INFLAMMATORY BOWEL SYNDROME

Objectives:

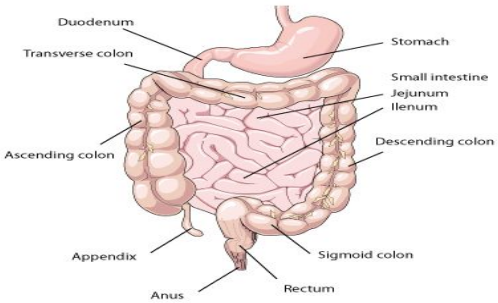
1. **Know the two forms of idiopathic inflammatory bowel disease (IBD).**
2. **Describe the pathogenesis of IBD.**
3. **Compare and contrast Crohn disease and ulcerative colitis with respect to:**

- clinical features and extraintestinal manifestations
- pathology (gross and microscopic features) of IBD.
- complications of IBD.(especially adenocarcinoma preceded by dysplasia)

Introduction

Anatomy

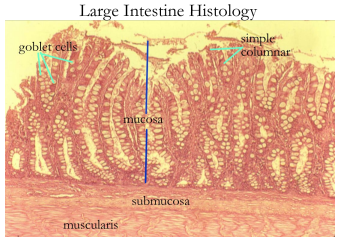
The large intestine is divided to :-
Cecum → Appendix → Ascending colon→ Transverse colon → Descending colon→ Sigmoid colon → Rectum → Anal canal



Histology

- Mucosa: simple columnar epithelium with numerous goblet cells
- Submucosa: showing numerous "**colonic crypts**" .
- longitudinal layer of muscles in muscularis externa known as "**taenia coli**".

Large Intestine Histology



Physiology

- **Reabsorb** water and compact material into feces.
- **Absorb** vitamins produced by bacteria.
- **Store** fecal matter prior to defecation.

Epidemiology

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

Ulcerative colitis	Crohn's disease
• More common in **whites** than blacks. • Occurs between 14 and 38 years of age. • **<u>Lower incidence in smokers</u>** and other nicotine users. • Lower incidence of previous **appendectomy** <20 years old. (يعتقد ان اللي شال الزايدة احتمال الاصابة بالمرض يقل)	• More common in **whites** than blacks, in **Jews** than non-Jews and more common in **childre**n than adults. • **Smoking is a risk factor.** • Majority (>75%) of cases occur between 11 and 35 years of age.

The *hygiene hypothesis*[1] suggests that these changes in incidence are related to **improved food storage conditions and decreased food contamination.**

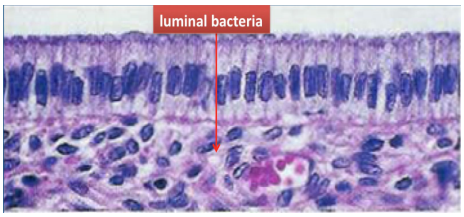
- improved hygiene has resulted in inadequate development of regulatory processes that **limit mucosal immune responses early in life.**
- As a result, exposure of susceptible individuals to normally innocuous[2] microbes later in life triggers inappropriate immune responses due to loss of intestinal epithelial barrier function.

لأنهم كانو يحافظو على اطفالهم و دايما يتأكدو انهم معقمين، فالاطفال لم يتم تعريضهم antigen فتم تقيد المناعة و قد تكون احدى السباب المؤدية الى الحركة المبالغ فيها للدفاع← immunologic hypersensitivity. (بمعنى اخر دعو اطفالكم يكتشفو العالم ليقوو مناعتهم)

[1] A theory suggests that the clean modern lifestyle and lack of early childhood exposure to dirt, bacteria and other pathogens weaken the immune system, and increase susceptibility to allergies and asthma.

[2] غير ضار

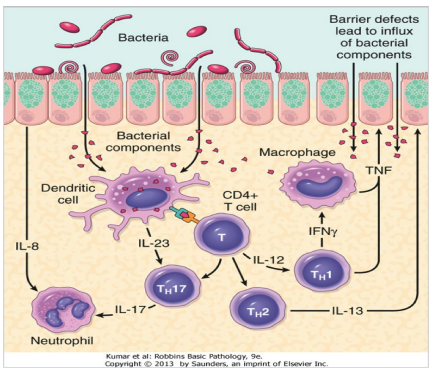
Inflammatory bowel disease



Definition

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

- Composed of two major groups **Crohn's disease** and **ulcerative colitis**.
- Although their causes are still not clear, the two diseases probably have an **immunologic hypersensitivity basis.**
- The distinction between CD and UC is based on the distribution of affected sites and morphological expression of disease at those sites.
- Crohn's most commonly affects the **end of the small bowel (the ileum) and the beginning of the colon,** but it may affect any part of the gastrointestinal (GI) tract. Ulcerative colitis is limited only to the colon(the large intestine).



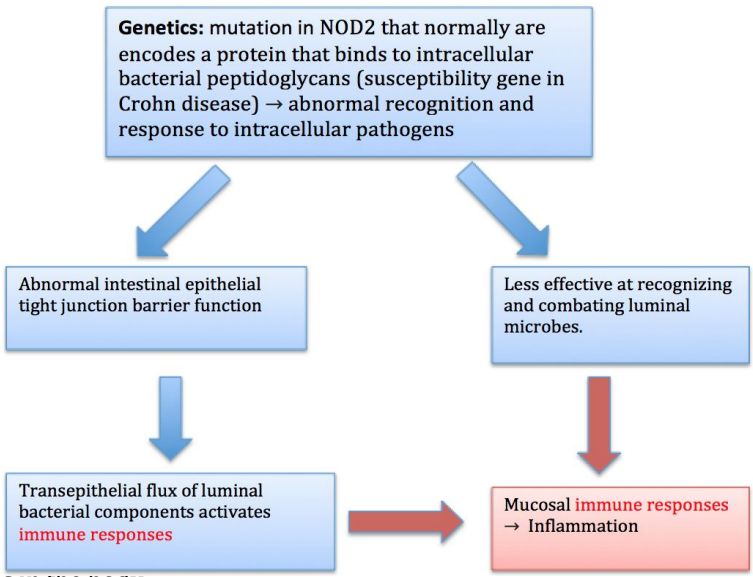
Clinical manifestations

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

Colon	Small intestine	Extraintestinal manifestations [3]
● Bloody diarrhea. ● Tenesmus[4]	● Abdominal pain. ● Intestinal obstruction. ● Steatorrhea	● Arthritis. ● Eye manifestation. ● Skin manifestation

Pathophysiology (Based on Theories)

- Immunosuppression is the mainstay of IBD therapy.
- NOD2 (Nucleotide-binding oligomerization domain).



Treatments:

immunosuppression is the mainstay therapy of IBD.

[3] The Immune reaction had affected other areas in the body.

[4] A feeling of constantly needing to pass stools despite an empty colon → pain during defecation .

Crohn's disease

Defenion

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.**
(crohn's disease also known as regional enteritis).

Sites of Involvement

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

Clinical Findings

- **Recurrent right lower quadrant** colicky pain due to (**obstruction)** with diarrhea and weight loss.
- **Bleeding** occurs only with **colon or anal involvement** → **(fistulas; abscesses).**
- **Aphthous ulcer in mouth.**
- Extragastrointestinal: **erythema nodosum**[5], **sacroiliitis**[6] (**HLA-B27 association**), pyoderma gangrenosum[7],Iritis **(CD>UD)**, primary sclerosing cholangitis [8]**(UC>CD)**.

Clinical Features

- Any age but has its highest incidence **in young adults**
- Extremely variable clinical feature.
- Thickening of the intestine may produce an ill-defined mass in the abdomen.

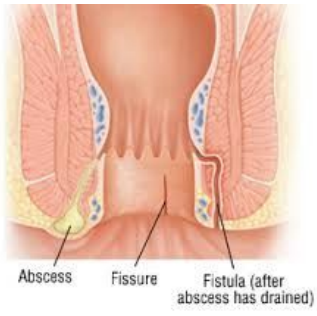
Acute phase	Chronic disease
fever, diarrhea, and right lower quadrant pain may mimic acute appendicitis or bowel perforation.	Remissions and relapses over a long period of time. (يتحسن بعدين يمرض و يتحسن و يرجع يمرض)

Morphology

Gross Appearance:

In general

- **Involvement is typically segmental**, with **skip areas** of normal intestine between areas of involved bowel.
- **Marked fibrosis** (to heal inflammation) → 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) ,it may extend deeply to become sites of perforation.

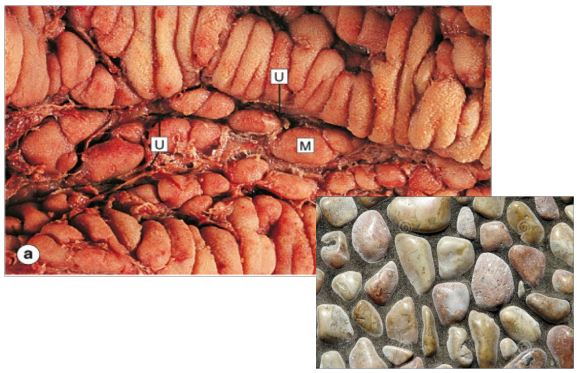


[5] rounded red lesion in skin
[6] inflammation of joint between sacrum and ilium
[7] is a condition that causes tissue to become necrotic, causing deep ulcers that u
[8] fibrosis around bile ducts leading to obstructive jaundice.

- **Fistula tracts** (communications with other viscera).

Mucosa:

longitudinal serpiginous[9] **ulcers** separated by irregular islands of edematous mucosa in the → **typical cobblestone**[10] **effect.** (مثل البلاط اللي بالحجر)

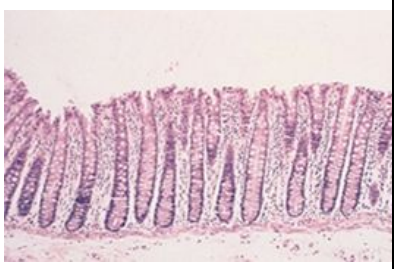
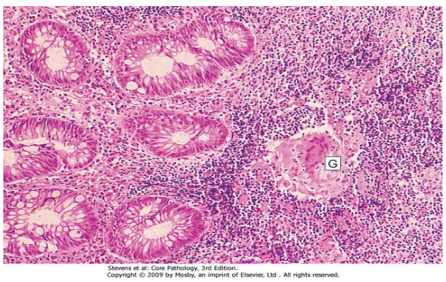
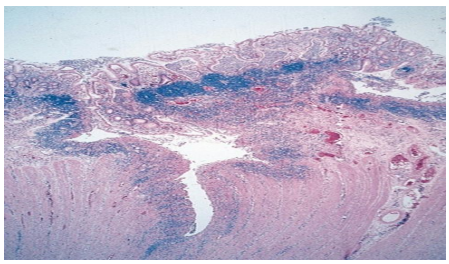


FAT :

In involved ileal segments, **the mesenteric fat creeps** from the mesentery to surround the bowel wall **(creeping fat)**[11].

Microscopic Features:

- Distortion of mucosal crypt architecture with mucosal inflammation.(because of repeated cycles of crypt destruction and regeneration.)
- Transmural inflammation(involving all layers mucosa, submucosa,muscularis..ect).
- **Noncaseating Epithelioid granulomas** [60%] (the hallmark in crohn' disease) but the absence of it does not exclude the diagnosis of crohn's disease.
- **Fissure-ulcers and fistulas** can be seen microscopically.

Normal	Crohn's diseases (granuloma)	Crohn's diseases (fissure)
		

Complications

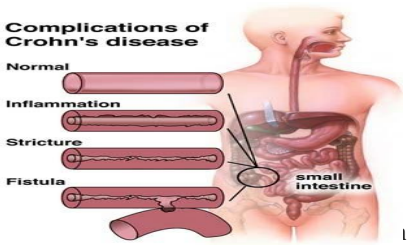
1.Intestinal obstruction

2.Fistula formation

A. between the ileum and the colon → **malabsorption**(steatorrhea)
B. Enterovesical fistulas → **urinary infections** , **passage of gas** and **feces with urine**.
C. Enterovaginal fistula → **fecal vaginal discharge**.

3. Extraintestinal manifestations (arthritis and uveitis).

4. Slight increased risk of development of carcinoma of the colon—much less than in ulcerative colitis.



[9] (of ı wavy margin.

[10] appearance in which diseased tissue is depressed below th

[11] This is because creeping fat is actually normal mesenteric fat that is behaving differently, extending from the mesenterium to the small or large intestine. In extreme cases, it wraps around more than 50% of the intestinal circumference.

Ulcerative Colitis

Defenion

- An ulceroinflammatory disease of undetermined etiology.
- It has a chronic course characterized by **remissions and relapses.**
- Common seen at 20- to 30-year age group but may occur at any age.
- **Most common IBD.**
- Ulcerations are in continuity (no skip areas).

Sites of Involvement

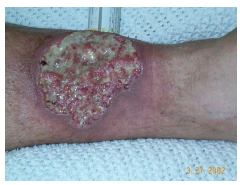
- **Rectum, and the colon.**(Pancolitis= involvement of the whole colon)
- **Rectum** is involved in **almost all cases.**
- The disease extends proximally from the rectum in a continuous manner **without** skip areas.
- **The ileum** is not involved as a rule. (but in severe cases could involve distal ileum called backwash ileitis).

Etiology

- The cause is **unknown.**
- **Antibodies** that cross-react with intestinal epithelial cells and certain serotypes of Escherichia coli(E.coli)have been demonstrated in the serum of some patients with ulcerative colitis.

Clinical Finding

- **Recurrent left-sided abdomina**l cramping with bloody diarrhea and mucus.
- Fever, tenesmus, weight loss (mostly seen in acute cases).
- **Toxic megacolon**[12] (up to 10% of patients). Mortality rate 50%.
- Extra-gastrointestinal: primary sclerosing cholangitis (UC > CD),erythema nodosum, iritis/uveitis (CD > UC), pyoderma gangrenosum[13] (see pic), **HLA-B27 positive arthritis.**
- **P-ANCA antibodies**[14] >45% of cases.



Clinical Features

Acute course (During relapse)	Chronic course
● Fever. ● Leukocytosis. ● Lower abdominal pain. ● **Bloody diarrhea**. ● **mucus** in the stool. These symptoms relieved by defecation	● Remissions. ● Exacerbations.[15]

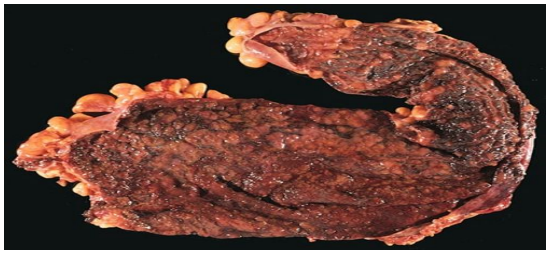
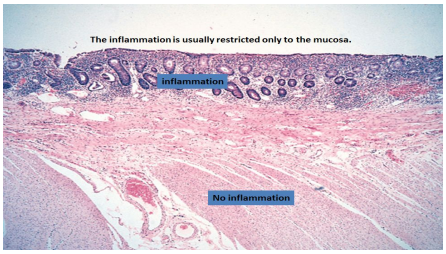
[12] Dilation of the colon, with functional obstruction → decreased motility

[13] تقيح الجلد الغرغريني

[14] **Anti-neutrophil cytoplasmic antibodies** (**ANCAs**) are a group of autoantibodies, mainly of the IgG type, against antigen in the cytoplasm of neutrophil granulocytes (the most common type of white blood cell) and monocytes.They are detected in a number of autoimmune disorders, but are particularly associated with systemic vasculitis.

[15] An increase in the severity of a disease or in any of its signs or symptoms.

Morphology

Gross Appearance	Microscopic Features
	
Involves mainly the mucosa ● **Diffuse hyperemia**[16] . ● **Numerous superficial ulcerations** These both seen in **acute phase** ● The regenerated or nonulcerated mucosa may appear **polypoid (inflammatory pseudopolyps)**[17] in contrast with the atrophic areas or ulcers.	● **The inflammation is** usually restricted to the mucosa. ● **In the active phase →** **neutrophils** (attack crypts) → **Cryptitis (Crypt abscess→** multiple neutrophil within crypts) ● **In the chronic phase →** **crypt atrophy and distortion.** Active inflammation correlates well with the severity of symptoms.

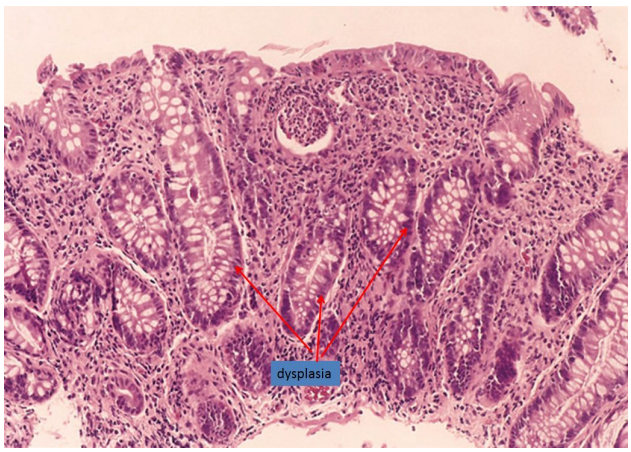
Complications

Acute phase:

- Severe bleeding
- **Toxic megacolon.**

Chronic ulcerative colitis

- Increase risk of developing **colon carcinoma.**
- The presence of **high-grade dysplasia** in a mucosal biopsy imposes a **high risk of cancer** and is an indication for colectomy.

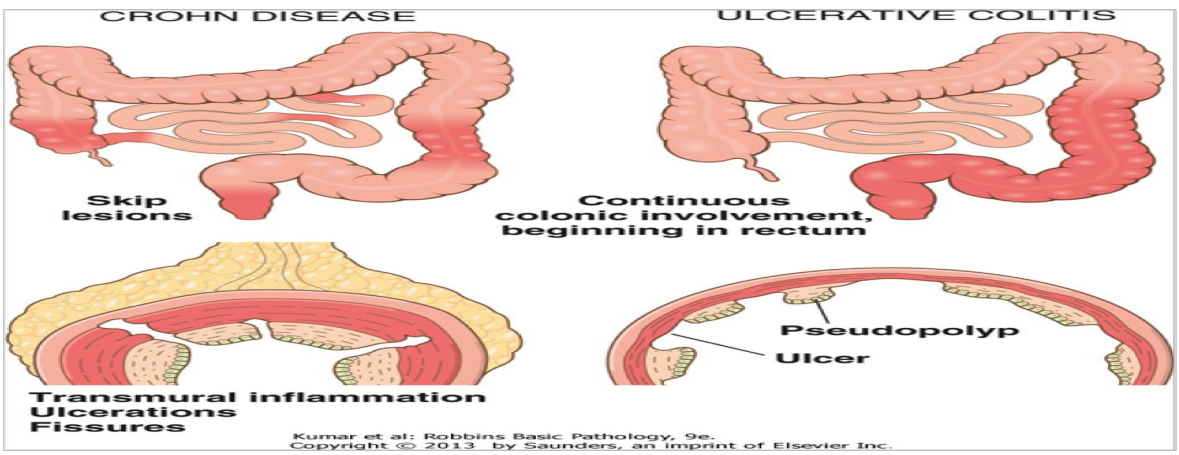


[16] An increase in the quantity of blood flow to a body part.

[17] are projecting masses of scar tissue that develop from granulation tissue during the healing phase in repeated cycle of ulceration. (these normal mucosa have polyp like appearance)

summary

	Crohn's	Ulcerative Colitis
Site	Any part of the GIT	Colon only
Pattern	Skip areas of normal mucosa	Diffuse involvement of mucosa
Symptoms	Right lower quadrant pain (ileum)with non bloody diarrhea.	Left Lower quadrant (rectum) with bloody diarrhea.
Depth of the ulcer	Deep ulcers (fissure)	Superficial ulcers
Extent of inflammation	Transmural inflammation	Mucosal inflammation only
Inflammation	Lymphoid aggregates with granulomas	Crypts abscesses with neutrophils
Fistula Formation	Yes	No
Creeping mesenteric Fat	Yes	No
Fibrous thickening wall	Yes	No
Granulomas	Yes	No
Dysplasia	rare	Common
Carcinoma	rare	More Common (10%)
Mucosal appearance	**Cobblestone**	**Pseudopolyps**
Bowel wall	Thickened wall narrow margin	Thin wall Dilated lumen
Complication	-Fistula formation -Bowel perforation -Stricture formation	-Haemorrhage -Toxic Megacolon -Systemic effects



MCQ

1) A 44-year-old man presents with multiple episodes of bloody diarrhea accompanied by cramping abdominal pain. A colonoscopy reveals the rectum and distal colon to be unremarkable, but x-ray studies find areas of focal thickening of the wall of the proximal colon, producing a characteristic "string sign." Biopsies from the abnormal portions of the colon revealed histologic features that were diagnostic of Crohn's disease. Which of the following histologic features is most character- istic of Crohn disease?

A. Dilated submucosal blood vessels with focal thrombosis
B. Increased thickness of the subepithelial collagen layer
C. Noncaseating granulomas with scattered giant cells
D. Numerous eosinophils within the lamina propria
E. Small curved bacteria identified with special silver stains

2) Which of the therapies listed below is used most often to treat an individual with a history of Crohn disease who acutely develops abdominal pain and bloody diarrhea but has no clinical evidence of obstruction or fistula formation?

A. Aspirin
B. Interleukin-10
C. Metronidazole
D. Prednisolone
E. Surgery

3) Which of the following findings is more characteristic of ulcerative colitis rather than Crohn disease?

A. Inflammation beginning in the rectum and extending proximally without "skip lesions"
B. Pericolonic fibrosis forming "creeping fat" around the outside of the gut
C. Intestinal obstruction resulting from a pericolonic abscess
D. Superficial noncaseating granulomas forming hamartomatous
E. polyps
F. Transmural inflammation producing fissures and fistulas

4) 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

5) 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-C
2-D
3-A
4-D
5-A

SAQ

A 22-year-old woman has had recurrent episodes of diarrhea, crampy **abdominal pain**, and slight fever over the last 2 years. At first the episodes, which usually last 1 or 2 weeks, were several months apart, but recently they have occurred more frequently. Other symptoms have included **mild joint pain** and sometimes **red skin lesions**. On at least one occasion, her stool has been guaiac-positive, indicating the presence of occult blood. Colonoscopy reveals several sharply delineated areas with thickening of the bowel wall and mucosal ulceration. Areas adjacent to these lesions appear normal. Biopsies of the affected areas show full-thickness inflammation of the bowel wall and several noncaseating granulomas.

◆ **What is the most likely diagnosis?**
Crohn disease
◆ **What are the common complications of this disease?**
Malabsorption and malnutrition, fibrous strictures of the intestine, and fistula to other organs, such as from bowel to skin or bowel to bladder.

For any suggestions or questions please don't hesitate to contact us on:
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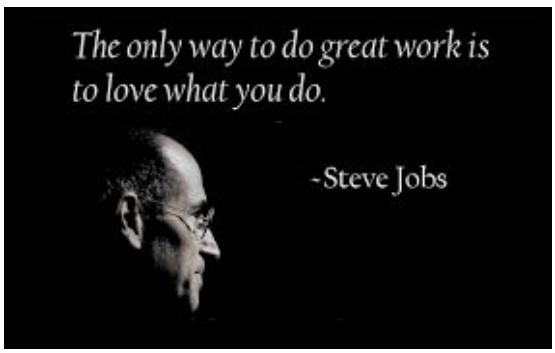
Ask us: www.ask.fm/Pathology434



Good Luck!

حسين الكاف
نواف الفوزان
سعد الخريجي
عمر الرهبيني
ريم لبني
ريما الرشيد
اشواق المطيري
رزان الصبحي