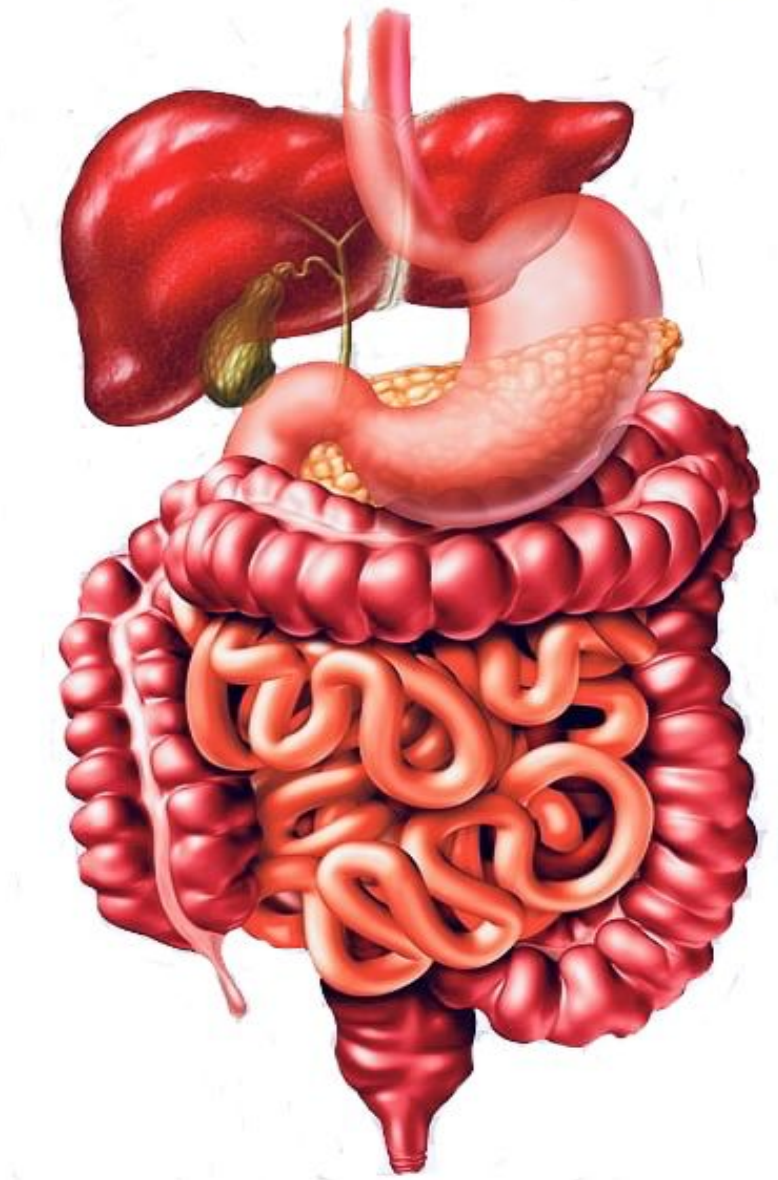
جامعة الملك سعود
King Saud University

MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

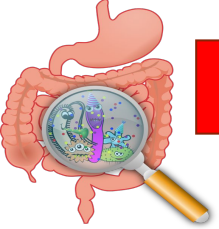
هذه المحاضرة هي تكريم لكل من يعمل ولا يكرّم،لكل من يعمل بالخفاء،لكل ايادي تدفعنا من ظهورنا لا نرى وجوه أصحابها

Please note:
This work is based on male slides except few points will appear pink



IBD I + II
&
Colonic Polyps And Carcinoma I + II

Content Explanation Notes Important



Objectives and there answers from Dr slides

1. Know the two forms of idiopathic inflammatory bowel disease (IBD).
Crohn's disease and ulcerative colitis.

2. Describe the pathogenesis of IBD.
a.Theories
b.Autoimmunity

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).

4. Know common types of intestinal polyps
A. Non-neoplastic polyps:
- no dysplasia
- 4 common types (hyperplastic, hamartomatous, inflammatory, lymphoid)

B. Neoplastic polyps:
- there is dysplasia
- 3 types (tubular, tubulovillous, villous)

5. Know the clinical presentation of left and right sided colon cancer, and the environmental factors that increase its risk
- Left colon…frank bleeding, obstruction
- Right colon…iron deficiency anaemia
- Tumor markers ……..CEA

6. Understand the pathogenesis of colon cancer
- Adenoma to Carcinoma Pathway
- Two genetic pathways APC/B-catenin and DNA mismatch repair genes
- Familial Polyposis Syndrome

7. Describe the Pathological features of colon cancer
- Adenocarcinoma most common ……carcinoid tumor { neurosecretory granules}
- 70% are in the rectum and/or sigmoid
- Duke classification is used for staging

Know The Two Forms Of Idiopathic Inflammatory Bowel Disease

Robbins: single episode of appendicitis is associated with reduced risk of developing ulcerative colitis.
the risk of Crohn disease is increased by smoking, whereas that of ulcerative colitis is reduced.

Disease	Crohn's disease and Ulcerative colitis are major types of IBD
Etiology	Although their causes are still not clear, the two diseases probably have an immunologic hypersensitivity basis.

Describe the pathogenesis of IBD

pathophysiology (theoretical)

mutation in NOD2

Robbins : along with NOD2, two Crohn disease–related genes of particular interest are **ATG16L1** and **IRGM**

susceptibility gene in Crohn disease more than 200 genes are related to these disease

Abnormal recognition and response to intracellular pathogens

Less effective at recognizing and combating luminal microbes

Abnormal intestinal epithelial tight junction barrier function

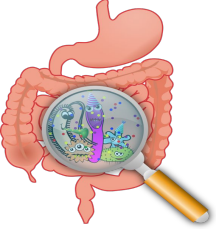
Transepithelial flux of luminal bacterial components activates immune responses

Mucosal immune responses.

Immunosuppression is the mainstay of IBD therapy.

inflammation

Mutations in **NOD2** are seen in about 15% of Crohn's disease patients but are also seen in a smaller percentage of the general population, so mutations in NOD2 are neither necessary nor sufficient for the development of Crohn's disease



Pathophysiology

IBD is an idiopathic disorder	The pathophysiology of IBD is under active investigation.	Persons with IBD have a genetic predisposition susceptibility for the disease

Most investigators believe that the two diseases result from a combination of:

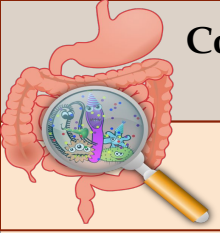
1.Defects in host interactions with intestinal microbes	2.Intestinal epithelial dysfunction	3.Aberrant mucosal immune responses.

For unclear reasons, research suggests that smoking increases the risk of Crohn disease but reduces the likelihood of ulcerative colitis.

Clinical

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

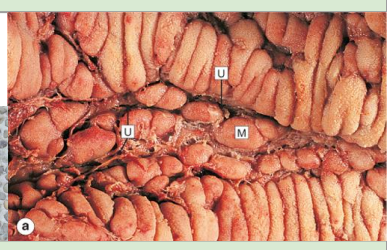
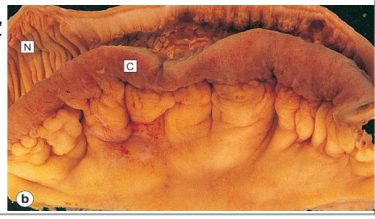
colon	small intestine	Extraintestinal manifestations
-Bloody diarrhea - Tenesmus pain during defecation Continual or recurrent inclination to evacuate the bowel.	-Abdominal pain -Intestinal obstruction. -Steatorrhea malabsorption manifestations	-Arthritis (joints) -Eye manifestation (uveitis) -Skin manifestation (erythema nodosum)



Compare And Contrast Crohn's Disease And Ulcerative Colitis

Crohn's Disease

Robbins: Crohn disease, also known as **regional enteritis**

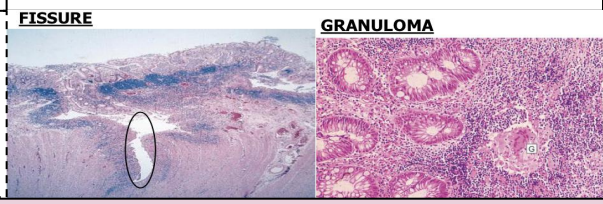
Definition	a chronic inflammatory disorder that most commonly affects the **ileum and colon** but has the potential to involve **any part of the gastrointestinal tract from the mouth to the anus.**	
Clinical features Extremely variable clinical feature.	Age group	Any age but has its highest incidence in **young adults** More common in females
	Acute phase:	Fever, diarrhea, and **right lower quadrant pain may mimic acute appendicitis.** Because it loves the terminal ileum and cecum, which are right
	Chronic phase	Remission and relapses over a long period of time patient is better from acute phase he enters chronic
Sites of Involvement	Any part of the GIT from the mouth to the anus. ileum (30%) colon (20%). most commonly **terminal ileum,** ileocecal valve, and the cecum. Commonly (75%) have **perianal lesions** such as abscesses, fistulas, and skin tags fibroepithelial polyp around anus	
Gross Appearance	• Involvement is typically **segmental**, with **skip** areas of normal intestine between areas of involved bowel. It's called **skip lesions**, or **discontinuous** or **regional ileitis** • Marked fibrosis causing luminal narrowing with intestinal obstruction. It's called **narrowing** or **stricture**, not completely closed. • Fissures (deep and narrow ulcers that look like stabs with a knife that penetrate deeply into the wall of the affected intestine) only found in Crohn disease. • Fistulas (communications with other viscera mostly bladder and vagina).	
	Mucosa	
	Typical Cobblestone appearance "longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa (pseudo polyps) This results in the typical cobblestone effect"  	
	Fat	
	Creeping fat: In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (creeping fat) يعني جاي من الجوانب The peritoneal tissue comes & tries to seal the perforation 	

Compare And Contrast Crohn's Disease And Ulcerative Colitis

Microscopic Appearance

Distortion of mucosal crypts architecture.	**Transmural inflammation.**	**Epithelioid granulomas.** **60%** a hallmark for Crohn Disease.
Also in ulcerative colitis it is branched, dilated, short and acutely inflamed	Involving the whole wall, from mucosa to serosa.	Fissure-ulcers and fistulas can be seen microscopically.

Another feature is **Crypt Abscess,** which is infiltration of neutrophils to the crypts during the active phase. This feature can also be seen in ulcerative colitis.

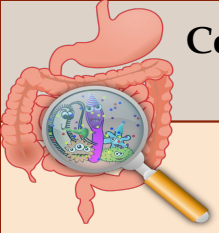


Complications of crohn's disease

Intestinal obstruction	**Fistula formation:** due to fissure ulcers	**Extraintestinal manifestation**	Slight increased risk of development of **carcinoma of the colon**
Due to fibrosis in terminal ileum by deep ulcer and inflammation	a) Between the ileum and the colon result in malabsorption b) Enterovesical fistulas lead to urinary infections and passage of gas and feces with urine. c) Enterovaginal fistulas produce a fecal vaginal discharge.	arthritis and uveitis	much less than in ulcerative colitis.) It means that ulcerative colitis has more risk of carcinoma

Ulcerative colitis

Definition	• Is an inflammatory disease of uncertain cause (idiopathic) • It has a chronic course characterized by: Remission & Relapse. • 20-30 year age groups are more susceptible to the disease but may occur at any time • It is continuous with no skip lesions
Etiology	• The cause is unknown. • Antibodies that cross react with intestinal epithelial cells & certain serotypes of E.coli have been demonstrated in the serum of some patients with ulcerative colitis antibodies that should be directed against E.coli are directed against the intestinal epithelium



Ulcerative colitis (con..)

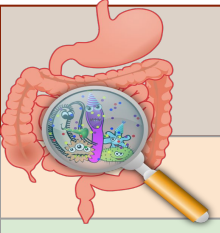
Complications

Acute phase	Chronic ulcerative colitis	Extra-intestinal manifestations
-Severe bleeding. -Toxic megacolon (dilation of the colon, with functional obstruction) Toxic megacolon will cause **obstruction** same as Crohn's disease but not due to Fibrosis. Toxic megacolon happens because there are a lot of chemical mediators and toxic substances (due to the inflammation) that will affect the smooth muscles of the colon so they're no longer working normally.	-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 (surgical removal of the colon).	(occur more commonly in ulcerative colitis than in Crohn's disease). -Arthritis -Uveitis -skin lesions (pyoderma gangrenosum) -sclerosing pericholangitis (fibrosis around bile ducts) leading to obstructive jaundice. Only in UC.

Comparison between crohn's disease and ulcerative colitis important

Crohn's disease	Ulcerative colitis
-Any part of GIT -Skip areas of normal mucosa -Deep ulcers (fissures) - Transmural inflammation - Fistula formation - Creeping mesenteric fat - Fibrous thickening of wall - Granulomas (60%) - Dysplasia is rare - Carcinoma is rare - Cobblestone appearance -Thickened wall Narrow lumen -Marked lymphoid reaction -Complications: Short gut syndrome "malabsorption" Fistula formation- Bowel perforation Stricture formation -Recurrence after surgery is common	-Colon only - Diffuse involvement of mucosa - Superficial ulcers - Mucosal inflammation only - Fistula formation is not seen - Creeping mesenteric fat is not seen - Fibrous thickening of wall is not seen - Granulomas are not seen - Dysplasia is common - Carcinoma is more common (10%) -Pseudopolyps appearance - Thin wall Dilated lumen -Moderate lymphoid reaction -Complications: Hemorrhage- Electrolyte loss Toxic megacolon- systemic effects -Recurrence is rare

Robbins:
Indeterminate Colitis histopathologic and clinical overlap between ulcerative colitis and Crohn disease and it is not possible to make a distinction in up to 10% of patients with IBD. In such cases the small bowel is not involved, and the continuous pattern of colonic disease typically would indicate ulcerative colitis. However, patchy disease, fissures, a family history of Crohn disease



Know common types of intestinal polyps

Polyps

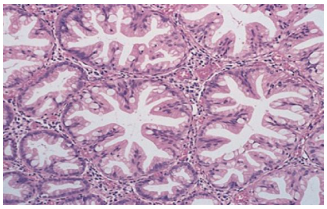
Non-neoplastic 90% No dysplasia only hyperplasia				Neoplastic 10% dysplasia
Hyperplastic polyp no malignancy potential	Hamartomatous (Juvenile and peutz - jeghers polyps)	Inflammatory polyps	Lymphoid polyps	Adenoma

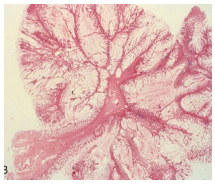
Differentiate between the neoplastic and non-neoplastic polyps

Non-neoplastic

Hyperplastic Polyp
hyperplasia of mucosal cells

- Asymptomatic.
- > 50% are located in the rectosigmoid.
- Sawtooth Surface. Irregular, crowded and elongated crypts
- Star shaped crypts.
- Composed of well-formed glands and crypts lined by differentiated goblet or absorptive cells.





This picture shows hyperplasia glands, and you can see goblets & absorptive cells around gland. The crypts show star shape look.

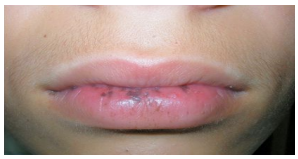
Hamartomatous polyp
affect multiple tissue types

Juvenile Polyps (retention polyp)
MCQs: what is the most common polyp in children

- Developmental malformations affecting the **glands** and **lamina propria.**
- Commonly occur in **children** under 5 years old in the rectum.
- In adult called retention polyp.

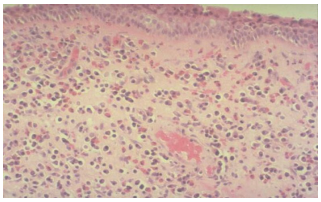
Peutz-Jeghers syndrome
Increase number of glands
Smooth muscle in Lamina propria

- Rare, autosomal dominant
- hamartomatous polyps accompanied by mucosal and cutaneous pigmentation around the lips, oral mucosa, face and genitalia.
- Polyps tend to be large and pedunculated.
- Increased risk of developing carcinoma of the pancreas, breast, lung,ovary and uterus



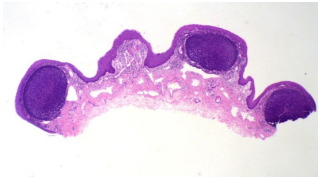
Inflammatory Polyps

- longstanding IBD, especially in chronic ulcerative colitis. Injury repair injury repair will lead to this
- Represent an exuberant reparative response to longstanding mucosal injury called pseudopolyps.



Lymphoid polyps
Not significant

Hype plastic lymphoid area
More likely in children (until 12 years old)

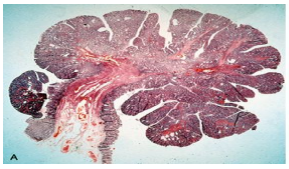
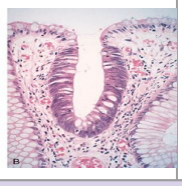
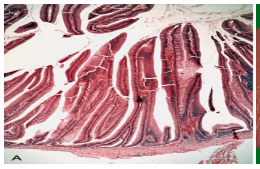
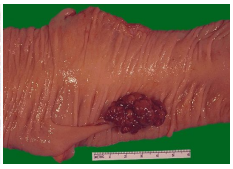


A **Polyp** is a mass that projects above a mucosal surface, as in the gut, to form a macroscopically visible structure. Those without stalks are referred to as **Sessile**. As sessile polyps enlarge, proliferation of cells adjacent to the polyp and the effects may combine to create a stalk. Polyps with stalks are termed **Pedunculated**.

Neoplastic Polyps (Adenoma /Adenomatous Polyp)

- Occur mainly in large bowl.
- Sporadic and familial.
- Vary from small pedunculated to large sessile.
- Epithelium proliferation and **dysplasia**

Tubular Adenoma	Villous Adenoma more aggressive	Tubulovillous Adenoma
- less than 25% villous architecture. - Represents 75% of all neoplastic polyps. - 75 % occur in the distal colon and rectum.	- villous architecture over 50% - The least common, largest and most ominous of epithelial polyps. - Age: 60 to 65 years, - Present with rectal bleeding or anemia, large ones may secrete copious amounts of mucoid material rich in protein. - 75% located in rectosigmoid area.	- villous architecture between 25 and 50%. - Intermediate in size, degree of dysplasia and malignant potential between tubular and villous adenomas.

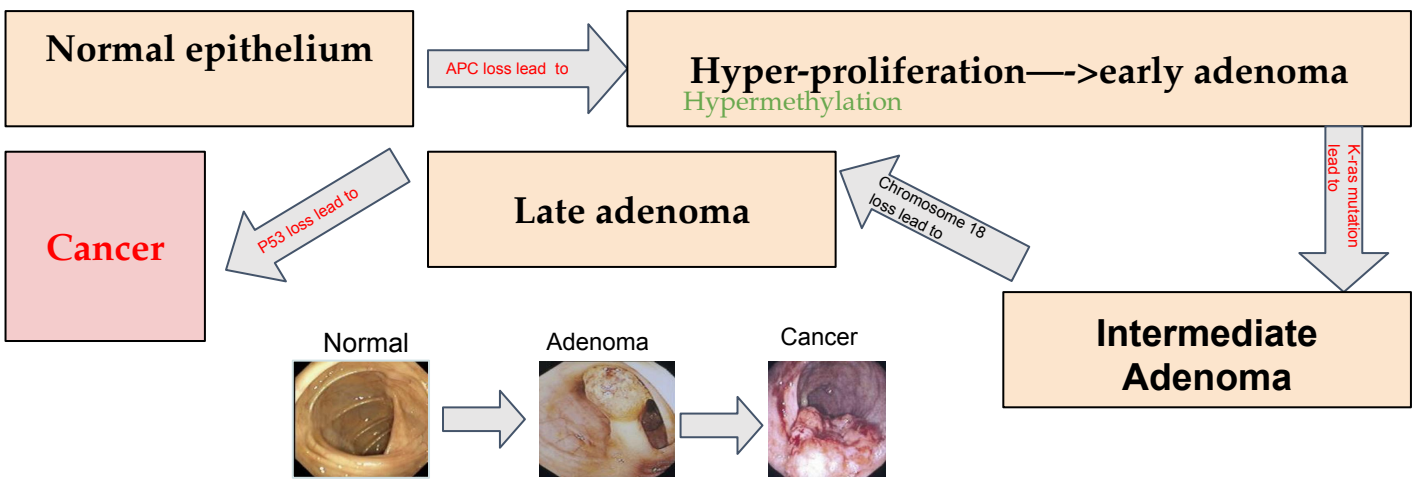
Relationship of Neoplastic Polyps to Carcinoma

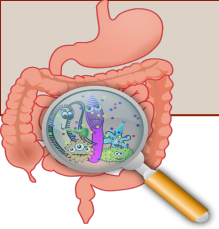
Adenoma to carcinoma sequence is documented by several genetic alterations.

The probability of carcinoma occurring in a neoplastic polyp is related to:

The size of the polyp.	The relative proportion of its villous features.	The presence of significant cytologic atypia (dysplasia) in the neoplastic cells

Understand The Pathogenesis Of Colon Tumors





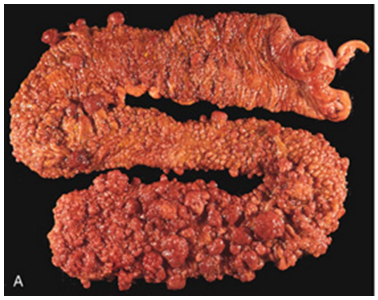
Understand The Pathogenesis Of Colon Tumors

Familial Polyposis Syndrome

Patients have genetic tendencies to develop neoplastic polyps.

Familial polyposis coli (FPC)

- Genetic defect of Adenomatous polyposis coli (APC).
- APC gene located on the long arm of chromosome 5 (5q21).
- APC gene is a tumor suppressor gene.
- Innumerable neoplastic polyps in the colon (500 to 2500).
- Polyps are also found elsewhere in alimentary tract.
- The risk of colorectal cancer is 100% by midlife.



Gardner's syndrome

- Polyposis coli, multiple osteomas(benign tumor of the bone), epidermal cysts, and fibromatosis.

Turcot syndrome

- Polyposis coli, glioma and fibromatosis

Malignant Tumors of Large Intestine

Adenocarcinoma	
Epidemiology	• Adenocarcinoma of the colon is the most common malignancy of the GI tract and is a major cause of morbidity and mortality worldwide. • Constitutes 98% of all cancers in the large intestine.
Predisposing factors	1.IBD, adenomas , polyposis syndrome. 2.Diet appears to play an important role in the risk for colon cancer: - Low fibre diet. -High fat content. -Alcohol - Reduced intake of vit A, C & E.

Understand The Pathogenesis Of Colon Tumors

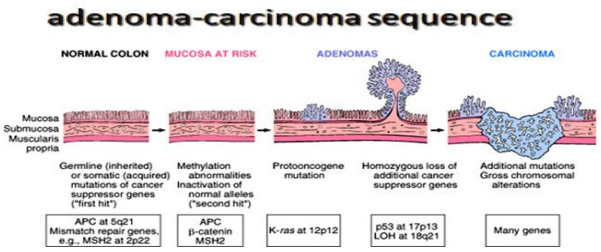
Adenocarcinoma of Large Intestine

Carcinogenesis

Two pathogenetically distinct pathways for the development of colon cancer, both seem to result from accumulation of multiple mutations:

1- The APC/B-catenin pathway (85 %)

- chromosomal instability that results in stepwise accumulation of mutations in a series of oncogenes and tumor suppressor genes. You should know three genes here: APC loss, K-ras, P53 loss is going to cause adenocarcinoma



2- The DNA mismatch repair genes pathway:
Not related to polyposis directly to adenocarcinoma

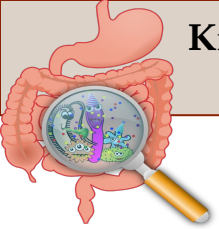
- 10% to 15% of sporadic cases.
- There is accumulation of mutations (as in the *APC/B-catenin schema)*
- Five DNA mismatch repair genes (**MSH2**, **MSH6**, **MLH1**, **PMS1, AND PMS2**) Dr Maha said all the genes her are important & they cause malignant tumors directly.
- give rise to the *hereditary non polyposis colon carcinoma (HNPCC)*

Hereditary mutation of the *APC* gene is the cause of familial adenomatous polyposis (FAP), where affected individuals carry an almost 100% risk of developing colon cancer by age 40 years.

Table 15.7 Common Patterns of Sporadic and Familial Colorectal Neoplasia

Etiology	Molecular Defect	Target Gene(s)	Transmission	Predominant Site(s)	Histology
Familial adenomatous polyposis (70% of FAP)	APC/WNT pathway	*APC*	Autosomal dominant	None	Tubular, villous; typical adenocarcinoma
Hereditary nonpolyposis colorectal cancer	DNA mismatch repair	*MSH2, MLH1*	Autosomal dominant	Right side	Sessile serrated adenoma; mucinous adenocarcinoma
Sporadic colon cancer (80%)	APC/WNT pathway	*APC*	None	Left side	Tubular, villous; typical adenocarcinoma
Sporadic colon cancer (10%–15%)	DNA mismatch repair	*MSH2, MLH1*	None	Right side	Sessile serrated adenoma; mucinous adenocarcinoma

FAP, Familial adenomatous polyposis.

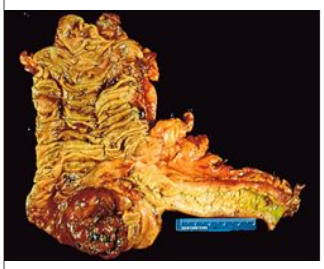
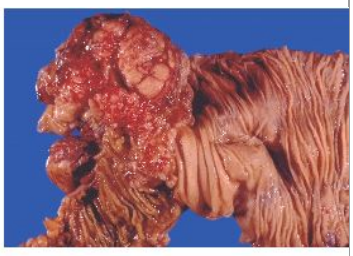
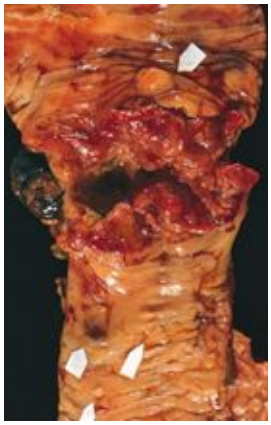


Know the clinical presentation of left and right sided colon cancer, and the environmental factors that increase its risk.

Colorectal Carcinoma

Morphology

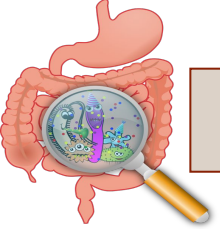
•70% are in the rectum, rectosigmoid and sigmoid colon.

Left-sided carcinomas	Right-sided carcinomas
 	
•tend to be annular, encircling lesions with early symptoms of obstruction. ★ **After defecation** the patient will start to develop bleeding or the stool will be **mixed with blood** (fresh blood). وهذا الشيء راح يخلي المريض يجي على الدكتور بسرعة يعني ما راح يفقد دم لمدة طويلة لدرجة يصير عنده انيميا ★ WHY there's obstruction? the tumor once it's involved, it will make desmoplastic reaction (fibrosis around tumor cells) so a lot of fibrosis will cause obstruction.	•tend to grow as polypoid, fungating masses, obstruction is uncommon. •Mucinous adenocarcinoma secret abundant mucin that may dissect through cleavage planes in the wall. ★ Ulceration will lead to bleeding and long term of bleeding will cause iron deficiency anemia, the stool will be black (**melena**). ★ Has better outcome than the left-sided carcinoma.

Signs and symptoms

•If located closer to the anus: change in bowel habit, feeling of incomplete defecation, PR bleeding

•A tumor that is large enough to fill the entire lumen of the bowel may cause bowel obstruction



Tumor Markers:

A **tumor marker** is a substance found in the blood , urine or body tissues that can be elevated in cancer, among other tissue types.

1. **Carcinoembryonic antigen (CEA)**
2. **Carbohydrate antigen (**CA19-9)

Both of them are useful to assess disease recurrence (late stage) , **NOT FOR DIAGNOSIS!**

Elevated in :

CEA	levels may also be raised in some non-neoplastic conditions like ulcerative colitis pancreatitis, cirrhosis COPD, Crohn's disease as well as in smokers
CA19-9	are raised in in patients with colon cancer and pancreatic cancer, esophageal cancer and hepatocellular carcinoma. Apart from cancer, elevated levels may also occur in pancreatitis, cirrhosis.

3. Tissue inhibitor of metalloproteinases 1 (TIMP1 3):
used for detection of early as well as late stage disease

Duke classification is used for staging

Malignant Small Intestine Neoplasm

Descending order of frequency:

1.Carcinoid

2.Adenocarcinomas

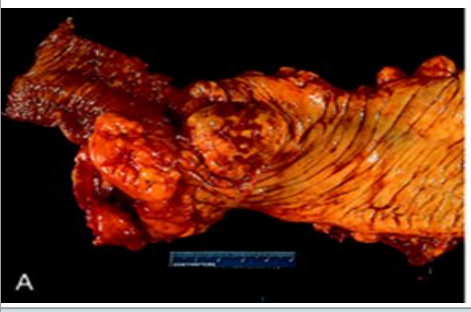
3.Lymphomas

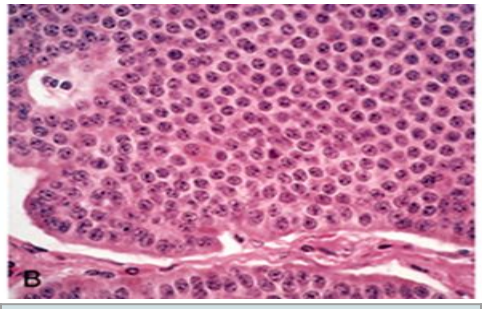
4.Leiomyosarcomas.

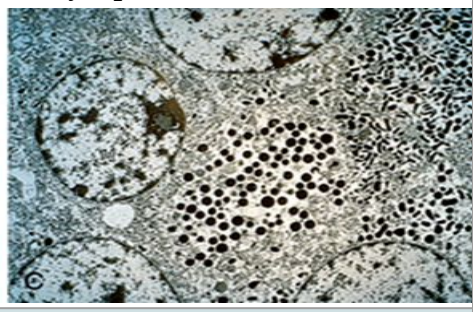
Small Intestinal Neoplasms

Carcinoid Tumors :

- Neoplasms arising from endocrine cells found along the length of GIT mucosa.
- 60 to 80% appendix and terminal ileum: 10 to 20% rectum.
- Ultrastructural features: neurosecretory electron dense bodies in the cytoplasm







Clinical features

- Asymptomatic
- May cause obstruction, intussusception* or bleeding**.
- May elaborate hormones: Zollinger-Ellison, Cushing's carcinoid or other syndromes.

(*): Segment of small bowel will be drawn into next segment of the bowl كأن كم تدخليه جوا كم ثاني.

(**): If it ulcerated it will bleed.

Carcinoid syndrome

It means patients who have carcinoid could present with other manifestations

- 1% of carcinoid tumor & in 20% of those of widespread metastasis
- Paroxysmal flushing, episodes of asthma-like wheezing, right-sided heart failure, attacks of watery diarrhea, abdominal pain,
- The principal chemical mediator is serotonin
- The syndrome is classically associated with ileal carcinoids with hepatic metastases. If there's no metastases serotonin will go ➜ portal circulation ➜ liver and there will be detoxify and then excreted in the urine, but if there's metastases the serotonin will go from the site of metastases in the liver ➜ hepatic vein ➜ systemic circulation so the symptoms will appear.

Lymphoma not significant

- Most often low-grade lymphomas arising in mucosal-associated lymphoid tissue (MALT) lymphoma

or

high-grade non-Hodgkin's lymphomas of B cell type.

- May occur in any part of the intestine;
- the ileocecal region is a favored site for Burkitt's lymphoma.

Comparison between crohn's disease and ulcerative colitis important

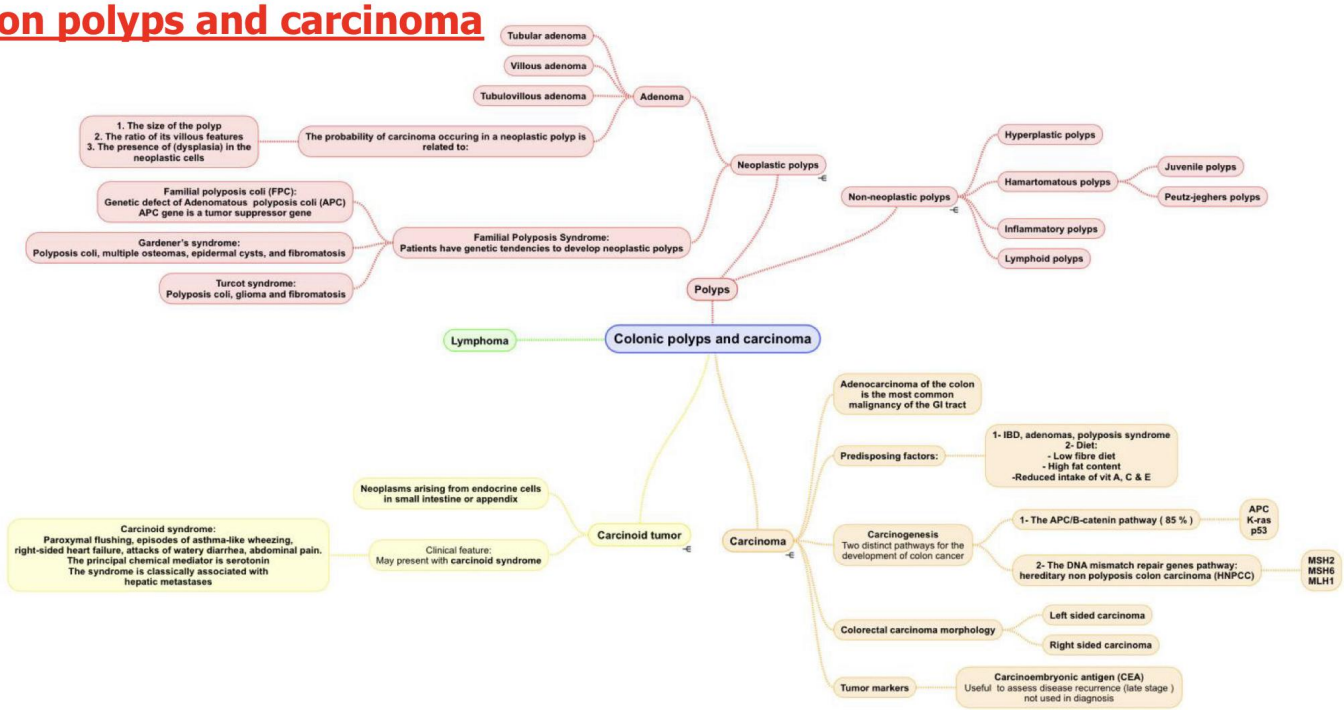
Crohn's disease	Ulcerative colitis
- Any part of the GIT - Skip areas of normal mucosa - Deep ulcers (fissure) - Transmural inflammation - Fistula formation - Creeping mesenteric fat - Fibrous thickening of wall - Granulomas - Dysplasia is rare - Carcinoma is rare	- Colon only - Diffuse involvement of mucosa - Superficial ulcers - Mucosal inflammation only - Fistula formation is not seen - Creeping mesenteric fat is not seen - Fibrous thickening of wall is not seen - Granulomas are not seen - Dysplasia is common - Carcinoma is more common (10%)

Summary

IBD

1-Inflammatory bowel disease is divided into: crohn's disease and ulcerative colitis both disease have immunological hypersensitivity.
2-The manifestation of IBD depend on the area of the intestinal (colon – small intestine – extraintestinal manifestation).
3-Crohn's disease is an inflammation that can affect any part of GIT, but the most common is the terminal ileum.
4- Crohn's disease commonly have perianal lesions (abscesses – fistulas – skin tags).
5- The gross appearance of Crohn's disease : segmental (skip area)– fibrosis – fissures – fistulas- in the mucosa (cobblestone effect) – fat (creeping fat).
6-The microscopic features of Crohn's disease :Distortion of mucosal crypt architecture – transmural inflammation – epithelioid granulomas .
7- The complication of Crohn's disease : intestinal obstruction – fistula .
8- Ulcerative colitis it's start from the rectum going to the colon with continuous manner (without skip).
9- Grossly the UC there is superficial ulceration and under the microscopic there is inflammation restricted only in the mucosa and there is active phase (neutrophil's) and in the chronic phase (crypt atrophy and distortion) and there is no epithelioid granulomas.
10-The complication of UC are toxic megacolon and sclerosing pericholangitis.
11- The dysplasia and carcinoma are common in UC more than CD.

Colon polyps and carcinoma



Questions

Q1: can affect any part of the GI?
A) Crohn's disease
B) Ulcerative colitis
C) Both
D) Neither

Q2: almost always involve the rectum?
A) ulcerative colitis
B) Crohn's disease
C) Both
D) Neither

Q3: on histological examination of the bowel, granulomas are highly suggestive of?
A) crohn's disease
B) Ulcerative colitis
C) Both
D) Neither

Q4: toxic megacolon is a common complication of?
A) crohn's disease
B) Ulcerative colitis
C) Both
D) Neither

Q5: involves the full thickness of the wall?
A) crohn's disease
B) Ulcerative colitis
C) Both
D) Neither

Q6: screening recommended due to increase risk of bowel cancer?
A) both
B) Neither
C) Crohn's disease
D) Ulcerative colitis

Q7: Q9: Strictures are a common complication of?
A) Crohn's disease
B) Ulcerative colitis
C) Both
D) PUD

Q8: on endoscopic or histological examination, pseudopolyps maybe found in:
A) Ulcerative colitis
B) Crohn's disease
C) Both
D) Neither

Q9: What is the most common site of GI polyps, diverticula and cancer?
A) Ascending colon
B) Descending colon
C) Sigmoid colon
D) Transverse colon

Q10: 6. Which one of the following abnormalities associated with adenocarcinoma of the colon?
A) Increase activity of TP53.
B) Over stimulation of ACP gene.
C) Increase activity of β-catenin.
D) Non of the above

Q11:Survival is decreased in Colorectal carcinoma in case of?
A) lymph node metastases
B) mucosal gland metastases
C) brain metastases
D) lung metastases

Q12:Which one of the following is a neoplastic polyp ?
A) Lymphoid polyps
B) Adenoma
C) Inflammatory polyps
D) Hyperplastic polyps

Q13:Which one of the following mechanisms is associated with morphological identifiable changes in adenocarcinoma of the colon?
A) The microsatellite instability pathway.
B) APC mutation\ β-catenin mechanism..

Q14:Most common site of metastatic lesions?
A) Pancreas
B) Heart
C) liver
D) spleen

Questions

Q15: A 57 years old man suffer from high fever, diarrhea, severe pain at his right lower quadrant part of his stomach the pain relieved and relapsed again multiple times, under microscope you saw a cobblestone appearance and fat creeping on sides what is your diagnose?

A)appendicitis
B)Acute phase of Crohn's D
C)chronic phase of Crohn's D
D)Ulcerative colitis

Q16)A 59-year-old man complains of progressive weakness. His friends have noticed that he has become pale, and he reports that his stools are tinged with blood. On abdominal palpation, there is fullness in the right lower quadrant. Laboratory studies show iron-deficiency anemia, Stool specimens are positive for occult blood. Colonoscopy reveals an elevated and centrally ulcerated lesion of the sigmoid colon. Which of the following is the most likely diagnosis?

A) Gastrointestinal stromal tumor
B) Carcinoid tumor
C) Lymphoma
D) Adenocarcinoma

Answers:
1)A
2)A
3)A
4)B
5)A
6)D
7)A
8)A
9)C
10)C
11)A
12)B
13)B
14)C
15)C
16)D

Case 1:

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 painand 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.

Case 2:

A 45-year-old man with a family history of colon cancer undergoes a screening colonoscopy. No invasive carcinomas are identified, but two small pedunculated tubular adenomas are removed and one villous adenoma measuring 5 mm in diameter is biopsied.

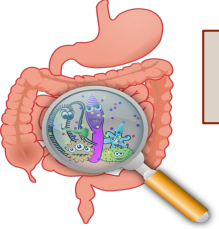
◆ What is the most likely diagnosis?

- Hyperplastic polyps or tubular adenomas.

◆ What are the syndromes that could predispose this individual to colon cancer?

- There are two common inherited colon cancer syndromes.
1-Familial adenomatous polyposis (FAP)
2-hereditary nonpolyposis colon cancer (HNPCC)

Thanks to 434 pathology team!!



Pathoma

IBD and colonic polyps and carcinoma

IV. IRRITABLE BOWEL SYNDROME

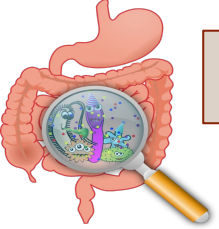
A. Relapsing abdominal pain with bloating, flatulence, and change in bowel habits (diarrhea or constipation) that improves with defecation; classically seen in middle aged females
B. Related to disturbed intestinal motility; no identifiable pathologic changes
C. Increased dietary fiber may improve symptoms.

VII. COLONIC POLYPS

A. Raised protrusions of colonic mucosa
B. Most common types are hyperplastic and adenomatous polyps.
I. Hyperplastic polyps are due to hyperplasia of glands; classically show a 'serrated' appearance on microscopy
i. Most common type of polyp; usually arise in the left colon (rectosigmoid)
ii. Benign, with no malignant potential
2. Adenomatous polyps are due to neoplastic proliferation of glands 2nd most common type of colonic polyp
i. Benign, but premalignant; may progress to adenocarcinoma via the adenoma-carcinoma sequence
3. Adenoma-carcinoma sequence describes the molecular progression from normal colonic mucosa to adenomatous polyp to carcinoma.
i. APC (adenomatous polyposis coli gene) mutations (sporadic or germline) increase risk for formation of polyp
. ii. K-ras mutation leads to formation of polyp.
iii. mutation and increased expression of COX allow for progression to carcinoma; aspirin impedes progression from adenoma to carcinoma.
C. Screening for polyps is performed by colonoscopy and testing for fecal occult blood; polyps are usually clinically silent, but can bleed.
1. Goal is to remove adenomatous polyps before progression to carcinoma.
D. On colonoscopy, hyperplastic and adenomatous polyps look identical. Hence, all polyps are removed and examined microscopically.
1. Greatest risk for progression from adenoma to carcinoma is related to size > 2 cm, sessile growth, and villous histology.

V1Il. FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

A. Autosomal dominant disorder characterized by lOOs to 1000s of adenomatous colonic polyps
B. Due to inherited APC mutation (chromosome 5); increases propensity to develop adenomatous polyps throughout colon and rectum
C. Colon and rectum are removed prophylactically; otherwise, almost all patients develop carcinoma by 40 years of age .
D. Gardner syndrome is FAP with fibromatosis and osteomas.
1. Fibromatosis is a non-neoplastic proliferation of fibroblasts; arises in retroperitoneum (desmoid) and locally destroys tissue
2. Osteoma is a benign tumor of bone that usually arises in the skull.
E. Turcot syndrome is FAP with CNS tumors (medulloblastoma and glial tumors).



IX. JUVENILE POLYP

A. Sporadic, hamartomatous (benign) polyp that arises in children(< 5 years)
l. Usually presents as a solitary rectal polyp that prolapses and bleeds
B. Juvenile polyposis is characterized by multiple juvenile polyps in the stomach and colon; large numbers of juvenile polyps increase the risk of progression to carcinoma.

X. PEUTZ-JEGHERS SYNDROME

A. Hamartomatous (benign) polyps throughout GI tract and mucocutaneous hyperpigmentation (freckle-like spots) on lips, oral mucosa, and genital skin; autosomal dominant disorder
B. Increased risk for colorectal, breast, and gynecologic cancer

XI. COLORECTAL CARCINOMA

A. Carcinoma arising from colonic or rectal mucosa; 3rd most common site of cancer and 3rd most common cause of cancer-related death
I. Peak incidence is 60-70 years of age.
B. Most commonly arises from adenoma-carcinoma sequence; a second important molecular pathway is microsatellite instability (MSI).
1. Microsatellites are repeating sequences of noncoding DNA; integrity of sequence (stability) is maintained during cell division.
2. Instability indicates defective DNA copy mechanisms (e.g., DNA mismatch repair enzymes).
3. Hereditary nonpolyposis colorectal carcinoma (H PCC) is due to inherited mutations in DNA mismatch repair enzymes.
1. Increased risk for colorectal, ovarian, and endometrial carcinoma
ii. Colorectal carcinoma arises de novo (not from adenomatous polyps) at a relatively early age; usually right-sided
C. Screening for colorectal carcinoma occurs via colonoscopy and fecal occult blood testing; begins at 50 years of age
1. Goal is to remove adenomatous polyps before carcinoma develops and to detect cancer early (before clinical symptoms arise).
D. Carcinoma can develop anywhere along entire length of colon.
I. Left-sided carcinoma usually grows as a 'napkin-ring' lesion; presents with decreased stool caliber, left lower quadrant pain, and blood-streaked stool 2. Right-sided carcinoma usually grows as a raised lesion; presents with iron deficiency anemia (occult bleeding) and vague pain. An older adult with iron deficiency anemia has colorectal carcinoma until proven otherwise.
E. Colonic carcinoma is associated with an increased risk for Streptococcus bovis endocarditis.
F. Staging
1. T - depth of invasion; tumors limited to the mucosa generally do not spread due to lack of lymphatics in the mucosa
2. N-spread to regional lymph nodes
3. M - distant spread; most commonly involves the liver
G. CEA is a serum tumor marker that is useful for assessing treatment response and detecting recurrence; not useful for screening

Sketchy pathology

Check the team drive for the video

Crohn's Disease & Ulcerative Colitis

1. **Fiery intestines** : inflammatory bowel disease (IBD) (ulcerative colitis and Crohn disease)
2. **Young white guy** : IBD is most common in young people with Caucasian and Jewish ancestry
3. **Fiery hat** : IBD presents with fever
4. **Thin guy** : IBD presents with weight loss
5. **Clutching abdomen** : IBD presents with abdominal pain
6. **Brown puddle** : IBD presents with diarrhea
7. **Union Cannon** : ulcerative colitis
8. **Rusty rectal stool** : ulcerative colitis ALWAYS affects the rectum
9. **Rust traveling proximally** : ulcerative colitis spreads proximally from rectum (in a CONTINUOUS pattern)
10. **Smooth end of cannon** : in ulcerative colitis, the colon has a "lead pipe" appearance on contrast enema (due to loss of normal haustral projections)
11. **First responders with perinuclear battle plan** : pANCA (PERInuclear anti-neutrophil cytoplasmic antibodies) are elevated in ulcerative colitis
12. **Eroding through 2 layers** : in ulcerative colitis, inflammation affects ONLY the mucosa and submucosa
13. **Dirt islands in hole** : in ulcerative colitis, the colon contains "pseudopolyps" (islands of normal mucosa within ulcerated tissue)
14. **Inflamed cannonball within wall** : on histology, ulcerative colitis displays abscesses within colonic crypts
15. **Shrapnel striking left side** : ulcerative colitis presents with LEFT-sided abdominal pain (due to location in rectum and distal colon)
16. **Bloody puddle** : ulcerative colitis presents with bloody diarrhea (frequent and small volume due to rectal inflammation)
17. **MEGA cannon** : ulcerative colitis can cause toxic megacolon (inflammation extends to colonic smooth muscle → smooth muscle paralysis → severe colonic dilation)
18. **Exploding cannon** : in ulcerative colitis, toxic megacolon can lead to perforation
19. **Cancer crab belt** : ulcerative colitis increases the risk of colon cancer (bigger risk factor than Crohn disease)
20. **Scaly snake in biliary tree** : ulcerative colitis increases the risk of primary sclerosing cholangitis (PSC)(autoimmune disorder of intra- and extrahepatic bile ducts)
21. **Cobblestone patches** : Crohn disease occurs as multiple separate areas of disease ("skip lesions")
22. **Cobblestone path from mouth to anus arch** : Crohn disease can affect ANY portion of the GI tract (from mouth to anus)
23. **Antibody sac** : anti-Saccharomyces cerevisiae antibodies are often present in ulcerative colitis
24. **Hit on right waist** : Crohn disease presents with RLQ abdominal pain (due to location in ileum and cecum)
25. **Debris-littered brown puddle** : Crohn disease presents with malabsorption of fats and fat-soluble vitamins (inflammation of distal ileum → poor reabsorption of bile acids → impaired absorption of fat)
26. **MacroCAGES** : Crohn disease causes formation of noncaseating granulomas (containing aggregations of macrophages)
27. **Broken through all wall layers** : Crohn disease causes TRANSMURAL bowel inflammation
28. **Tight abdominal gauze** : Crohn disease can cause fibrotic strictures (transmural inflammation → bowel wall thickening → narrowed lumen)
29. **Pulling strings** : in Crohn disease, X-ray shows "string sign" (due to strictures)
30. **Obstructing rocks** : in Crohn disease, strictures can cause bowel obstruction
31. **Fistulizing trench** : Crohn disease can lead to fistulas (transmural inflammation leads to epithelization across bowel wall → connections between bowel and bladder, skin, vagina, or other bowel segments)
32. **Pale erosions on mouth arch** : Crohn disease causes aphthous ulcers in the mouth and esophagus
33. **Wrapped joints** : inflammatory bowel disease can cause arthritis (migratory polyarthritis, sacroiliitis, ankylosing spondylitis)(often HLA-B27)
34. **Red spots on shin columns** : inflammatory bowel disease can cause erythema nodosum (painful erythematous nodular rash on shins)(due to inflammation of fat cells)
35. **Skin wounds** : inflammatory bowel disease can cause pyoderma gangrenosum (skin ulcers due to neutrophil dysfunction) (not infectious or gangrenous)
36. **Shrapnel on kidney tray** : inflammatory bowel disease can cause renal calculi (due to increased absorption of oxalate)
37. **Red-rimmed goggles** : inflammatory bowel disease can cause eye disease (anterior uveitis, iritis, episcleritis)(presents with eye pain and redness)
38. **5-pointed star of USA** : inflammatory bowel disease is treated with 5-ASA (sulfasalazine, mesalamine)

كل الشكر والتقدير للجهود العظيمة
من قبل أعضاء فريق علم الأمراض الكرام.

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