Lecture 8 & 9

Inflammatory bowel disease

432 ***Pathology*** Team

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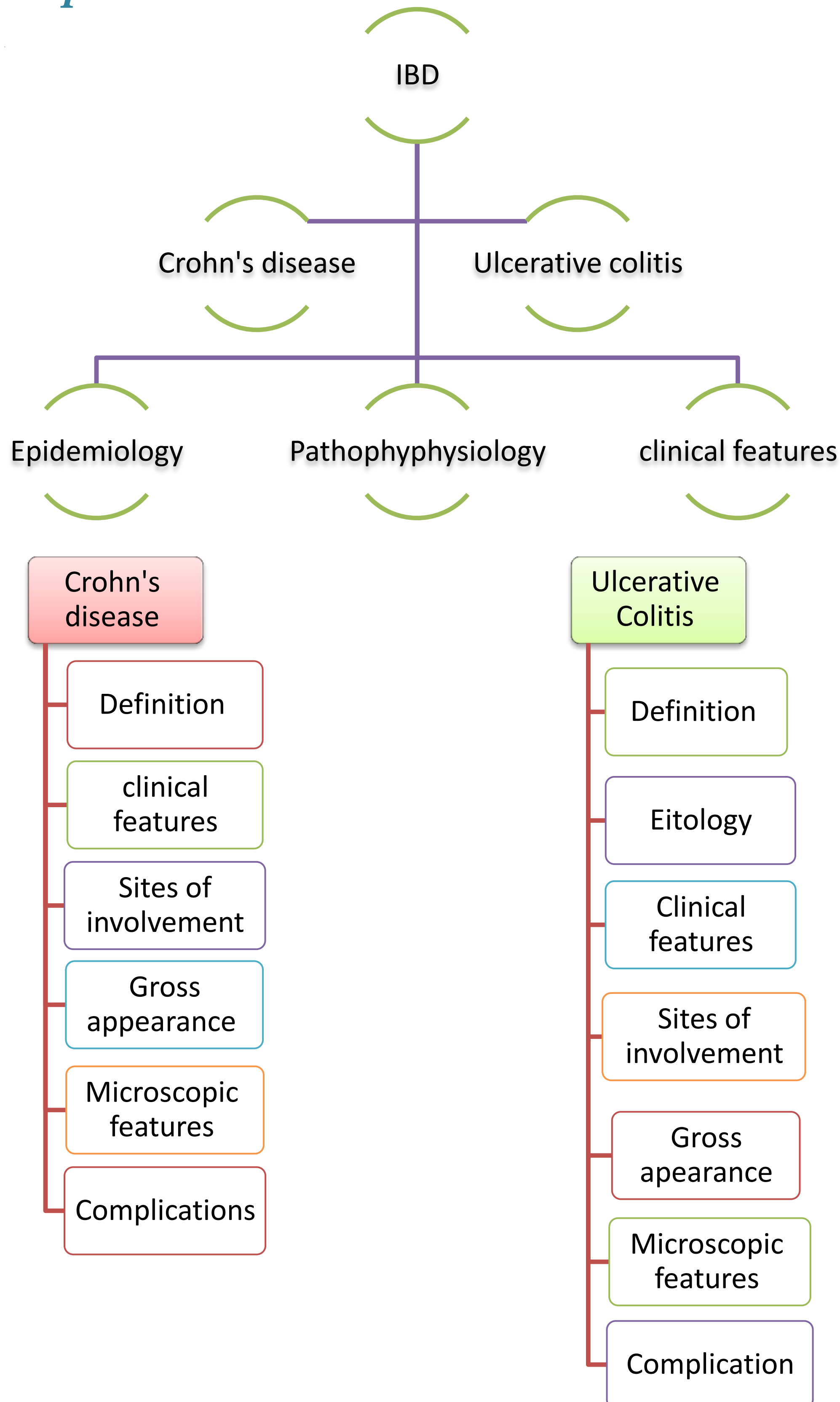
GIT Block

Color Index: female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Inflammatory bowel disease

Mind Map:



Inflammatory bowel disease

Definition:

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

- Crohn's disease and ulcerative colitis.
- Although their causes are still not clear, the two diseases probably have an immunologic hypersensitivity basis.

Epidemiology:

- Both Crohn's disease and ulcerative colitis are more common in females and in young adults.
- 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.
- 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:

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

Abnormal intestinal epithelial tight junction barrier function

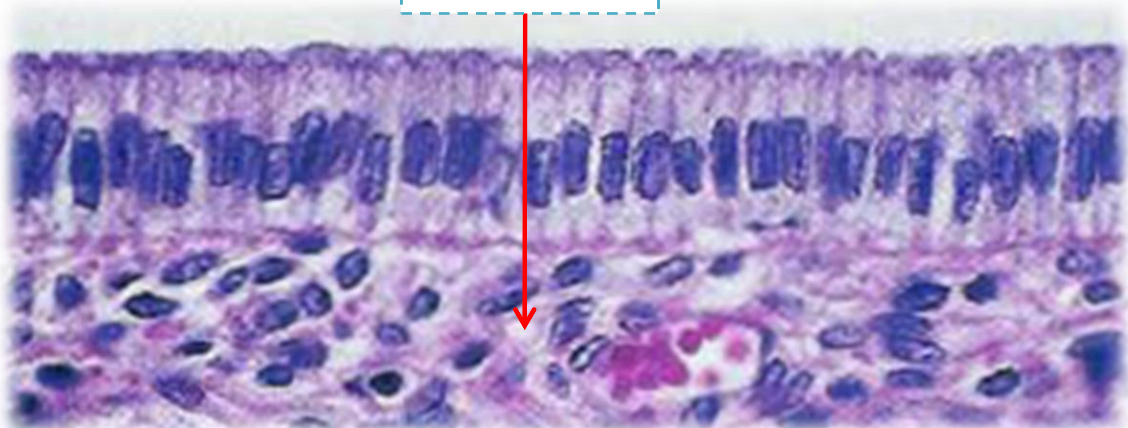
Transepithelial flux of luminal bacterial components activates immune responses

Less effective at recognizing and combating luminal microbes

Mucosal immune responses

Inflammation

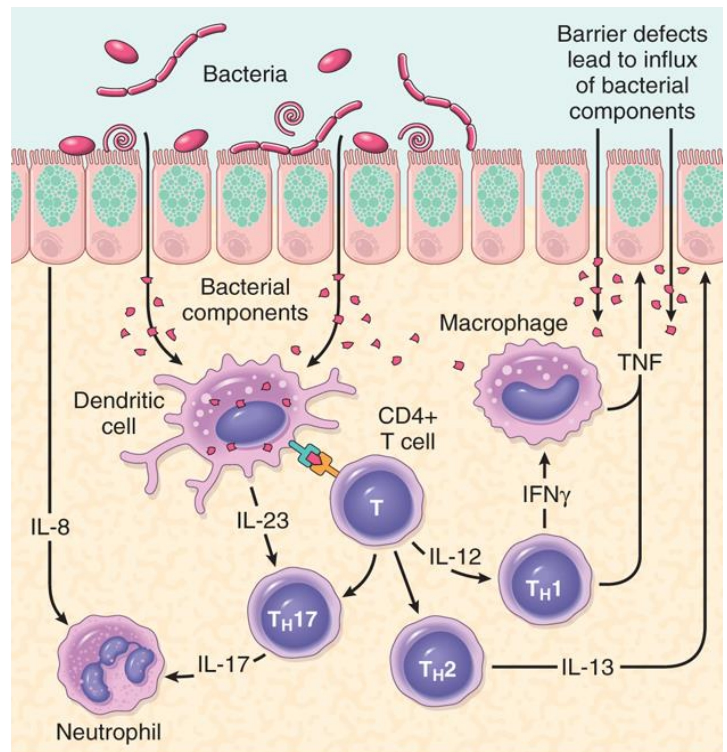
Immunosuppression is the mainstay of IBD therapy.



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 disease but reduces the likelihood (chance to develop) of ulcerative colitis.



Kumar et al: Robbins Basic Pathology, 9e.
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Clinical manifestation:

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

NOTE: Tenesmus: is a clinical symptom where there is a feeling of constantly needed to pass stools despite an empty colon.

Crohn's Disease

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.

Clinical Features

- Affects any age but has its highest incidence in **young adults**.
- Has extremely variable clinical features, depending on the phase:
    1. Acute phase: fever, diarrhea, and right lower quadrant pain may mimic acute appendicitis.
    2. Chronic disease: remissions and relapses over a long period of time.

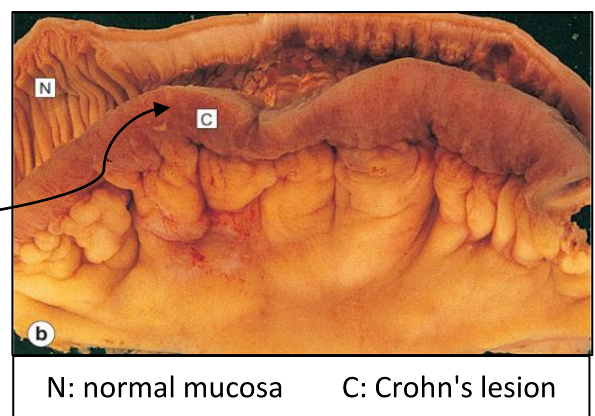
- Thickening of the intestine may produce an ill-defined mass in the abdomen.

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.

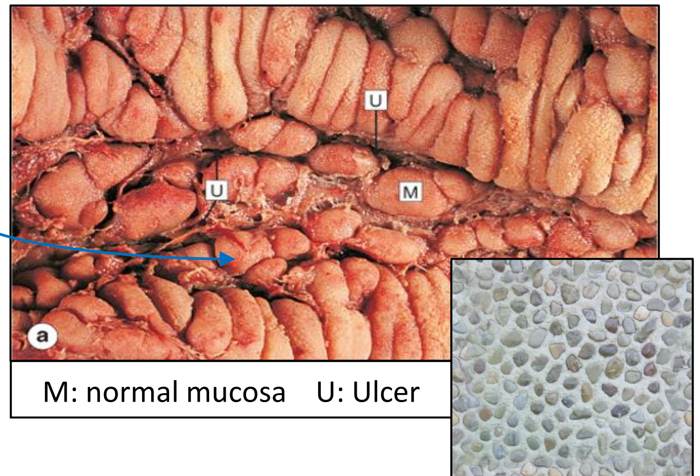
Gross Appearance

- 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).



N: normal mucosa C: Crohn's lesion

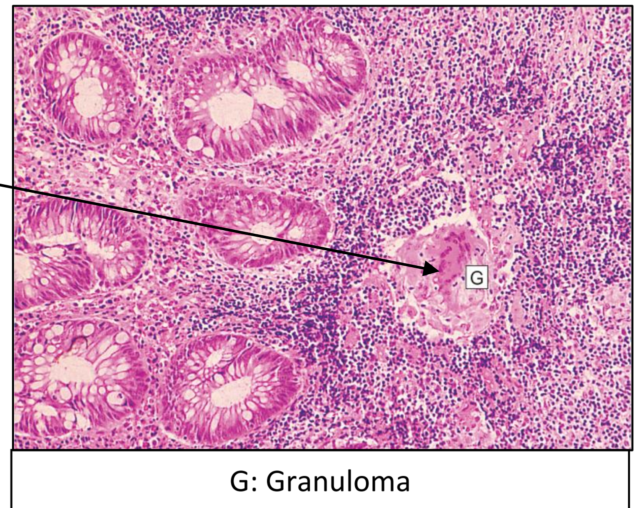
- Mucosa: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa. This results in the typical cobblestone effect.
- FAT: In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (creeping fat).



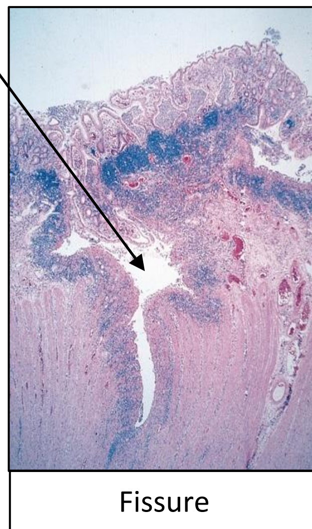
M: normal mucosa U: Ulcer

Microscopic Features

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



G: Granuloma


Fissure

NOTES:

- **Transmural inflammation reaching to serosa, cobblestone effect and creeping fat are seen in Crohn's but not in ulcerative colitis.**
- **Ulcerative fissures are narrow and deep. They might cause peritonitis or lead to fistula formation.**

Complications

- Intestinal obstruction.
- Fistula formation:
    - If it was between the **ileum and the colon**, it'll 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.

> ***REMEMBER:***
>
> **Crohn's is characterized by:**
> - 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

- Is an inflammatory disease of uncertain cause.
- It has a **chronic** course characterized by **remissions and relapses**.
- 20 to 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. (This leads to an acute inflammation), it also lead to an imbalance between T-cell activation and regulation. The CD4+ T cells present in the lesions secrete damaging substances.

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.
- Acute symptoms are temporarily relieved by defecation.
- Colectomy cures intestinal disease, but extraintestinal manifestations may persist.

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. (1- downwards ascending upward 2-can involve the left side or the entire colon)**
- The **ileum is not involved** as a rule.

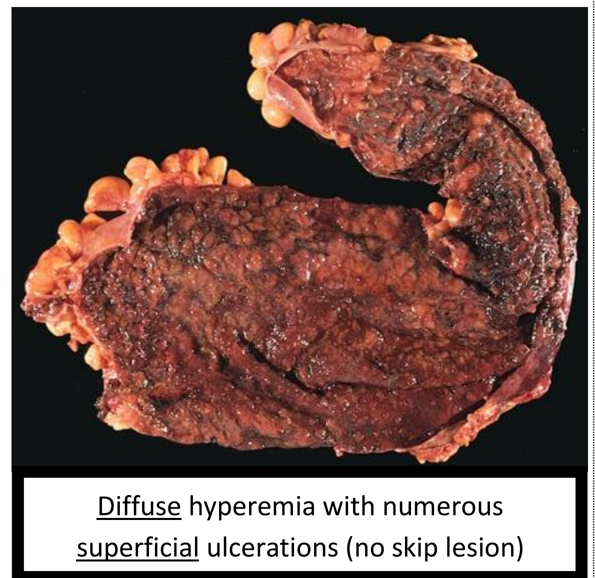
From Robbins:

- Disease of the entire colon is termed **pancolitis**.
- Disease limited to the rectum or rectosigmoid may be referred to descriptively as **ulcerative proctitis** or **ulcerative proctosigmoiditis**

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.

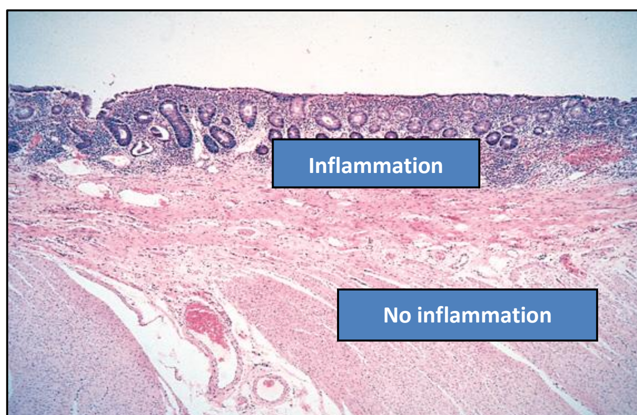
The repeated injury and regeneration of the epithelium →dysplasia →Cancer

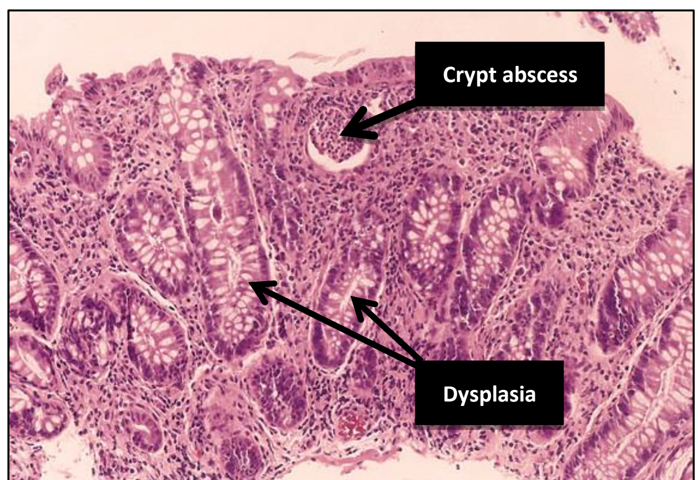


Diffuse hyperemia with numerous superficial ulcerations (no skip lesion)

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 (in the form of branched ,dilated glands with decreased goblet cells)
- Active inflammation correlates well with the severity of symptoms. (higher neutrophils →more crypt abscess →more signs of the disease will manifest)





Cryptits: its active and, neutrophils are attacking the epithelium.

Crypt abscess: it is the presence of neutrophils within the lumen and the crypts are dilated.

From Robbins:

- There is epithelial metaplasia.
- **skip lesions are absent and inflammation generally is limited to the mucosa and superficial submucosa**
- In severe cases, mucosal damage may be accompanied by ulcers that extend more deeply into the submucosa, but the muscularis propria is rarely involved.
- Submucosal fibrosis, mucosal atrophy, and distorted mucosal architecture remain as residua of healed disease, but the histologic pattern also may revert to near normal after prolonged remission.

Complications

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

- **Chronic ulcerative colitis**:
  1. **Increase risk of developing colon carcinoma**.
  2. The presence of **high-grade dysplasia** in a mucosal biopsy imposes a **high risk of cancer** and is an **indication for colectomy**. (1-**dysplasia includes nuclear enlargement ,over stratification and crowding of the nuclei , hyperchromasia , pleomorphisim , increased mitotic ratio → if too high it's an in sito state and you need to treat before the invasive carcinoma develops . 2-adenocarcinoma superimposed on ulcerative colitis is very aggressive with poor prognosis).**

From Robbins:

Toxic mega colon:

- Inflammation and inflammatory mediators can damage the muscularis propria and disturb neuromuscular function leading to colonic dilation and **toxic megacolon,** which carries a significant risk of perforation. **(The tone and peristalsis are gone)**
- **It's a medical emergency where surgery and resection of the colon is required.**

- **Extraintestinal manifestations:**
  (Occur more commonly in ulcerative colitis than in Crohn's disease)
  1. Arthritis
  2. Uveitis
  3. Skin lesions (pyoderma gangrenosum),
  4. Sclerosing pericholangitis (fibrosis around bile ducts), leading to obstructive jaundice.

Summery From Robbins:

Inflammatory Bowel Disease

- Inflammatory bowel disease (IBD) is an umbrella term for Crohn disease and ulcerative colitis.
- Crohn disease most commonly affects the terminal ileum and cecum, but any site within the gastrointestinal tract can be involved; skip lesions and noncaseating granulomas are common.
- Ulcerative colitis is limited to the colon, is continuous from the rectum, and ranges in extent from only rectal disease to pancolitis; neither skip lesions nor granulomas are present.
- Both Crohn disease and ulcerative colitis can have extraintestinal manifestations.
- The risk of colonic epithelial dysplasia and adenocarcinoma is increased in patients who have had IBD for more than 8 to 10 years.

Comparison:

	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
Complications	Short gut syndrome Fistula formation Bowel perforation Stricture formation	Haemorrhage Electrolyte loss Toxic megacolon Systemic effects

Questions

1/ A 25-year-old man presents with weight loss, abdominal pain, and bloody diarrhea. Sigmoidoscopy, colonscopy reveals mucosal erythema and ulceration extending in a continuous fashion proximally from the rectum. Which of the following pathological findings would also be characteristic of this patient's illness?
(A) Bowel wall thickening
(B) Cobblestone appearance of mucosa
(C) Fistula
(D) Pseudopolyps

2/ 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) Carcinoid tumor
(C) Crohn disease
(D) Ulcerative colitis

3/ 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 . Abdominal palpation reveals tenderness over the left lower quadrant. Microscopic examination of the stool reveals numer- ous red and white blood cells. A diffusely red, bleeding, friable colonic mucosa is visualized by colonoscopy. Which of the following is the most likely diagnosis?
(A) Adenocarcinoma
(B) Carcinoid tumor
(C) Crohn disease
(D) Ulcerative colitis

4/ The patient described in Previous Q is at increased risk of developing which of the following complications?
(A) Adenocarcinoma
(B) Fistula
(C) Granulomatous lymphadenitis
(D) Transmural inflammation

Answers:
- 1- D
- 2- C
- 3- D
- 4- A

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*Good Luck ^_^*