Revised & Approved

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GNT pathology cases file
Don't forget to check it frequently Click

Pathology

Inflammatory bowel disease
(crohn's disease)
(ulcerative colitis)

439

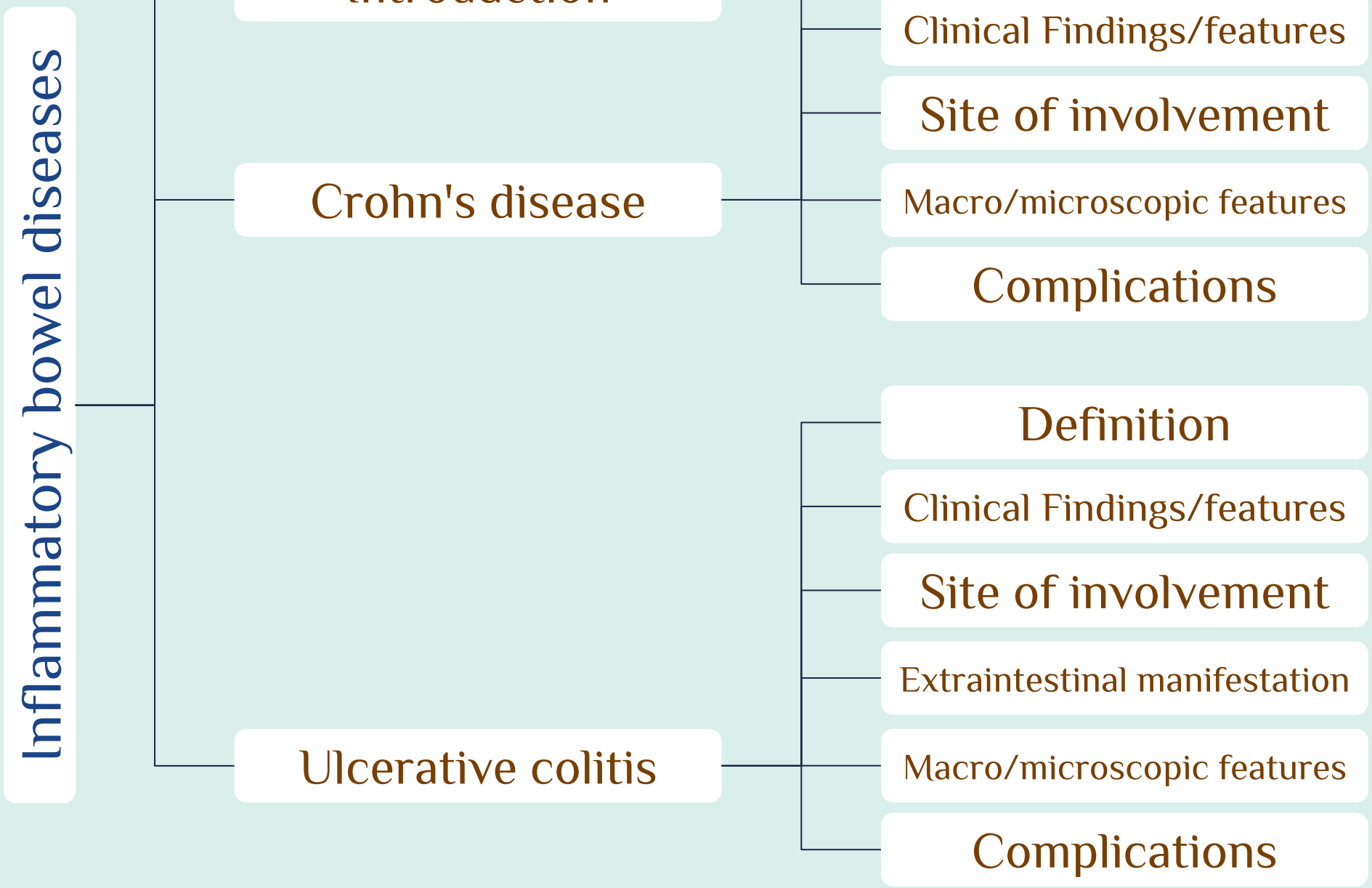
Color index
- Important
- Doctor's note
- Extra info
- Main text
- ★ Male's slide
- ★ Female's slide

" اللهم لا سهل الا ماجعلته سهلا و انت تجعل الحزن إذا شئت سهلا "

Objective

1. Know the two forms of idiopathic inflammatory bowel disease (IBD)
2. Describe the pathogenesis of IBD.
3. 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)

Overview



Inflammatory bowel disease

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Definition

- It is a chronic condition resulting from complex interactions between intestinal microbiota and host immunity in genetically predisposed individuals resulting an inappropriate mucosal immune activation (inflammation of the mucosa of the bowel).

- **It has 2 Types**
  - Crohn's Disease (CD)
  - Ulcerative colitis (UC)

- The distinction between **ulcerative colitis** and **Crohn disease** is based on the distribution of affected sites and the morphologic expression of disease at those sites
- 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

Ulcerative colitis	Crohn's disease
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	More common in **whites** than **blacks** More common 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**

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

- The geographic distribution of IBD is highly variable
- 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:

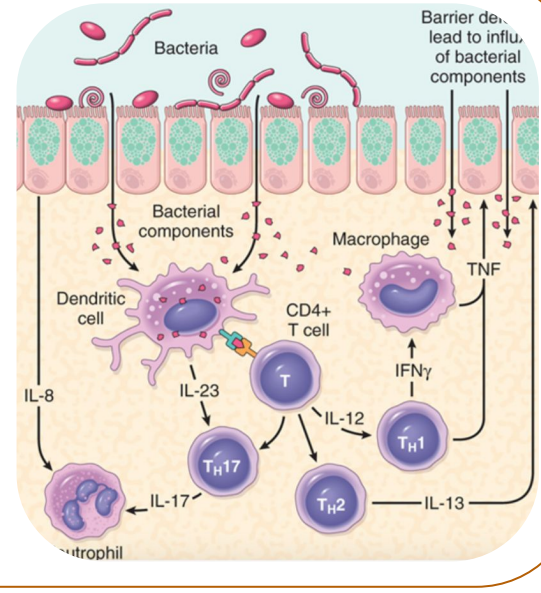
- Improved food storage conditions and decreased food contamination.
  - improved hygiene has resulted in inadequate development of regulatory processes that limit mucosal immune responses early in life.
  - As a result, exposure of susceptible individuals to normally innocuous microbes later in life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

There is inadequate development of regulatory process that limit mucosal immune response early in life (children are less exposed to antigens due to the hygiene areas which elicits an immune reaction when they get exposed to it later in life) . But people in non-hygienic areas won't develop any excessive immune reaction due to the early exposure to these antigens .

Pathophysiology

1. **Defects in host interactions with intestinal microbes**
2. **Intestinal epithelial dysfunction** (There's some epithelial dysfunction that allow the products of these bacteria to go into the lamina propria & induce an immune reaction)
3. **Aberrant/exaggerated mucosal immune responses.**
4. **altered composition of the gut microbiome** leading to exaggerated proliferation of T lymphocytes & production of cytokines which exaggerate the injury of the mucosa

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



Genetics:

- Risk for disease is increased when there is an affected family member
  - in Crohn disease, the concordance rate for monozygotic twins is approximately 50%.
  - By contrast, concordance of monozygotic twins for ulcerative colitis is only 16%, suggesting that genetic factors are less dominant in this form of IBD
- So, genetic factors are less dominant in ulcerative colitis the CD

First: 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 intracellular pathogens

THEORY

Less effective at recognizing and combating luminal microbes

Abnormal intestinal epithelial tight junction barrier function

↓

Transepithelial flux of luminal bacterial components activates immune responses

Mucosal immune responses.

Immunosuppression is the mainstay of IBD therapy.

INFLAMMATION

Clinical features

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

Colon	Small intestine	Extraintestinal manifestations
Bloody diarrhea, Tenesmus (feeling of open the bowel frequently)	Abdominal pain, Intestinal obstruction (due to fibrosis) , Steatorrhea (due to malabsorption)	Arthritis, Eye manifestation, Skin manifestation

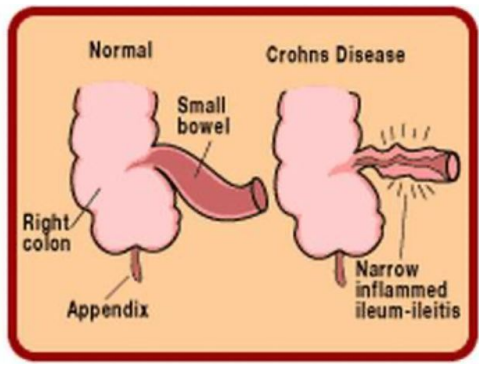
Crohn's disease

Definition

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.

Sites of involvement

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

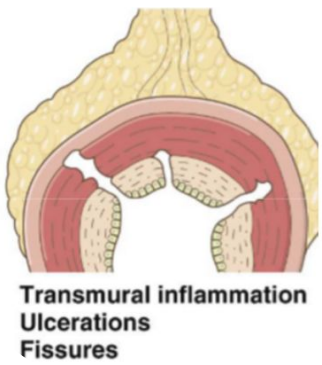


Clinical features

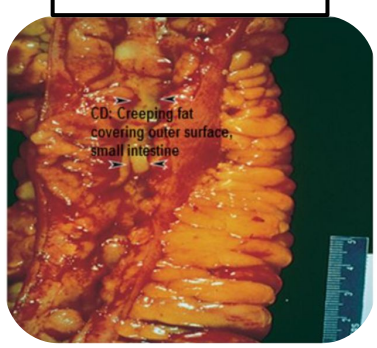
- Any age but has its highest incidence in young adults (11-35 years old) .
- Extremely variable clinical feature.
  - ➢ **Acute phase:** fever, diarrhea, and right lower quadrant pain may mimic acute appendicitis.
  - ➢ **Chronic disease:** remissions and relapses over a long period of time.
  - ➢ In long-standing crohn's disease, thickening of the intestine may produce an ill defined mass in the abdomen.

Gross appearance

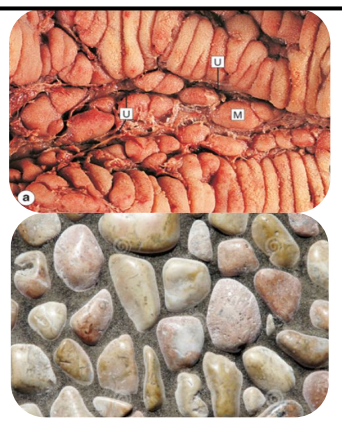
- Involvement is typically segmental, with **skip areas** of normal intestine between areas of involved bowel. Also called "regional enteritis"
- Transmural inflammation will repair by Marked fibrosis causing luminal narrowing with intestinal obstruction.
- **Fissures "deep fissuring ulcers"**: deep 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 (from bowel to : urinary bladder, vagina or skin)
- **Mucosa**: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa. This results in the typical **cobblestone effect/appearance.**
- **Fat**: In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (**creeping fat**).



creeping fat



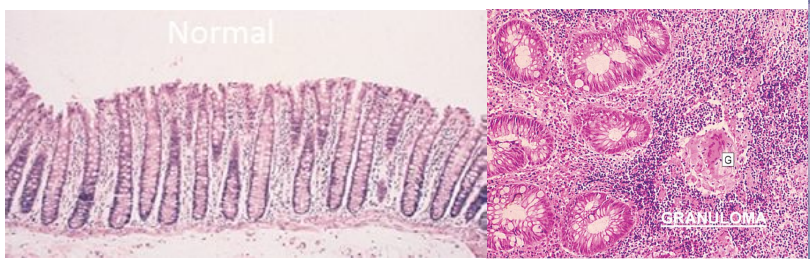
cobblestone effect



Microscopic features

1. Distortion of mucosal crypt architecture with mucosal inflammation.
2. Transmural inflammation.
3. Epithelioid granulomas [60%] "collection of epithelioid histiocytes"

- Fissure-ulcers and fistulas can be seen microscopically.



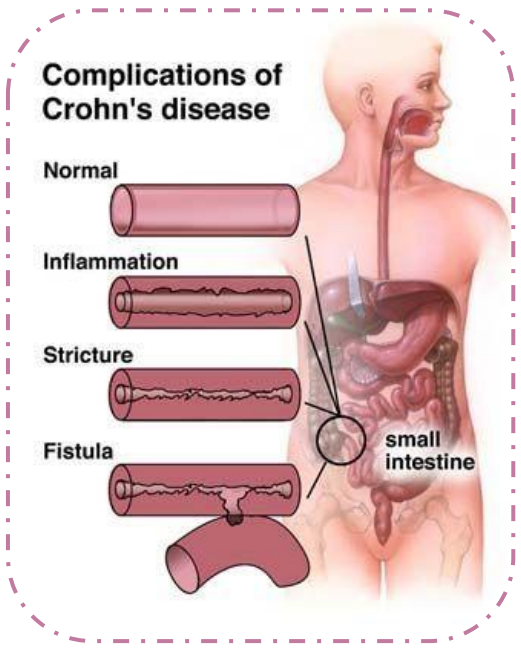
Clinical findings

(Only found in the girl's slides)

- Recurrent right lower quadrant(place of appendix) colicky "مغص" pain (obstruction) with diarrhea and weight loss
- Bleeding occurs only with colon or anal involvement (fistulas; abscesses)
- Aphthous (superficial) ulcers in mouth
- Extragastrointestinal: erythema nodosum (nodules in the skin), sacroiliitis (HLA-B27 association) (inflammation of the joint between sacrum & ileum), pyoderma gangrenosum, iritis (CD > UC), primary sclerosing cholangitis (UC > CD)

Complications

1. Intestinal obstruction (fibrosis & narrowing of lumen)
2. Malabsorption (steatorrhea, vitamin & iron deficiency)
3. 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. (between the bowel & bladder)
   -Enterovaginal fistulas produce a fecal vaginal discharge. (between the bowel & vagina)
   -Peritonitis
4. Extraintestinal manifestations (arthritis and uveitis)
5. Slight increased risk of development of carcinoma of the colon - much less than in ulcerative colitis.



Practice 1

Feature	Inflammatory diseases
1. Fistula formation	A. Crohn's disease
2. Transmural inflammation	
3. Granulomas	
4. Deep ulcers (fissure)	B. Ulcerative Colitis
5. Dysplasia is common	
6. Carcinoma is more common (10%)	

Answer key:
1;A 2;A 3;A 4;A 5;B 6;B

Ulcerative Colitis

Definition

- Chronic relapsing ulcero-inflammatory disease of undetermined etiology.
- Most common inflammatory bowel disease.
- Ulcerations of the colon are in continuity (non-segmental) unlike Crohn's disease
- 20- to 30-year age group but may occur at any age.

Sites of involvement

- Ulcerative colitis is a disease of the rectum, and the colon.
- Rectum is involved in almost all cases (it starts at the rectum then extend proximally)
- The disease extends proximally from the rectum in a continuous manner without skip areas, it may involve a part or the whole colon "pancolitis".
- The ilium is not involved as a rule
- Lesion is limited to the mucosa, ulcers are wide based but not deep penetrating, the normal mucosa between them appear like polyps "pseudopolyps"

Clinical features

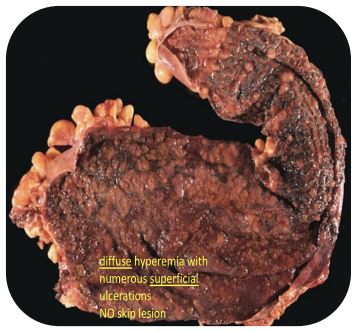
- In the **acute phase** and during relapse, the patient has fever, leukocytosis, lower abdominal pain, bloody diarrhea and mucus in the stool (dysentery).
- The disease usually has a **chronic course**, with remissions and exacerbations.

Etiology

- The cause is **unknown**
- Antibodies that cross-react with intestinal epithelial cells and certain serotypes of Escherichia coli (normal flora) have been demonstrated in the serum of some patients with ulcerative colitis.
- For unclear reasons, research suggests that smoking increases the risk of Crohn's disease but reduces the likelihood of ulcerative colitis.

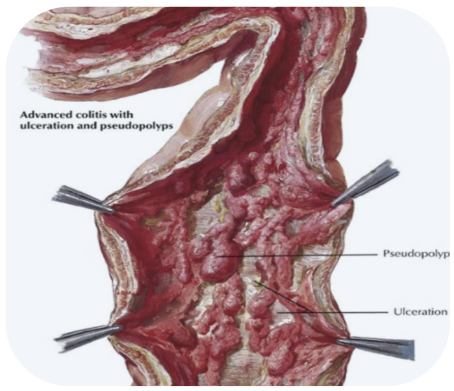
Gross appearance

Involves mainly the mucosa (diffuse hyperemia with numerous superficial ulcerations in the acute phase)



Pancolitis "the whole colon is involved" with hyperemia, superficial ulceration & hemorrhagic areas but no skip areas (**toxic megacolon**)

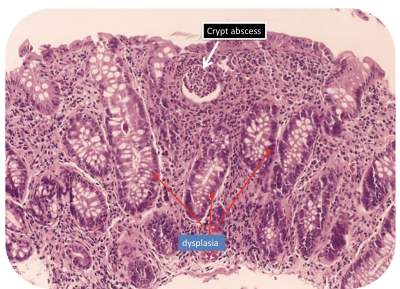
The regenerated or nonulcerated mucosa may appear polypoid (inflammatory **pseudopolyps**) in contrast with the atrophic areas or ulcers.



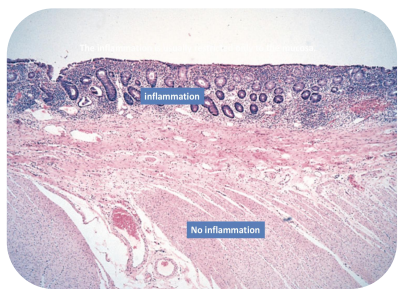
Microscopic features

- The inflammation is usually restricted to the mucosa.
- Active inflammation correlates well with the severity of symptoms.

In the active/acute phase....neutrophils (Cryptits, crypt abscess)



In the chronic phase.....crypt atrophy and distortion (crypts are short & dilated)



Clinical findings	1. Recurrent left-sided abdominal cramping with bloody diarrhea and mucus 2. Fever, tenesmus, weight loss 3. Extra-gastrointestinal: primary sclerosing cholangitis (UC > CD), erythema nodosum, iritis/uveitis (CD > UC), pyoderma gangrenosum, HLA-B27 positive arthritis. 4. p-ANCA antibodies >45% of cases 5. **Toxic megacolon** (dilated colon, removed by surgery) (up to 10% of patients). Mortality rate 50%.
Extraintestinal manifestations	1 Arthritis 2 Uveitis 3 Skin lesions (pyoderma gangrenosum), 4 Sclerosing cholangitis (fibrosis around bile ducts), leading to obstructive jaundice.
Complications	**Acute phase** 1. Severe bleeding, fever & abdominal pain 2. Toxic megacolon (dilation of the colon, with functional obstruction) **Chronic ulcerative colitis** "girls' dr: Very important مافيه اختبار يخلو منها" 1. **Increase risk of developing colon carcinoma (ADENOCARCINOMA)** 2. The presence of high-grade dysplasia in a mucosal biopsy imposes a high risk of cancer and is an indication for colectomy.

Practice 2

Feature	Inflammatory diseases
1. Colon only	A. Crohn's disease
2. Diffuse involvement of mucosa	
3. Superficial ulcers	
4. Any part of the GIT	B. Ulcerative Colitis
5. Skip areas of normal mucosa	
6. Mucosal inflammation only	

Answer key:
1;B 2;B 3;B 4;A 5;A 6;B

Summary

	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

QUIZ!

MCQs

01 | A 46 years old male complaining of bloody diarrhea and abdominal pain for the past month. Colonoscopy shows ulceration and edema in some areas while other areas are normal. Mucosal biopsy showed focal mucosal inflammation, with non caseating granuloma, crypt distortion and crypt abscess. What is the diagnosis?			
A) Ulcerative colitis	B) Crohn's disease	C) Adeno-carcinoma	D) Hyperplastic polyp
02 | Which one of the following is a characteristic for Crohn's disease more than ulcerative colitis?			
A) Epithelial dysplasia	B) Rectum involvement	C) Deep mucosal ulcer	D) Pseudo-membranous polyps
03 | Strictures are common complication of which of the following?			
A) Crohn's disease	B) Ulcerative colitis	C) both	D) none of them
04 | Ulcerative colitis is characterized by			
A) Segmental areas	B) Discontinuous segments	C) Continues segments	D) Skip areas
05 | A patient has severe arthritis involving the lower back. Before making a diagnosis of ankylosing spondylitis, the patient should be questioned about which of the following diseases ?			
A) Carcinoid syndrome	B) Celiac disease	C) Crohn's disease	D) Peptic ulcer
06 | Which Inflammatory bowel disease mimics appendicitis ?			
A) Crohn's / chronic disease	B) Crohn's / Acute phase	C) Ulcerative colitis	D) Acute pancreatitis

MCQs Answer key	01	02	03	04	05	06
	B	C	A	C	C	B

" اللهم علمنا ماينفعنا ، وانفعنا بما علمتنا وزدنا علما يارب العالمين "

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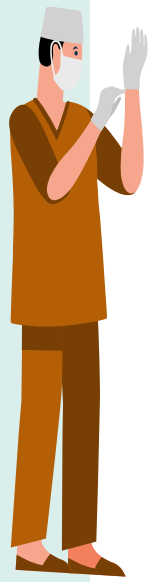

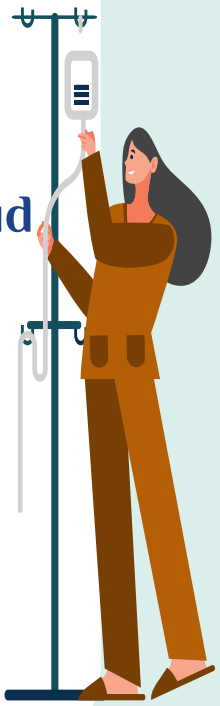

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