

13.10.2021

5th Lecture

Pathology - GI

Intussusception

- * Bowel is tube-like and a hollow organ
- * Intussusception process is similar to "telescoping" ^{"triggering factor"}
- * Due to some reasons, a leading point or mass (polyp, tumor, ...) induces peristalsis → increase in peristalsis → the segment telescopes into the immediately distal segment

- can be folded or multilayered → all that leads to obstruction

→ very common among children (< 2 years) & infants

- In elder people usually tumor, polyp or any mass lesion

→ Reasons: types of infections → prominence of MALT
& vaccines

↳ bulging → Mass
↓
telescoping

* If there's no clear reason for the disease it's called **idiopathic**

Clinically:

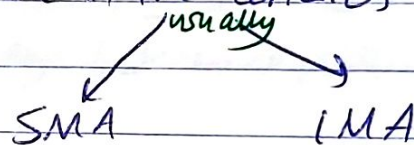
- Barium enema → شلج
- شلج
- in most cases → surgery is required

Ischemic Bowel disease

- A common disease among elderly
- Related to / most common reason: atherosclerosis

atherosclerosis: atheroma plaques → sometimes thrombosis happens

- build fast or slow according to case
- parts of thrombus can fall apart and can move in the arterial system until they find a new place in the arteries



- sometimes in the heart itself atheroma plaques or valvular lesions or thrombus in atria can fall apart → leading to embolism
"thrombo embolism"

- according to its degree & time needed to form ~~obstruction~~ / blood supply compromise
- If fast and in a short time → predict ischemia & infarction in bowel
- If slow (slowly growing) → Collateral in blood supply & anastomoses in vascular system (especially arterial)

SMA branches to reach to SI, wide part of colon - nearly to splenic flexure

IMA branches reach → Descending colon, Sigmoid, Rectum (waves)

⇒ Their branches are characterized by making loops that allow them to get blood supply from various other branches (other sources)

↳ Obstruction would not cause a serious problem

Vasa recta from arbor → أفرع يدخلها شرياني جدار القولون
وذلك يتفرع إلى ما قبل (capillaries)

↳ There are different anastomoses between these branches

↳ the lower part of rectum (supplied by internal iliac a.) or coccygeal

→ There are also other anastomoses as in celiac trunk, SMA

Infarction → mucosal infarction
 ↳ mural infarction (mucosa & sub mucosa)
 ↳ transmural " (if muscularis propria also)
 usually in acute cases - fast ones

* : Thrombus can also happen in veins ^{dilated thin wall}

blood flow can be slow sometimes due to compression on P.V, problem in coagulation system

- * Thrombus in vein is different, at first blood supply will continue normally and ischemia isn't easy to develop, but if obstruction holds on $\rightarrow$ blood flow will be disabled,

$\hookrightarrow$ has many reasons: sclerosis, tumor around P.V

- * Ischemia can happen without obstruction, due $\Rightarrow$

إفلال في مرور الدم

- cardiac failure

- shock

- some drugs

watershed zones $\leftarrow$

for ex. at SMA end (flexure) & inferior starts ^{splenic}

regions that receive dual blood supply from most distal branches of 2 arteries

at this point $\rightarrow$ slow blood flow $\rightarrow$ possible for ischemia

Obstruction due Ischemia happens in two phases

① Oxygen deprivation $\rightarrow$ reperfusion due ^{مزيد في القرب}

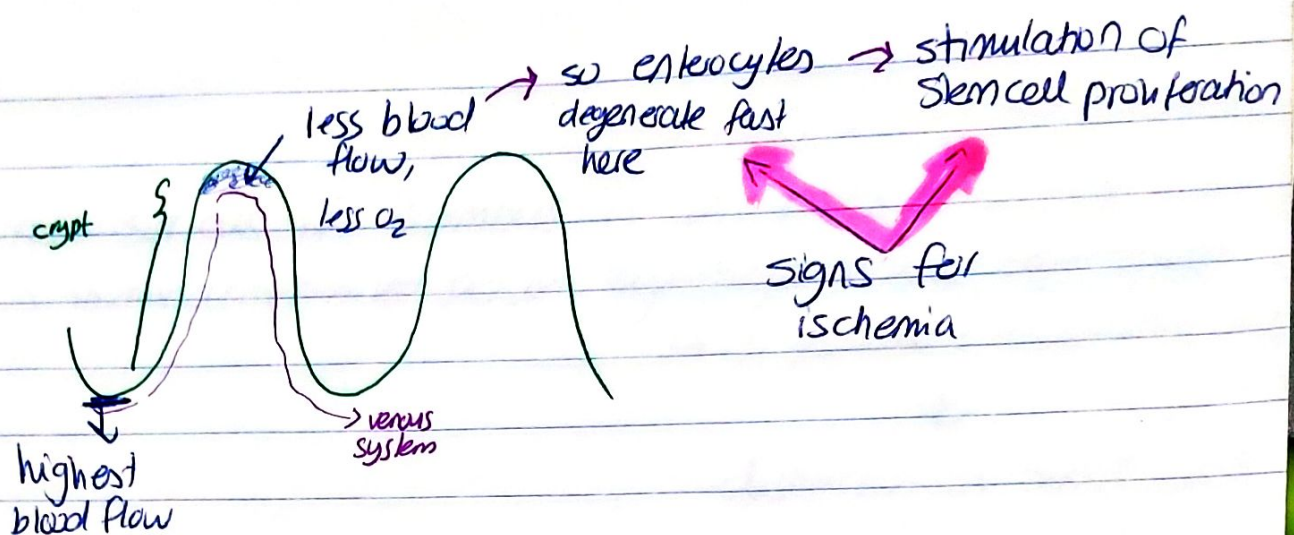


thrombus goes away and blood flow comes too fast $\rightarrow$ destruction also called "reperfusion injury"

②

أسبابها $\downarrow$

- ischemia in tissue ($O_2 \downarrow$)
- $\hookrightarrow$ free radical affect badly
- calcium deposition
- mediators
- neutrophil leukocytes
- microorganism Proliferation



- most common places for ischemia is the colon as watershed zones. Ischemic part is removed surgically
- **macroscopically**
 - looking of a healthy bowel with enough O_2 disappears and turns dark, bluish
 - edema
 - mucosa dark red and hemorrhage, lumen full with blood
 - venous thrombosis sometimes visible
- **Microscopically**:
 - ischemia leads to infarction

Infarction types

Coagulation type infarction:

Same cell is found but with lost nucleus (destroyed) but shadow of cell is found.

- ↳ contaminated and susceptible for bacteria
- ↳ proliferation
- ↳ enters wall & causes more destruction, especially in transmural infarction

* more serious if thrombus is in field of SMA

other reasons for ischemia → * in immunocompromised persons Cytomegalovirus infection
↳ its favourite: endothelial cells



destruction in small vessels

↓
local ischemic changes

* Radiation → "radiation related-enterocolitis"

* Necrotizing enterocolitis

Angiodysplasia

disease that came up due to anatomy of bowel:

- Organ has continuous peristalsis
- distended by material → distention + peristalsis → pressure on B.V

* There's no problem in Arteries, due to "waves" and lots of anastomoses

* But in veins not; they have a thin wall^{& full lumen}, and it's easy for an obstruction to happen → dilatation
↳ tortus in B.V

↳ microscope II C3

thick wall, dilated, congested vein

↳ injury → massive bleeding, especially elderly

- most common place: cecum → 3/4s of cecum → more filled → wall tension ↑

Malabsorption

Failure of absorbance of various components of food material

leading to steatorrhea → greasy stool, with high fat contents

most common reasons:

- pancreatic insufficiency due to chronic pancreatitis
- and sometimes in females: gallbladder stones
- celiac disease
- Crohn disease
- Graft versus host disease (GVH) after bone marrow transplantation (reaction happens)

Four places in where a defect leads to malabsorptions

① Intraluminal

علة اليع في المساحة بين الخلايا
التي تحدث في الـ stomach & pancreas

② Terminal digestion

Brush border, glycocalyx: peptidase^x → A.A
, disaccharidases^x

③ transepithelial transport

علة اليع في جدار الـ epithelium

④ Lymphatic system

lymphatic vessels → lacteal → transports fat components to blood

Malabsorption $\rightarrow$ more food that $\rightarrow$ defecation $\uparrow$ $\rightarrow$ diarrhea stays

Diarrhea:

increase in frequency or amount of stool or increase in fluidity of stool.

$\Rightarrow$ to diagnose diarrhea correctly, a proper history taking is required, due to differences among people

Categories:

- **Secretory**: secretion of fluid & electrolyte, but isotonic (same osmolarity of plasma)

related to food intake { - **Osmotic**: especially in lactose intolerance or lactose deficiency
lactose stays in stool

- **malabsorptive**: Problem in absorbance (as panc. deficiency)

- **Exudative**: related to infections $\rightarrow$ stool has components of inflammatory process

Cystic Fibrosis

- very rare disease $\frac{Cl}{HCO_3}$ due to
→ defect in electrolyte and fluid transport

- * secretion is important for intraluminal transport, as digestive & respiratory system
- * sometimes the pancreatic canals - if a defect happens in their amount of electrolyte & fluid - → a viscous material will be build that does obstruction

↓
chronic pancreatitis (التهاب البنكرياس)
↓
atrophy

→ cystic fibrosis transmembrane conductance regulator (CFTR)
(defect in this protein)

- 80% of patients get pancreatic insufficiency
↓
malabsorption

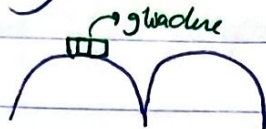
Celiac disease

- immune system related disorder triggered by protein containing diet (in some predisposed people)
↳ wheat rye and barley

- 0.5% - 1%

Pathogenesis:

Protein is partly digested resulting in gliadine



IL5 stimulates cytotoxic T Lymphocytes → does expression to natural killer G2D (NK G2D) → acts as a receptor to MIC-A (on enterocytes) → T Lymphocytes will find ligand specific for receptor and will bind to it → destruction of enterocytes (Barrier) → more gliadine will enter → high amounts of gliadine → result: tissue transglutaminase tTG, which does deamination.

The deaminated glutamine is a stimulator for antigen-presenting cells (type of macrophages) APC for persons that have HLA (DQ2 or DQ8) antigen

autoimmunity → immunosystem ↓
relativ disease

⇒ if people have that antigen (HLA...), deaminated gliadine will be presented to T-lymphocytes that in order will secrete cytokines as interferon gamma $IFN\gamma$ → more destruction in epithelial layer

إذا واصلت (لها) وفتة خبث جبري يـ

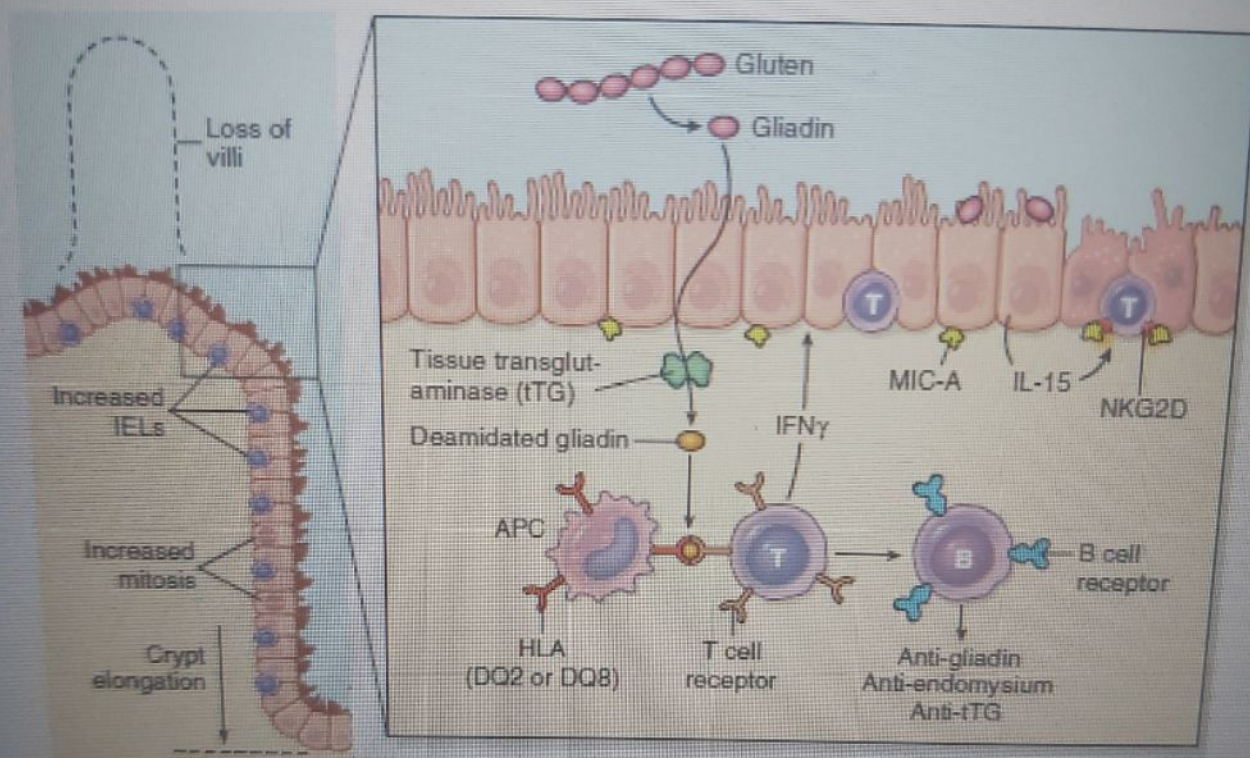


Figure 17.26 The left panel illustrates the morphologic alterations that may be present in celiac disease including villous atrophy, increased numbers of intraepithelial lymphocytes (IELs), and epithelial proliferation with crypt elongation. The right panel depicts a model for the pathogenesis of celiac disease. Note that both innate (CD8⁺ intraepithelial T cells, activated by IL-15) and adaptive (CD4⁺ T cells and B cells sensitization to gliadin) immune mechanisms are involved in the tissue responses to gliadin.

The presence of HLA antigens explains half of the cases, the other half goes back to polymorphism (meaning that people have thousands of various genes)

Clinical

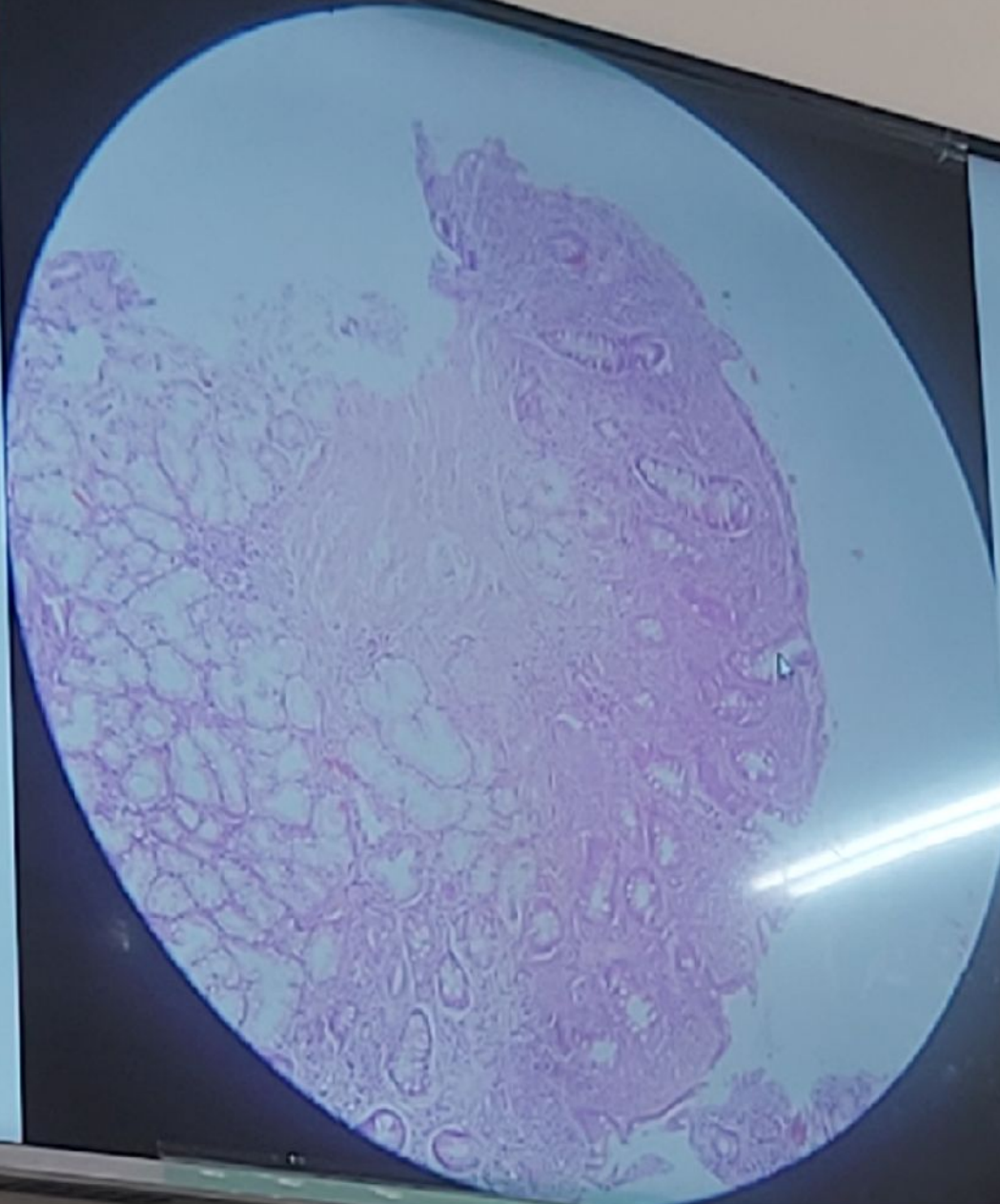
- 30-60 (in Gaza younger)

* malabsorption → loss of weight

- silent celiac: serology +, villus atrophy
- latent celiac: serology +, but no change in tissue
- Extraintestinal conditions: Aphthous stomatitis, short stature, anemia
- * usually tissue is taken from 2nd part of duodenum (biopsy)

Microscopically:

- villi projections are flat (villus atrophy)
 - Lymphocytes number amount increases
 - Lamina propria Populated by dense population of lymphocytes and plasma cells and inflammatory system cells
 - destruction of villus is characteristic → proliferation in stem cells → crypt hyperplasia
- * 10% of patients have a dermatologic disease called herpetiformis



celiac disease:

- villus atrophy
- dense population of lymphocytes
- crypt hyperplasia

Serological's

Anti tTG Ig A

Antibody Ig A

- * Patients have increased risk of lymphoma and adenocarcinoma

Lactase deficiency's

can be

congenital or acquired

↳ defect
in gene itself

↳ in adults due following or viral
infection

Irritable bowel syndrome

- Patients ~~say~~ = intermittent abdominal pain & bloating
- is often falsely diagnosed
- من مفردون يكون اول زحمة

⇒ Crohn disease & ulcerative colitis
related to many factors that promote diseases

- 1- Immunesystem
- 2- Environmental factor (microorganisms found in lumen)
- 3- Genetic predisposition

most commonly in rectal area (ileorectal)

Crohn disease

Inflammatory process related to environmental factors and genetic predisposition

- Patchy involvement (skip lesions), not only colon but from oral cavity to anal.
↳ inflammation leaves جدار → fistulas tract
- Transmural inflammatory process. Fistulation/Fistula common
↳ bowel & skin
↳ anal & perianal region

Ulcerative colitis

- characterized by that it affects only the colorectal part
- in vast majority → rectum is affected

Terminal - Mucosa only in inflammatory process

→ * Ulcerative proctitis → rectum only

→ * Ulcerative proctosigmoiditis → rectum & colon
↳ sigmoid

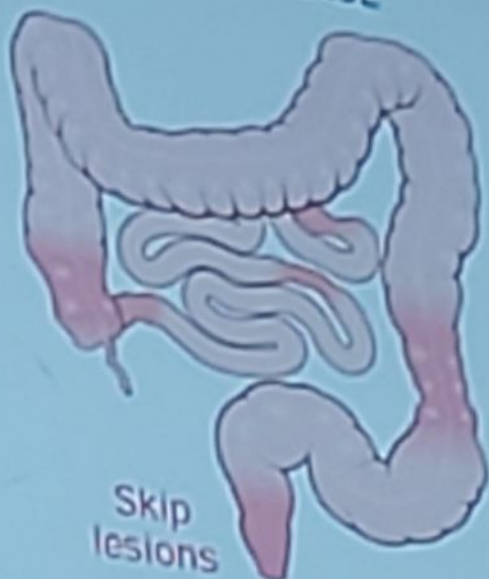
→ * Ulcerative pan colitis → all the colon

→ * Backwash ileitis → involves ileum (terminal)

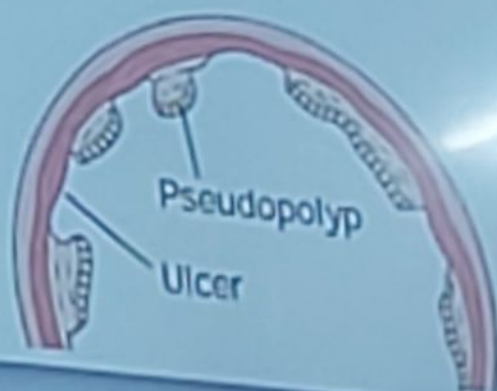
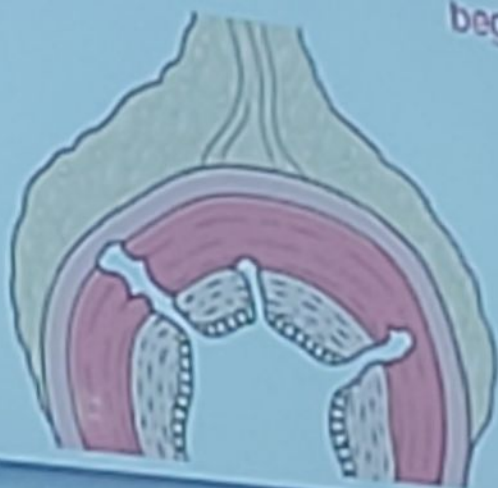
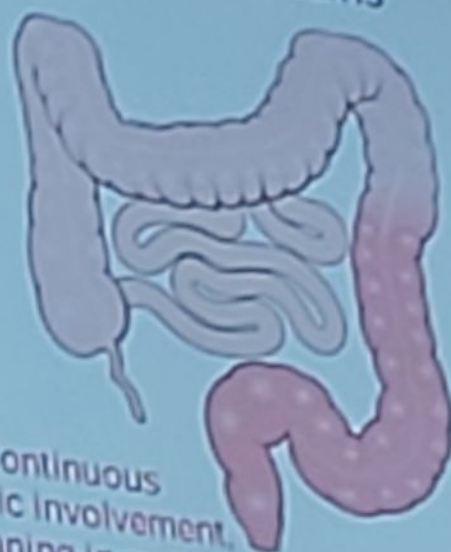
Inflammatory bowel disease

- Crohn or Ulcerative colitis is meant here
- detected relatively early in age (in teenage)
- related to high socioeconomic level
- Hygiene theory: immune system isn't anymore exposed to same amount of antigenic stimulation as in the past. → some regulatory processes ↓
- food preservative theory: may trigger some epithelial infection leading to reaction

CROHN DISEASE



ULCERATIVE COLITIS



Pathogenesis

⇒ it's a combination of immun^①system regulating mechanism and micro^②b interaction (flora & person) and epithelial barrier^③ function

↳ $\text{GIT} \rightarrow \text{Mucosal Immune System}$

Function of epithelial barriers:

1) separation between two planes

+++ $\Rightarrow$ genetic predisposition^④ (environmental factors have also an important role)

Mucosal immunity

(mucosal environment and different mediators)

- HLA and cytokines (proinflammatory, IFN- γ , anti-inflammatory, IL-10)
- TH1 Polarization Present in both
- TH2 activation in UC
- TH17 signaling in both

* Autophagy and cellular stress responses

↳ digestion of self components of the cell. Happens when a defect in the environment (blood supply, nutrients) $\rightarrow$ shrinks its size to fit environment $\rightarrow$ digests parts of its own components.

↳ related with phagolysosome ATG16L1

* Host microbial interactions

* relation between M.O in lumen & immun^①system (local, general)

* very rare cases in newborns (gene mutation related problem)



التهاب القولون
النشيط

Crohn disease (more specific)

- Most commonly ileocecal area
- 40% limited to small intestine
- 30% SI and colon
- the remainder only colon

Macroscopically: (Gross)

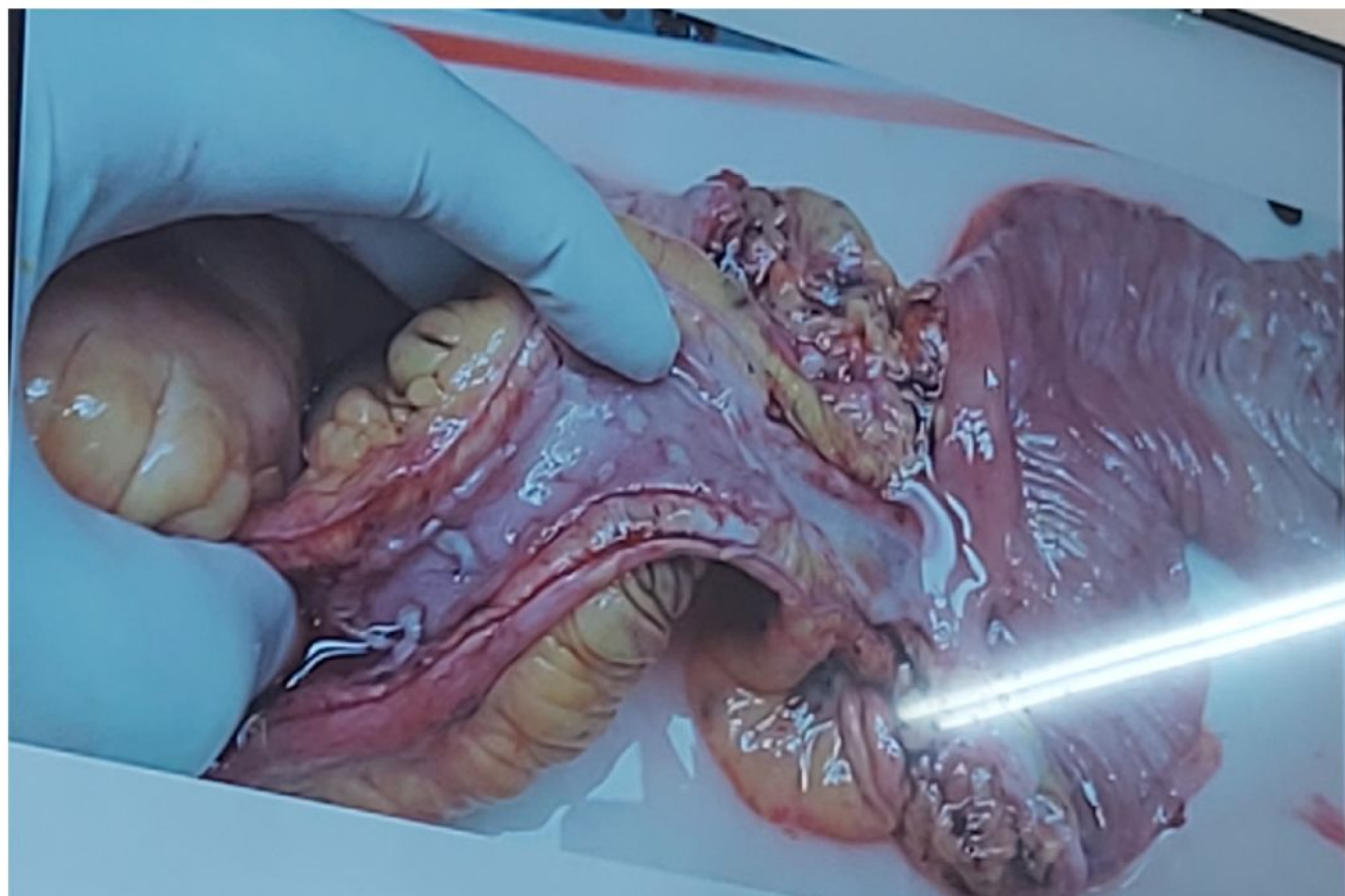
- aphthous ulcer
- narrowing of lumen (stricture)
- "creeping up" Fat of mesentery encloses all circumference of small bowel
- "Cobble-stone appearance": parts have ulcerations, others not.
- Transmural → inflammation through all the wall
 - ↳ Fistula, abscess
 - ↳ usually in anal area

Microscopically

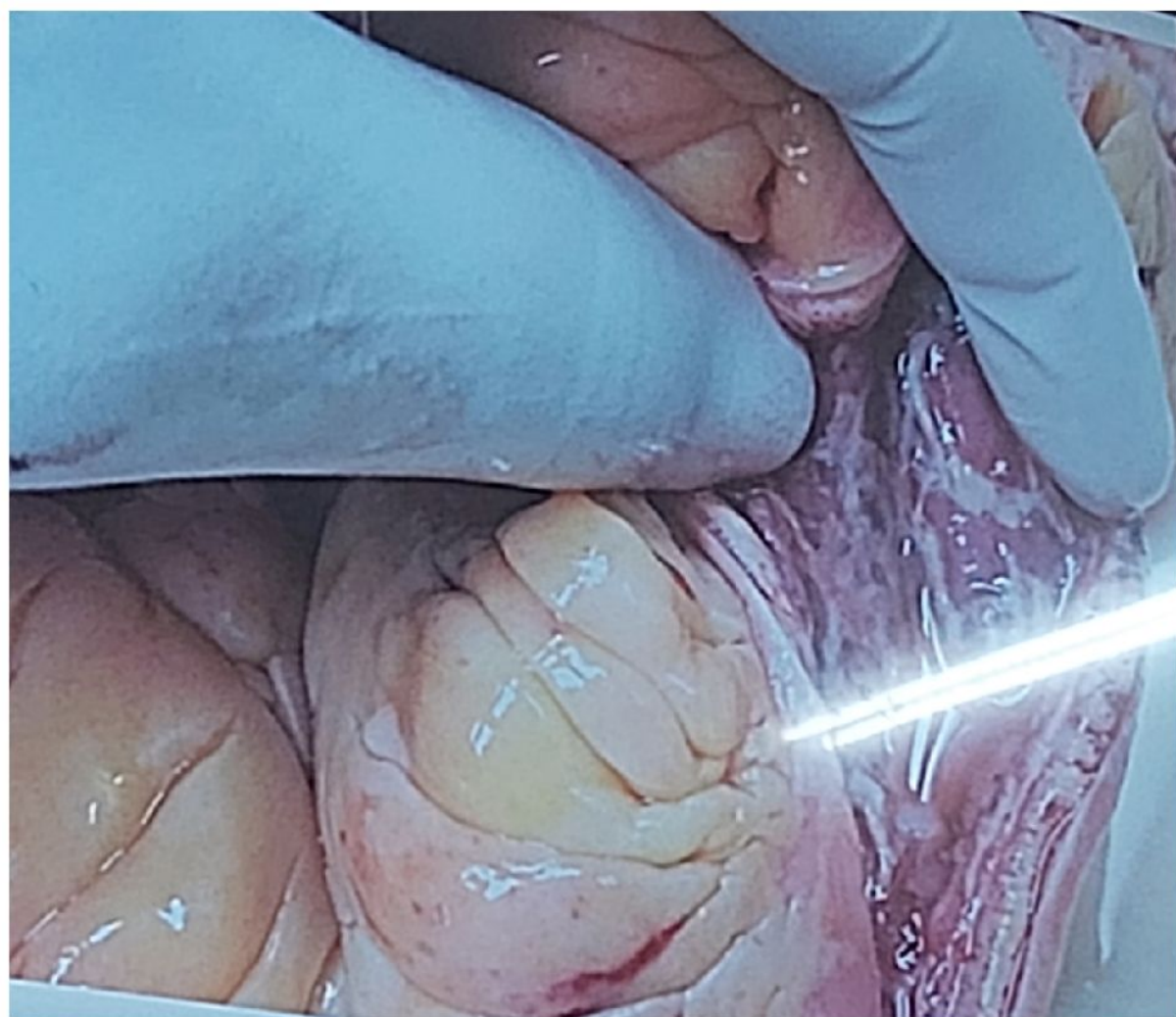
- Inflammatory process along all layers of bowel
- crypt abscess (neutrophil leukocytes collect in crypt)
 - ↳ also seen in ulcerative colitis

- metaplasia: - pseudopyloric metaplasia

immune system ↓ op ↓ [Paneth cell] metaplasia (always not found in left colon)
↳ so, if found → metaplastic change and normally found in Rt colon



Crohn diseases



- granuloma: important characteristic for Crohn
- بوجودها يمكن تشخيص المرض، لكن معاكاً مرتابين أكثر
- found in 35-50% of cases

Clinicals

- Extraintestinal manifestations (as skin)
- "مشى موضوعيا"

- Risk of colonic adenocarcinoma, whether ulcerative or Crohn disease, especially ulcerative colitis

Ulcerative colitis (more specific)

- most importantly must be: rectum affected
- (plus other parts can be)

• backwash ileitis

or
inflammatory
pseudopolyps

• pseudo polyps/mucosal bridges

→ new formed blood vessels

↳ not real polyp → ulceration, granulation tissue, inflamm. cells + edema

↳ polyps can fuse together → bridge

↳ toxic megacolon → rupture (perforitis)

Microscopically

- inflammatory process dense inflammatory process (mucosa only)
- histologically serious condition
- it's a chronic disease (fibrotic mucosa) distorted

* hard to differentiate between Crohn & ulcerative

Clinically

- severe pain, bloody diarrhea + improves with smoking

ulcerative colitis



intermediate colitis: Colitis indeterminate
↳ can be overlap clinically and endoscopically

* Dysplasia → related to increase in adenocarcinoma, as mentioned
↳ regular checkup is important

Diversion colitis "أكل" (3)

↳ after operations specific for digestive system or colon
a blind loop results → empty and has no purpose
↳ an inflammatory process can occur here

Sigmoid diverticular disease

Diverticulum: outpouching ⇒ complications of diverticulum: obstruction
↳ perforation
↳ diverticulitis
↳ abscess (3)

↳ **True** = as Meckel diverticulum

2-3 cm patent (open) can contain stomach mucosa
leading to peptic ulcer + ectopic pancreatic tissue

↳ **Pseudo** = outpouching of mucosa • vasa recta enters
at specific place in colon

most favorable: sigmoid or left colon

↳ longitudinal layer ✓
↳ circular layer not found on all
colon

• Some parts have muscularis propria
only

Heba Edwan

