Pathology

# Pathology sheet

DONE BY:

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Inflammatory Bowel Disease &
Ischemic bowel disease

These two diseases are very important in the clinical so you have to be familiar with. so by the name of ALLAH we start:

Inflammatory Bowel Disease (IBD):

- The two disorders that comprise IBD are: ulcerative colitis
  
  Crohn disease

Both share some characteristic and differ in others, you have to know the characteristic for each one and how to differentiate between them.

<table>
<thead>
<tr>
<th>ULCERATIVE COLITIS</th>
<th>CROHN'S DISEASE</th>
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<tbody>
<tr>
<td>Mainly affect the colon and the rectum, usually starts in rectum (anus, mouth, esophagus, stomach, small bowel are NOT involved)</td>
<td>Can affect any part of the GI from mouth to anus.</td>
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<tr>
<td>Limited to the mucosa and submucosa</td>
<td>Transmural (usually). Involve mucosa, submucosa, and muscularis propria and can reach serosa.</td>
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<tr>
<td>Inflammation is continuous along the colon</td>
<td>Occurs in skip area (you will</td>
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found that some regions are involved and others are not.

**Morphologically:**

| Pseudo polyp in it is a main sign, because the inflammatory area become elevated. | Characterized by the presence of fissure (i.e.: breaks inside the lumen, unlikely those breaks may reach the serosa and cause perforation) |

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• 5:50 min
  
the distinction between ulcerative colitis and Crohn disease is based, in large part, on the distribution of affected sites and the morphologic expression of disease at those sites.

**Ulcerative colitis** is limited to the colon and rectum and extends only into the mucosa and submucosa.

**Crohn disease**, which has also been referred to as regional enteritis (because of frequent ileal involvement) may involve any area of the GI tract and is typically transmural.
• Epidemiology:

Ulcerative colitis and Crohn disease frequently present in the teens and early 20s, with the former being slightly more common in females (especially ulcerative colitis).

IBD is most common among Caucasians (white color people) and, in the United States, occurs 3 to 5 times more often among eastern European (Ashkenazi) Jews than the general population.
The hygiene hypothesis suggests that this increasing incidence is related to improved food storage conditions, decreased food contamination, and changes in gut microbiome composition. Apparently this results in inadequate development of regulatory processes that limit mucosal immune responses. This in turn allows some mucosa-associated microbial organisms to trigger persistent and chronic inflammation in susceptible hosts.

We can see that these diseases are most common in people with familial history of IBD. Therefore, it is very important to ask the patient he has a family history of IBD. As it is also important to know the immune response status for that patient.
and if he has a defect in the epithelial barrier, which can greatly affect the development of IBD.

10:36
for unknown cause it has been found that the patient with IBD has developed a problem in the immune system; immunosuppressor decreased and immunoactivator increased so, we have excessive immune activation for genetic reasons and so one of the most important drugs we give to the patient is the immunosuppressor therapy, In order to decrease the activation of immunity.

• Pathogenesis:

Although precise causes are not yet defined, most investigators believe that IBD results from the combined effects of:

Alterations in host interactions with intestinal microbiota,

Intestinal epithelial dysfunction,

Aberrant mucosal immune responses,

Altered composition of the gut microbiome

• Genetics. There is compelling evidence that genetic factors contribute to IBD. Risk of disease is increased when there
is an affected family member. Genetic factors are more dominant in Crohn disease.

3 genes strongly associated with Crohn disease: NOD2, ATG16L1, and IRGM.

These genes involved in recognition and response to intracellular pathogens

- **Mucosal immune responses:** it is clear that deranged mucosal immune activation and defective immunoregulation contribute to the development of ulcerative colitis and Crohn disease.

Immunosuppressive agents remain the mainstay of treatment for these conditions.

- **Epithelial defects:** Defects in intestinal epithelial tight junction barrier function

11:30

: pathogenesis of bone disease 

1. Usually we have normal flora but some condition, lead to change in these pathogens in colon or in any elsewhere in the GI , that make the patient more susceptible .
2. And cause destruction of the mucosal barrier
3. Bacterial component influx to the lamina propria where the innate immune system is
4. Innate system become activated now (i.e.: the first line of the protective mechanism for any disease that differ from adaptive one

5. Once bacterial components bind to the innate system the patient that was already susceptible for IBD will have a chronic inflammation

We are going to talk about chron disease now:

In books, you'll read another name for crohn disease called regional ileitis which named so because this disease occur as terminal ileitis inflammation and it occurs as a skip
region (some area are involved, others are NOT) involved areas are depressed and non-involved areas are elevated. Therefore, we say that Crohn disease has cobblestone appearance.

- Crohn disease may occur in any area of the GI tract, but the most common sites involved at presentation are the terminal ileum, ileocecal valve, and cecum.
- Disease is limited to the small intestine alone in about 40% of cases; the small intestine and colon are both involved in 30% of patients; the remainder have only colonic involvement.
- The presence of multiple, separate, sharply delineated areas of disease, resulting in skip lesions, is characteristic of Crohn disease and may help in the differentiation from ulcerative colitis. Sparing of interspersed mucosa, a result of the patchy distribution of Crohn disease, results in a coarsely (خشن) textured, cobblestone appearance in which diseased tissue is depressed below the level of normal mucosa.

The earliest lesion called aphthous ulcer.

*aphthous ulcer* إنها لو ظلت أكثر من 10 أيام underlying pathology cause ومنهم كان الـ Crohn disease ومنها إنها تعتبر من الـ fistula complication of Crohn disease ومن التي تعتبر من الـ fistula* أو fissure* والمضايجات أيضًا عنا الـ perforation

*fistula: which is a connection between two followed organs lined by epi- cells, and it is one of the most common complications.
Histologically, we see dispersed architecture of GI, fibrosis, Glands abnormal in shape, glands have branches, some drop of gland & most important, in 35% we see non-caseating granuloma that distinguish it from the granuloma of TB

- **Fissures** frequently develop between mucosal folds and may extend deeply to become **fistula** tracts or sites of **perforation**.
- The **intestinal wall is thickened** and rubbery as a consequence of transmural edema, inflammation, submucosal fibrosis, and hypertrophy of the muscularis propria, all of which contribute to **striction formation**.
- In cases with extensive transmural disease, mesenteric fat frequently extends around the serosal surface (**creeping fat**)
Figure 17-35 Microscopic pathology of Crohn disease. A, Haphazard crypt organization results from repeated injury and regeneration. B, Noncaseating granuloma. C, Transmural Crohn disease with submucosal and serosal

Figure 17-34 Gross pathology of Crohn disease. A, Small-intestinal stricture. B, Linear mucosal ulcers, which impart a cobblestone appearance to the mucosa, and thickened intestinal wall. C, Perforation and associated serositis. D, Creeping fat.
From the Clinical Features:

- Diarrhea *(which called on and off) / (remission or relapsing found in all IBD)*. + malabsorption in both IBD but more in crohn because the small intestine here is also involved.

- Cigarette smoking is one of the factors that help showing the first presentation for the disease, unlike ulcerative colitis where cessation of smoking will trigger the first presentation.

- If the patient had developed fistula between bowel and urinary bladder he will have feces in the urea.

- Non-caseating granulomas, a hallmark of Crohn disease, are found in approximately 35% of cases.

- Clinical Features:
  - Diarrhea, fever, and abdominal pain *Periods of active disease are typically interrupted by asymptomatic periods that last for weeks to many months.*
  - Disease re-activation can be associated with a variety of *external triggers*, including physical or emotional stress, specific dietary items, and cigarette smoking.
  - nutrient malabsorption (small bowel disease)
  - Iron-deficiency anemia (colonic disease)
• Fistulae develop between loops of bowel and may also involve the urinary bladder, vagina, and abdominal or perianal skin.

• **Extra intestinal manifestations of Crohn disease:**
  - Uveitis: *inflammation in the eye, loss of vision may develop.*
  - Migratory polyarthritis: *first ly in one joint then appear in the other one, not specific for chron but for any autoimmune disease.*
  - Sacroiliitis
  - Ankylosing spondylitis,
  - Erythema nodosum: *skin lesion in the lower limb, inflammation of the subcutaneous part*
  - Clubbing of the fingertips,

Any of which may develop before intestinal disease is recognized.

Pericholangitis and primary sclerosing cholangitis occur in Crohn disease, but are more common in those who have ulcerative colitis.
21:30

Risk of colonic adenocarcinoma is increased in patients with long-standing IBD affecting the colon.
Anti-TNF antibodies have revolutionized treatment of Crohn disease, and other biologic therapies are becoming available.

Ulcerative Colitis
The disease in ulcerative colitis is limited to the colon and rectum.
Common extra intestinal manifestations of ulcerative colitis overlap with those of Crohn disease (but Pericholangitis and primary sclerosing cholangitis are more in UC)

- Ulcerative colitis always involves the rectum *usually short area, called “ulcerative proctitis”*, and extends proximally in a **continuous fashion** to involve part or the entire colon.
- Disease of the entire colon is termed panniculitis, *and in this case malignancy incidence increase.*
- *Can the small intestine be involved? Yes, in some cases in backwash ileitis. But do not start in the small bowel.*
- The small intestine is normal, although mild mucosal inflammation of the distal ileum, termed *backwash ileitis*, may be present in severe cases of panniculitis.
- broad-based ulcers
- Isolated islands of regenerating mucosa often bulge into the lumen to create *pseudo polyps*, and the tips of these polyps may fuse to create **mucosal bridges**
• Inflammation and inflammatory mediators can damage the muscularis propria and disturb neuromuscular function leading to colonic dilation and toxic mega colon, which carries a significant risk of perforation.

Toxic megacolon occur because the inflammation reach the neuromuscular joint of the wall. Lead to destruction of the normal junction of the wall, which cause thining in the wall of the lamina propria and increase the risk of perforation.

crohn disease

mucosal bridges
We see drops of crypts in some area because of fibrosis, glands & bud of glands BUT WE DON’T SEE GRANULOMA.

For the treatment; surgical treatment for the ulcerative colitis "colectomy" can be done, while it can NOT be done in case of crohn disease ☹ coz we have a skipped area lesions, but can be done only in the case of complication (fistula, perforation & stenosis).
Clinical Features:

Ulcerative colitis is a **relapsing disorder**

Characterized by attacks of bloody diarrhea with stringy, mucoid material, lower abdominal pain, and cramps that are temporarily relieved by defecation. These symptoms may persist for days, weeks, or months before they subside.

The initial attack may, in some cases, be severe enough to constitute a medical or surgical emergency.

**Colectomy** effectively cures intestinal disease in ulcerative colitis, but extra intestinal manifestations may persist.

- The factors that trigger ulcerative colitis are not known, but infectious enteritis precedes disease onset in some cases.
- In other cases the first attack is preceded by psychologic stress, which may also be linked to relapse during remission.
- The initial onset of symptoms has also been reported to occur shortly after smoking cessation in some patients, and smoking may partially relieve symptoms.
Irritable Bowel Syndrome

History of diarrhea and abdominal pain with distension. However, it is NOT ORGANIC because it does not cause complications such as fistula, anemia, and other gastrointestinal symptoms. It is benign, benign, but can recur at any time. It is a non-organic disease that cannot be seen under the microscope.

Table 17-9: Features That Differ between Crohn Disease and Ulcerative Colitis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Crohn Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macroscopic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bowel region</td>
<td>Ileum ± colon</td>
<td>Colon only</td>
</tr>
<tr>
<td>Distribution</td>
<td>Skip lesions</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Stricture</td>
<td>Yes</td>
<td>Rare</td>
</tr>
<tr>
<td>Wall appearance</td>
<td>Thick</td>
<td>Thin</td>
</tr>
<tr>
<td><strong>Microscopic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation</td>
<td>Transmural</td>
<td>Limited to mucosa</td>
</tr>
<tr>
<td>Pseudopolyps</td>
<td>Moderate</td>
<td>Marked</td>
</tr>
<tr>
<td>Ulcers</td>
<td>Deep, knife-like</td>
<td>Superficial, broad-based</td>
</tr>
<tr>
<td>Lymphoid reaction</td>
<td>Marked</td>
<td>Moderate</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Marked</td>
<td>Mild to none</td>
</tr>
<tr>
<td>Serositis</td>
<td>Marked</td>
<td>Mild to none</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Yes (~35%)</td>
<td>No</td>
</tr>
<tr>
<td>Fistulae/sinuses</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perianal fistula</td>
<td>Yes (in colonic disease)</td>
<td>No</td>
</tr>
<tr>
<td>Fat/vitamin malabsorption</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Malignant potential</td>
<td>With colonic involvement</td>
<td>Yes</td>
</tr>
<tr>
<td>Recurrence after surgery</td>
<td>Common</td>
<td>No</td>
</tr>
<tr>
<td>Toxic megacolon</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

All features may not be present in a single case.
Irritable bowel syndrome (IBS) is characterized by chronic, relapsing abdominal pain, bloating, and changes in bowel habits.

IBS is currently divided into several subtypes, as defined by successive revisions of the Rome criteria:
- IBS with diarrhea (IBS-D),
- IBS with constipation (IBS-C),
- Mixed IBS (IBS-M)

Pathogenesis:
The pathogenesis of IBS remains poorly defined, although there is clearly interplay between psychologic stressors, diet, perturbation of the gut.
microbiome, increased enteric sensory responses to gastrointestinal stimuli, and abnormal GI motility. Other data link disturbances in enteric nervous system function to IBS, suggesting a role for defective brain-gut axis signaling.

stress conditions بما إنا حكينا إنها تكثر بالـ female وفي حالات الـ . brain-gut axis signaling لذلك لها علاقة إما بالـ أو علاقة بالـ أو علاقة بالـ serotonin receptors and cannabinoid receptors والتي مرة أخرى لها علاقة بالـ appetite , emotion and mood.

- Several candidate genes to IBS, including:
  Serotonin reuptake transporters,
  Cannabinoid receptors,
  TNF-related inflammatory mediators.
  5-HT3 receptor antagonists are effective in many cases of diarrhea-predominant IBS.
  Opioids and psychoactive drugs with anti-cholinergic effects are also commonly used to treat diarrhea predominant IBS.

A separate group of IBS patients, relate onset to a bout of infectious gastroenteritis, suggesting that immune activation or, alternatively, a shift in the gut microbiome.

- Clinical Features.
The peak prevalence of IBS is between 20 and 40 years of age, and there is a significant female predominance.
Other causes, such as enteric infection or inflammatory Bowel disease must be excluded.
IBS is not associated with serious long-term sequelae

- The **Rome IV criteria** for the diagnosis of irritable bowel syndrome require that patients have had:
  - recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with 2 or more of the following:
    * Related to defecation (may be increased or unchanged by defecation)
    * Associated with a change in stool frequency
    * Associated with a change in stool form or appearance

Ischemic Bowel Disease:
- The colon is the most common site of gastrointestinal ischemia.
The severity of vascular compromise, the time frame during which it develops, and the vessels affected are the major variables in ischemic bowel disease.

- Two aspects of intestinal vascular anatomy also contribute to the distribution of ischemic damage and are worthy of note:
  - Intestinal segments at the end of their respective arterial supplies are particularly susceptible to ischemia. These **watershed zones** include the **splenic flexure**, where the superior and inferior mesenteric arterial circulations terminate, and, to a lesser extent, the **sigmoid colon** and
rectum where inferior mesenteric, pudendal, and iliac arterial circulations end.

- Intestinal capillaries run alongside the glands, from crypt to surface, before making a hairpin turn to empty into the post-capillary venules. This arrangement makes the surface epithelium particularly vulnerable to ischemic injury, relative to the crypts. Organization of the blood supply in these patterns has advantages, as it protects the epithelial stem cells, which are located within the crypts and are necessary for recovery from epithelial injury.

- **Mucosal and mural infarctions** can follow acute or chronic hypoperfusion (non-occlusive), causes: cardiac failure, shock, dehydration, or use of vasoconstrictive drugs.

  Transmural infarction is typically caused by acute vascular obstruction (occlusive), causes: severe atherosclerosis, aortic aneurysm, hypercoagulable states, oral contraceptive use, and embolization of cardiac vegetation or aortic atheroma

- Intestinal responses to ischemia occur in two phases.
  - The initial hypoxic injury occurs at the onset of vascular compromise. While some damage occurs during this phase, the epithelial cells lining the intestine are relatively resistant to transient hypoxia.
  
  The second phase, reperfusion injury, is initiated by restoration of the blood supply and it is at this time that the greatest damage occurs. In severe cases this may trigger multiorgan failure. Leakage of gut lumen bacterial products into the systemic circulation, free radical production,
neutrophil infiltration, and release of additional inflammatory mediators

• Clinical Features:
  Ischemic disease of the colon is most common in patients older than 70 years of age, and occurs slightly more often in women.
  **Acute colonic ischemia** typically presents with sudden onset of cramping, left lower abdominal pain, a desire to defecate, and passage of blood or bloody diarrhea. ----- resemble acute abdomen.
  **Chronic ischemia**: episodes of bloody diarrhea interspersed with periods of healing------ resemble IBD
  Necrotizing enterocolitis (NEC): transmural necrosis-- neonates