

## Lec 9

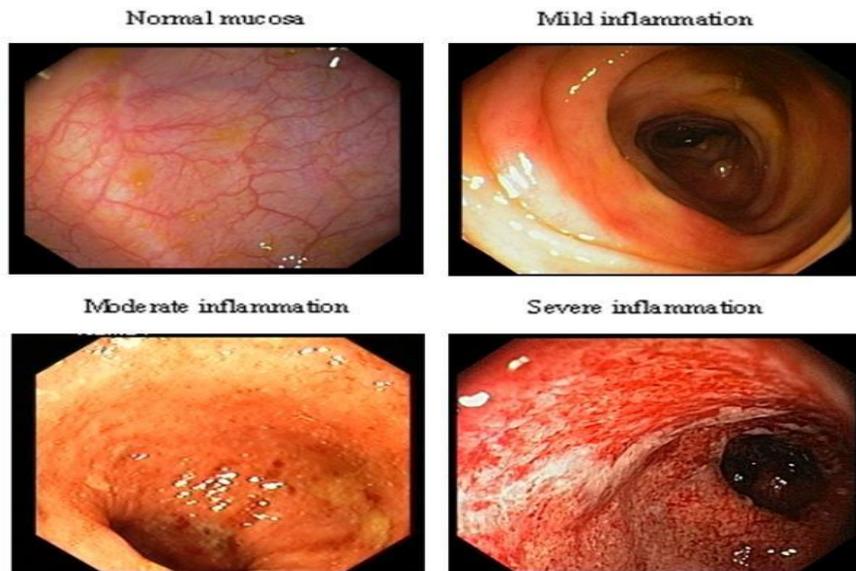
## *Inflammatory bowel diseases*

### *(1)Ulcerative Colitis*

**Ulcerative colitis** (colitis ulcers) (التهاب القولون التقرحي) (UC) is a form of inflammatory bowel disease (IBD). Ulcerative colitis is a form of colitis a disease of the intestine specifically the **large intestine or colon** that include characteristic ulcers or open area in the colon or open sores.

Because of the name, **IBD is often confused with irritable bowel syndrome (IBS), a troublesome (مزعج), but much less serious, condition.**

- Ulcerative colitis is however, believed to have **systemic etiology** that **lead to many symptoms outside the intestine**
- Ulcerative colitis has similarities' to Crohn's disease, another form of IBD.
- Ulcerative colitis is an intestinal disease with periods of exact **hared symptoms** (اعراض حادة) and periods that are relatively **symptom-free** (بدون اعراض) .
- Although the symptoms of ulcerative colitis can sometimes **diminish** (تتضاءل) on their own, the disease usually requires treatment to go into remission.



**Endoscopic images of ulcerative colitis**

### **Characteristic of ulcerative colitis (symptoms)**

- Visible blood and pus cells in stool > 90 % of patients.
- Diarrhea mixed with blood of gradual onset (main symptom of active disease)

- Fever and weight loss
- Abdominal pain and cramping with **gurgling sound** (صوت قرقرة) in the intestine
- Tenesmus (rectal pain) and rectal bleeding.
- Children's growth may slow.

## **Epidemiology**

Ulcerative colitis (UC) has **2 incidence peaks**, one in adolescents and young adults (مرحلة المراهقة والشباب) and the other in middle-aged men and women. **Men and women are about equally affected**. Overall, inflammatory bowel disease is more common **in white individuals than in black** or Asian Americans. This disease occur in 30-100 people for every 100,000 in United States or **less than 0.1% of the populations**. Although ulcerative colitis has no known cause, there is a presumed genetic component to susceptibility.

## **Classification of disease**

Doctors often classify ulcerative colitis according to **its location**. Types of ulcerative colitis include:

- **Ulcerative proctitis** (التهاب المستقيم التقرحي): Inflammation is **confined** (يتقيد او يقتصر) to the area closest to the **rectum** (rectum), and **rectal bleeding** may be the only sign of the disease.
- **Proctosigmoiditis** (التهاب المستقيم السيني): Inflammation involves the **rectum** and **sigmoid colon** the lower end of the colon. Signs and symptoms include bloody diarrhea, abdominal cramps and pain, and an inability to move the bowels in spite of the urge to do so (tenesmus الزحير).

- **Left-sided colitis** (التهاب القولون من الجانب الأيسر): is a form of ulcerative colitis (UC) that begins at the rectum and extends up to the left colon (sigmoid colon and descending colon (القولون النازل). Signs and symptoms include bloody diarrhea, abdominal cramping and pain on the left side, and urgency to **defecate**(التبرز) .
- **Pancolitis or universal colitis** (التهاب القولون العام): This type often affects the entire colon and causes bouts of bloody diarrhea that may be severe, abdominal cramps and pain, fatigue, and significant weight loss.

### **Etiology (risk factors)**

- **Diet** when colon is exposed to many dietary substances (dietary fiber) which may encourage inflammation and its play role in pathogenesis.
- **Breastfeeding** (الرضاعة الطبيعية) may be development of inflammatory bowel disease.
- **Accutane** (دواء آيزوترتينوين) is a possible trigger of ulcerative colitis.
- **NSAID** and postmenopausal hormone used
- **Genetics**: The **IBD-5 locus on chromosome 5q1** has been associated with both Crohn disease and ulcerative colitis.

### **Common Extraintestinal Manifestations of Ulcerative Colitis**

Arthritis (21%)

Aphthous stomatitis (4%) (التهاب الفم القلاعي)

Primary sclerosing cholangitis (4%) (التهاب الأفتنية الصفراوية المصلب الأولي)

Uveitis (4%) (التهاب القرنية)

Erythema nodosum (3%) (التهاب الجلد الاحمراري) (حمامي عقدي)

Ankylosing spondylitis (2%)

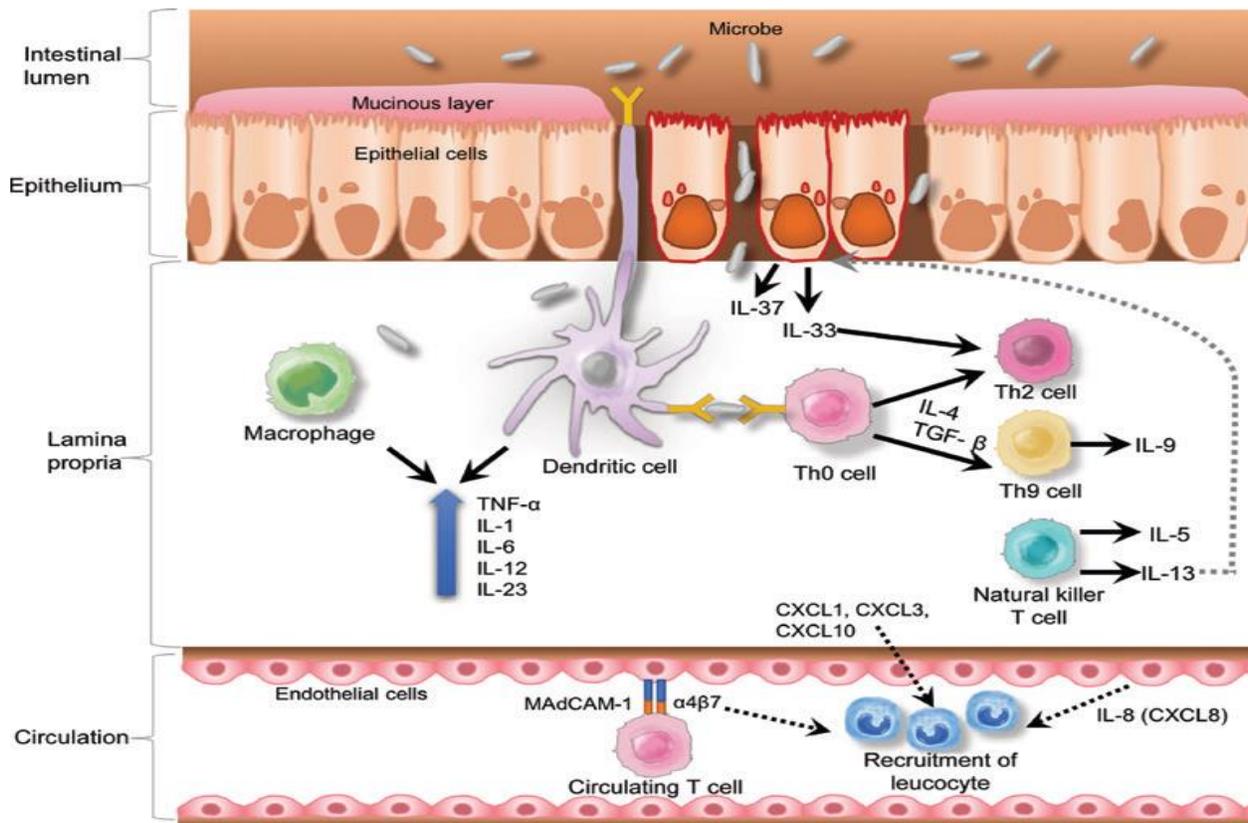
Pyoderma gangrenosum (2%) (تقيح الجلد الغنغريني)

Psoriasis (1%)

### **Immunopathophysiology (pathogenesis)**

- The mucinous layer plays an important role in luminal protection of the gastrointestinal tract. Lack of **mucin** (بروتين عالي الوزن الجزيئي/مخاطي) causes a **leaky barrier** (حاجزا متسربا) , and bacteria can subsequently interact with epithelial cells in the mucosa.
- In the colon, the mucinous layer consists of the outer layer, which is habitat for **commensal bacteria** (البكتريا المتعايشة), and the inner layer, which is resistant to bacteria.
- Bacteria produce (protease enzyme) which can damage mucin, resulting in a **defective mucinous layer** that allows bacterial penetration into the epithelium.
- The impaired mucosal barrier allows foreign bodies into the lamina propria.
- The defense mechanism is initiated from innate immune cells; macrophages and dendritic cells (DCs) are activated by the antigens (bacteria) via Toll like receptors (TLR). Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. TLR-2 and TLR4 are related with Gram Negative and gram positive bacteria respectively.
- Activation of the **nuclear factor kappa (NF-κB)** pathway by both cells stimulates transcription of pro-inflammatory genes, and consequently results in the production of pro-inflammatory cytokines, TNF-α, IL-1β, IL-6, IL-12, and IL-23.
- Hereafter, macrophages and DCs present them to **naïve CD4 T cells (Th0 cells)** to promote differentiation to Th2 cells via activation of IL-4.
- Th2 and NKT cells produce IL-13, **which disrupts the epithelial cell barrier**, consequently leading to increased permeability and enhanced absorption of bacterial products, **and IL-5, which contributes to recruitment and activation of eosinophils**

- IL-9 which produce from Th9 cells interacts with epithelial cells by inhibition of cellular proliferation, impairs tissue-repair mechanisms in response to cellular damage, and disrupts the tight junction.
- When epithelial cells are injured, the cells release IL-33 to recruit immune response by promoting the Th2 immune response.
- In systemic circulation, circulating T cells bearing ( $\alpha 4\beta 7$  integrin molecules) binds to colonic endothelial cells by mucosal vascular addressin cell adhesion molecule 1 (**MAdCAM-1**). This molecule induces intestinal inflammation and increases the entry of gut-specific T cells into the lamina propria.



## **Differential diagnosis**

The differential diagnosis for ulcerative colitis includes

- 1- Crohn's disease
- 2- Infectious colitis (typically detected on stool culture) caused by bacterial, viral, or parasitic pathogens. **Pseudo membrane colitis** or *Clostridium difficile*- associated colitis were seen following administration of antibiotics.
- 3- Radiation colitis in patient with previous pelvic radiotherapy.
- 4- Ischemic colitis
- 5- Chemical colitis due to introduction of harsh chemicals into the colon.

## **The initial lab Diagnosis**

- 1- CBC (to check anemia, thrombocytosis and a high platelet count), ESR and CRP.
- 2- Liver function tests to screen for liver and bile duct problems, which are occasionally seen in some people with Crohn's disease.
- 3- X-ray
- 4- Colonoscopy with biopsy is generally used to diagnose ulcerative colitis.  
Colonoscopy is also used to screen people with ulcerative colitis for colon cancer.  
Ulcerative colitis increases the risk of colon cancer.

### **Endoscopic determine:**

Loss of the vascular appearance of the colon

Erythema or redness of the mucosa and friability of the mucosa

Superficial ulceration which may be confluent and pseudopolyps (انماط زائفة)