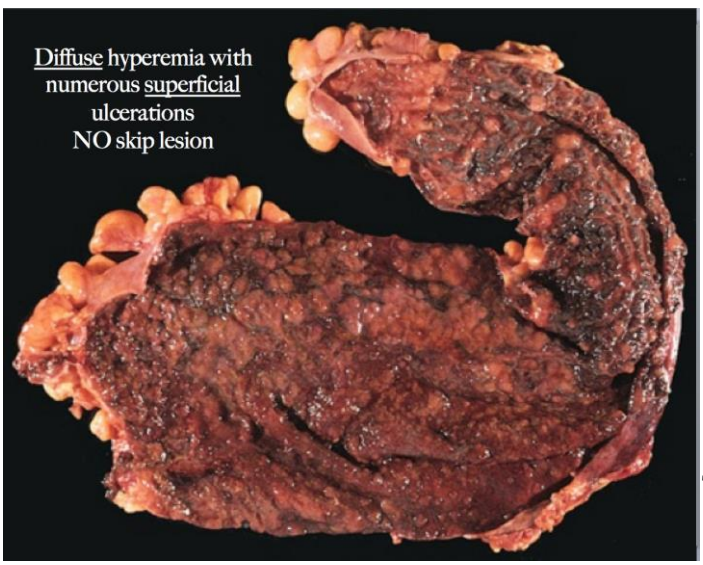
UC starts with **RECTUM** then spread to colon

- 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

Could affect parts of the colon, or the entire colon "pancolitis"

Gross Appearance: (Very Important)

- 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.
- Absent skip lesions.



- The ulceration limited to the mucosa
- The mucosa will become red because of the increase in blood supply "hyperemia"
- inflammatory pseudopolyps mean there is inflammation but without the feature of true polyps (like hyperplasia) → because some fluid from colon will diffuse to this area

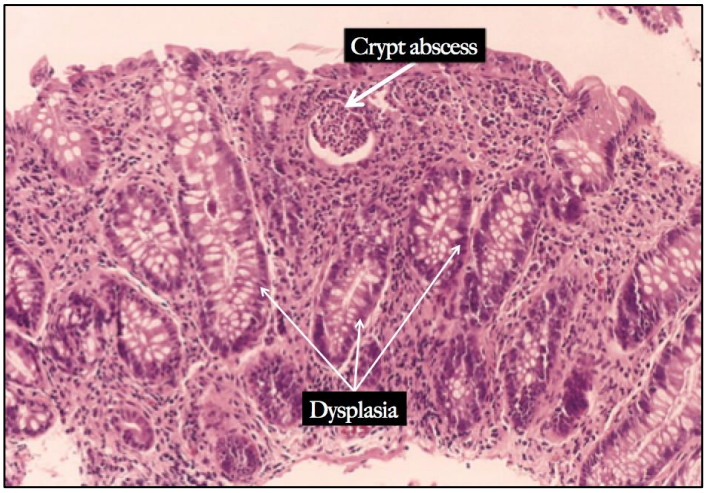
Crypt abscess means accumulation of neutrophils in lumen of the crypt

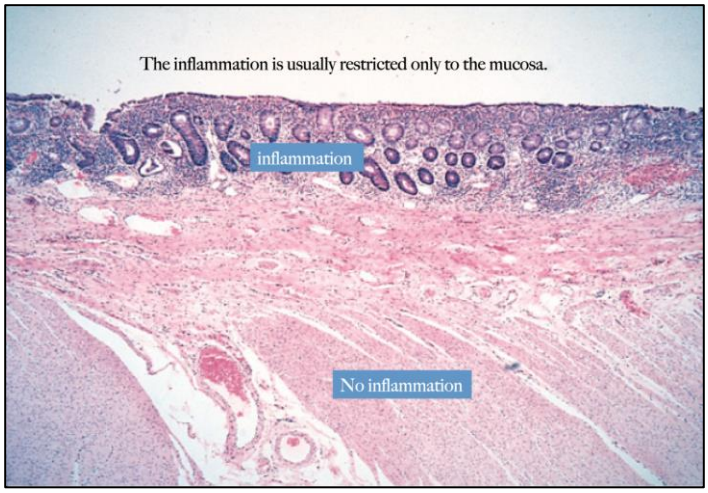
Microscopic Appearance:

- The inflammation is usually restricted to the mucosa.
- In the active phase → neutrophils (Cryptits, crypt abscess).
- In the chronic phase → crypt atrophy and distortion.
- Active inflammation correlates well with the severity of symptoms.
- Colonic dilation and toxic megacolon caused by damage to muscularis propria by inflammatory mediators.
- Absent granulomas.

Crypt distortion (of normal picture) so some crypt dilates and some branches

- There will be depletion of goblet cell (decrease in number)
- In acute phase the patient will have symptoms while in chronic Asymptotic





Dysplasia → the base of premalignant lesion that leads to adenocarcinoma

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%.

Complications:

Megacolon happens when the entire muscle becomes weak so the bowel wall will dilate → needs colectomy

Acute phase:

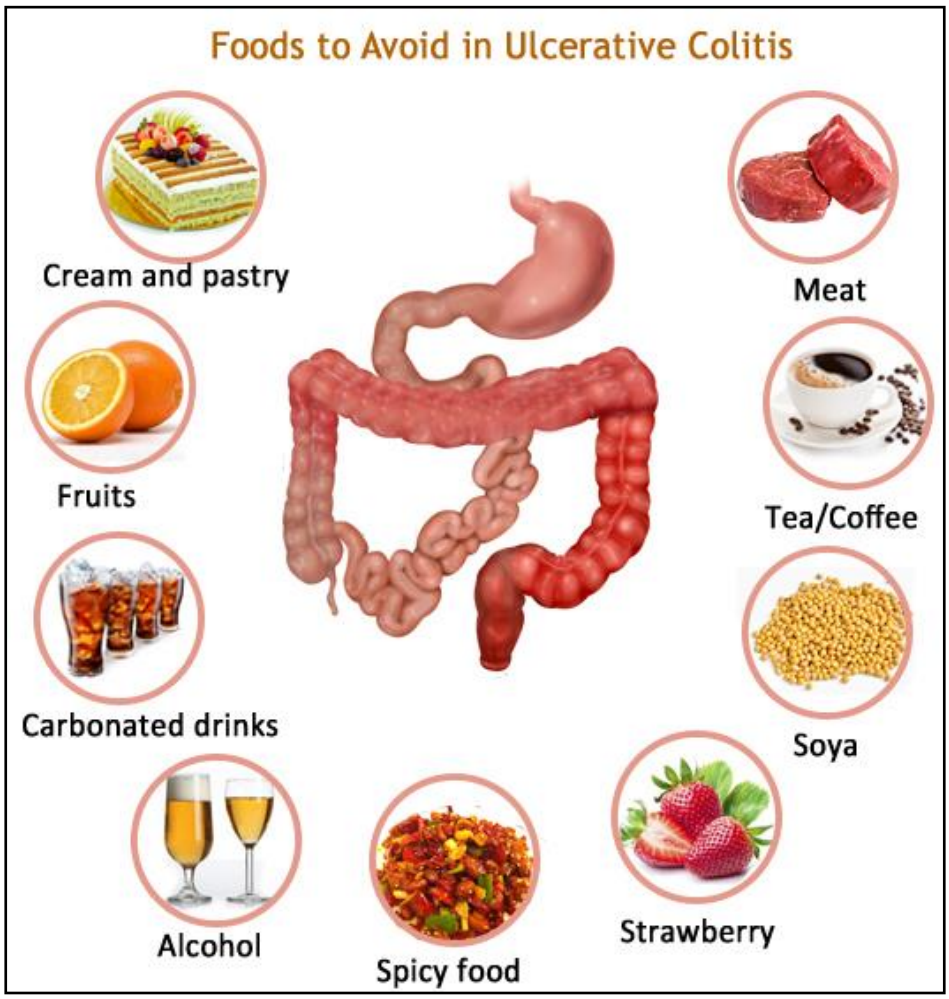
- Severe bleeding.
- Toxic megacolon (dilation of the colon, with functional obstruction).

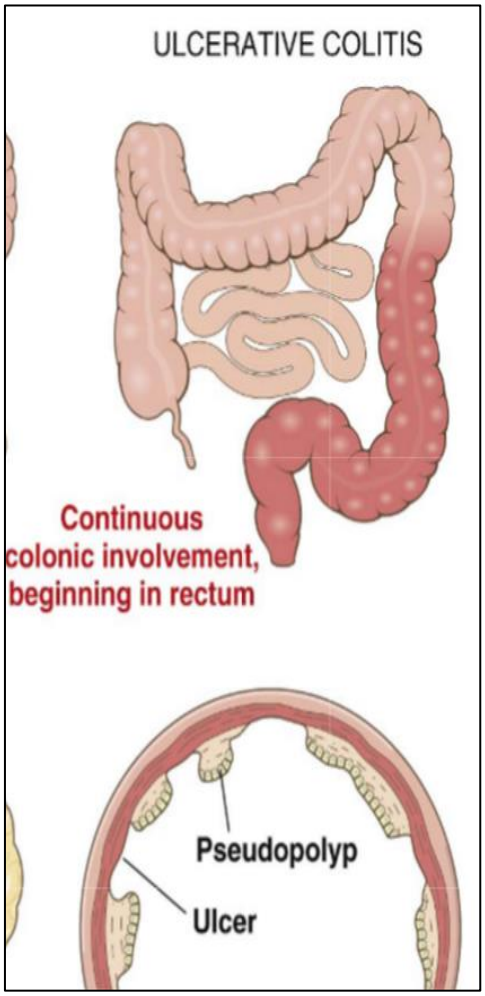
Chronic ulcerative colitis:

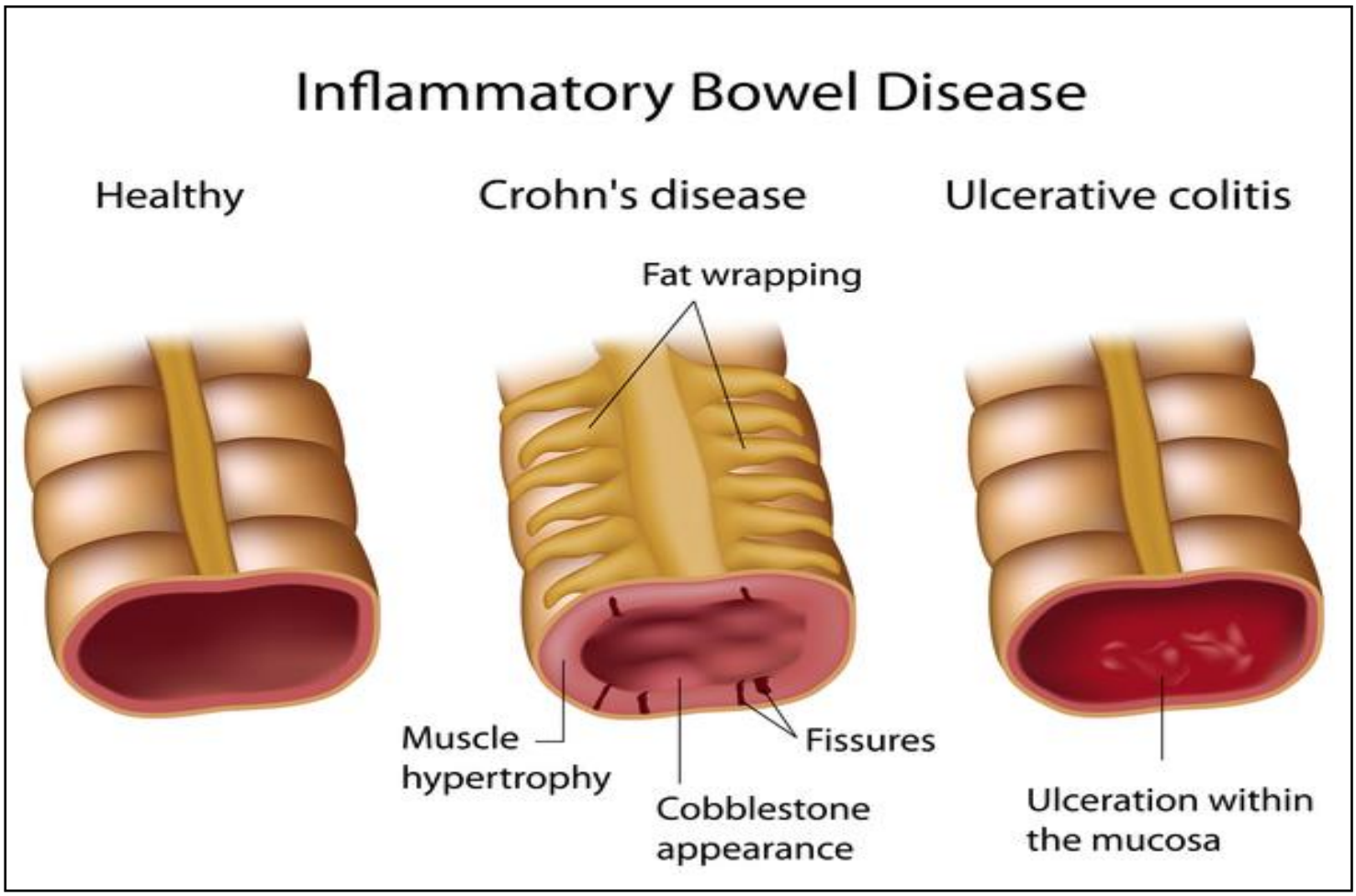
- Increase risk of developing colon carcinoma.
- The presence of high-grade dysplasia in a mucosal biopsy imposes a high risk of cancer and is an indication for colectomy.

Extraintestinal manifestations:

- Arthritis.
- Uveitis.
- Skin lesions (pyoderma gangrenosum).
- Sclerosing cholangitis (fibrosis around bile ducts), leading to obstructive jaundice.

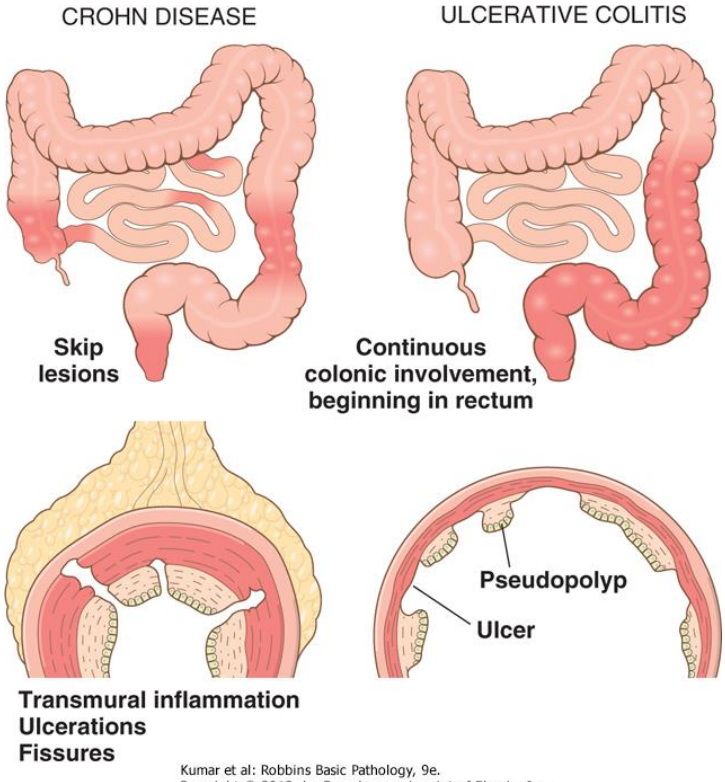

Foods to Avoid in Ulcerative Colitis
Cream and pastry
Meat
Fruits
Tea/Coffee
Carbonated drinks
Soya
Alcohol
Spicy food
Strawberry


ULCERATIVE COLITIS
Continuous colonic involvement, beginning in rectum
Pseudopolyp
Ulcer


Inflammatory Bowel Disease
Healthy
Crohn's disease
Ulcerative colitis
Fat wrapping
Muscle hypertrophy
Fissures
Cobblestone appearance
Ulceration within the mucosa

This table is super important

	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



Summary

Crohn's disease	Ulcerative Colitis
Any part of the GIT	Colon only
Skip areas of normal mucosa	Diffuse involvement of mucosa
Deep ulcers (fissure)	Superficial ulcers
Transmural inflammation	Mucosal inflammation only
Fistula formation	Not seen
Creeping mesenteric fat	Not seen
Fibrous thickening of wall	Not seen
Granulomas	Not seen
Dysplasia is rare	Dysplasia is common
Carcinoma is rare	Carcinoma is more common (10%)

Table 14–5 Features That Differ Between Crohn Disease and Ulcerative Colitis

Feature	Crohn Disease	Ulcerative Colitis
Macroscopic		
Bowel region affected	Ileum ± colon	Colon only
Rectal involvement	Sometimes	Always
Distribution	Skip lesions	Diffuse
Stricture	Yes	Rare
Bowel wall appearance	Thick	Thin
Inflammation	Transmural	Limited to mucosa and submucosa
Pseudopolyps	Moderate	Marked
Ulcers	Deep, knifelike	Superficial, broad-based
Lymphoid reaction	Marked	Moderate
Fibrosis	Marked	Mild to none
Serositis	Marked	No
Granulomas	Yes (~35%)	No
Fistulas/sinuses	Yes	No
Clinical		
Perianal fistula	Yes (in colonic disease)	No
Fat/vitamin malabsorption	Yes	No
Malignant potential	With colonic involvement	Yes
Recurrence after surgery	Common	No
Toxic megacolon	No	Yes

NOTE: Not all features may be present in a single case.

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

A. Crohn's disease

B. Ulcerative Colitis

1: B 2: B 3:B 4:A 5:A 6:B 7:A 8:A 9:A 10:A 11:B 12:B

Check Your Understanding

MCQs:

1- What's from the following is true about Ulcerative colitis:

A. Smoking is a risk factor
B. It's more common in males
C. Appendectomy is a risk factor
D. Smoking reduce the risk of developing UC

2- Crohn disease has:

A. More genetic dominance than UC
B. Less genetic dominance than UC
C. Equal genetic factors with UC
D. Genetics play no role

3- IBD is due to:

A. suppression of mucosal immune reaction
B. Decrease permeability of epithelial tight junction
C. Intestinal microbiota

1:D 2:A 3:C

4- Which of the following histological findings is seen under the microscope of a biopsy taken from a 27-year-old male with acute ulcerative colitis?

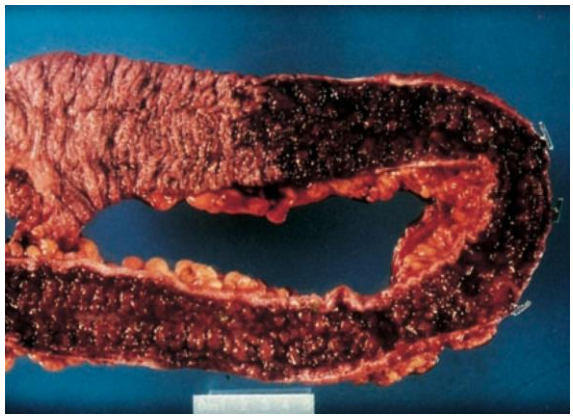
A. Granulomas
B. Mesenteric adipocytes
C. Pseudopolyps
D. Lymphocytes

5- Which of the following is NOT an extraintestinal manifestation of ulcerative colitis?

A. Glossitis
B. Uveitis
C. Arthritis
D. Jaundice

6- A 27-year-old woman presents with a 9-month history of bloody diarrhea and crampy abdominal pain. Three weeks ago, she noticed that her left knee was swollen, red, and painful. Her temperature is 38°C (101°F), respirations are 32 per minute, and blood pressure is 130/90 mm Hg. Abdominal palpation reveals tenderness over the left lower quadrant. Laboratory studies show moderate anemia, with a hemoglobin level of 9.3 g/dL. Microscopic examination of the stool reveals numerous red and white blood cells. A diffusely red, bleeding, friable colonic mucosa is visualized by colonoscopy. The colon is subsequently removed and the surgical specimen is shown in the image. Which of the following is the most likely diagnosis?

A. Adenocarcinoma
B. Crohn disease
C. Pseudomembranous colitis
D. Ulcerative colitis



4:C 5:A 6:D

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قال ﷺ: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق
