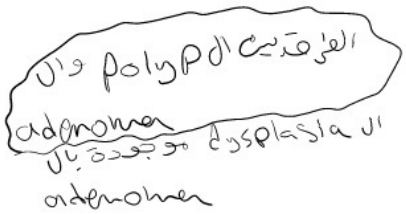
COLONIC POLYPS AND NEOPLASTIC DISEASE



- Colon is most common site for polyps
- *Sessile polyp:* no stalk
- *Pedunculated polyp:* stalk
- *Non neoplastic polyps:* inflammatory, hamartomatous, or hyperplastic.
- *Neoplastic polyps: adenoma.* (there is dysplasia

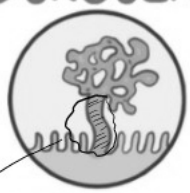
POLYPS CLASSIFIED by APPEARANCE

FLAT

* DON T PROTRUDE into the LUMEN
* FLAT AGAINST the MUCOSA

- تغرقها كن ال tissue
العادي كنا طريق اللون (يكون
لونها أكثر احمرار)

PEDUNCULATED



* PROTRUDE into the LUMEN
* ATTACHED to the WALL by a STALK

SESSILE

* PROTRUDE into the LUMEN
* BASE ATTACHED to the MUCOSA

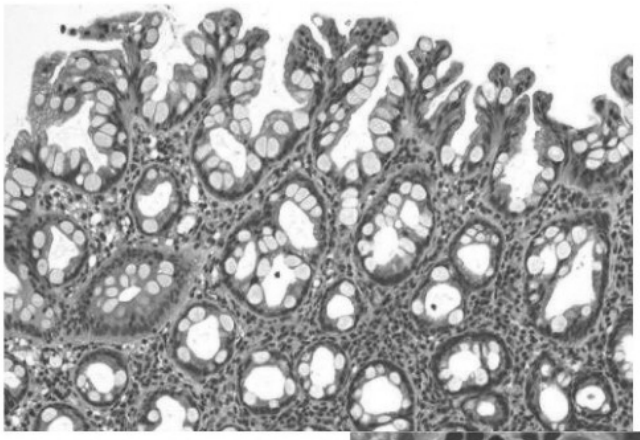
Hyperplastic Polyps

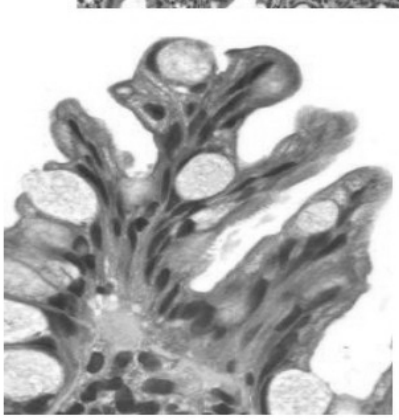
- Common
- 5th-6th decade.
- Decreased epithelial turnover and delayed shedding of surface epithelium >>> pileup of goblet cells & epithelial overcrowding
- No malignant potential

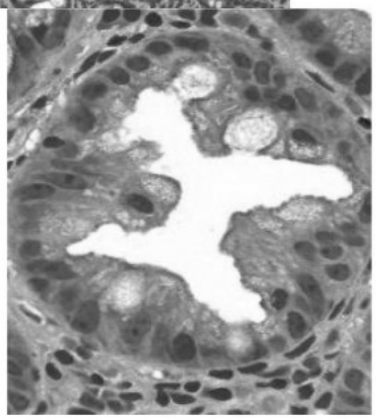
Hyperplastic polyp

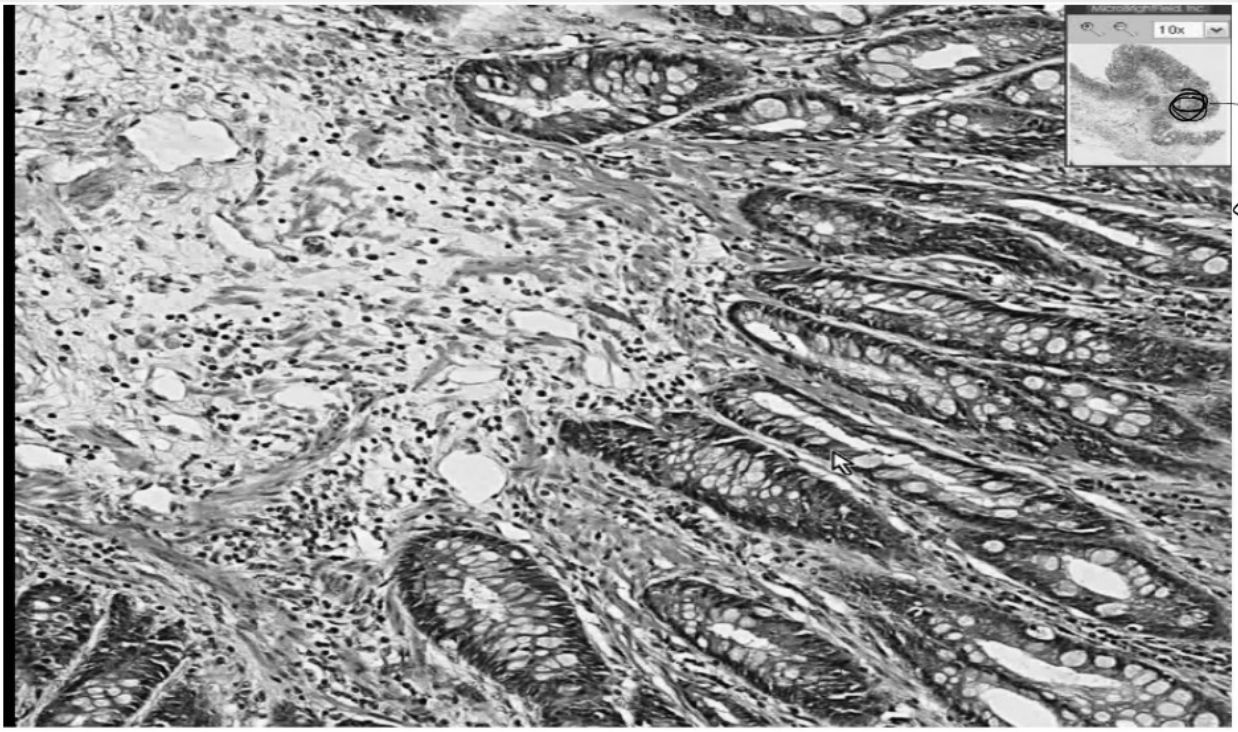
- Left colon (common site)
- Rectosigmoid.
- Small < 5 mm
- Multiple

- Crowding of goblet & absorptive cells. بعض كل منتظم
- Serrated surface: hallmark of these lesions (Serrated polyps)



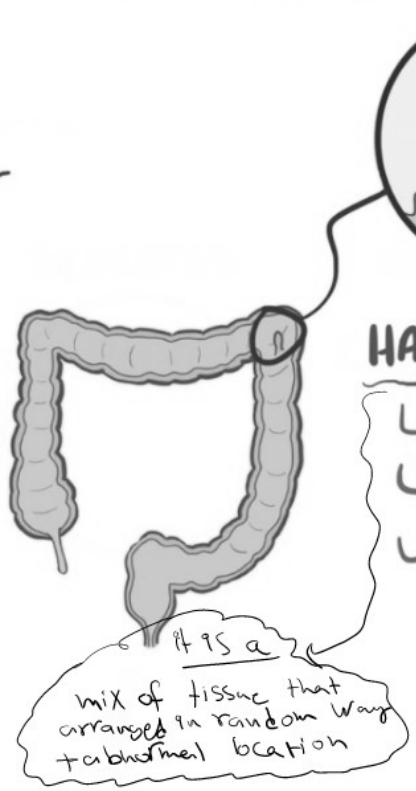





10x
NO
- hyperchromatic
nucleus

INFLAMMATORY POLYPS

- FOLLOW BOUTS of
  - * ULCERATIVE COLITIS
  - * CROHN'S DISEASE
- NOT MALIGNANT



HAMARTOMATOUS POLYPS

- MIX of TISSUES
- DISTORTED ARCHITECTURE
- ASSOCIATED WITH:
  - * JUVENILE POLYPOSIS
  - * PEUTZ-JEGHER'S SYNDROME

it is a mix of tissue that arranged in random way + abnormal location

2 Inflammatory Polyps

- *Solitary rectal ulcer syndrome.* + ulcerative colitis + crohn disease
- Recurrent abrasion and ulceration of the overlying rectal mucosa.
- **Chronic cycles of injury and healing give a polypoid mass of inflamed and reactive mucosal tissue.** + proliferation of muscularis layar and reach mucosa

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MACROCEPHALY

HYPOTONIA

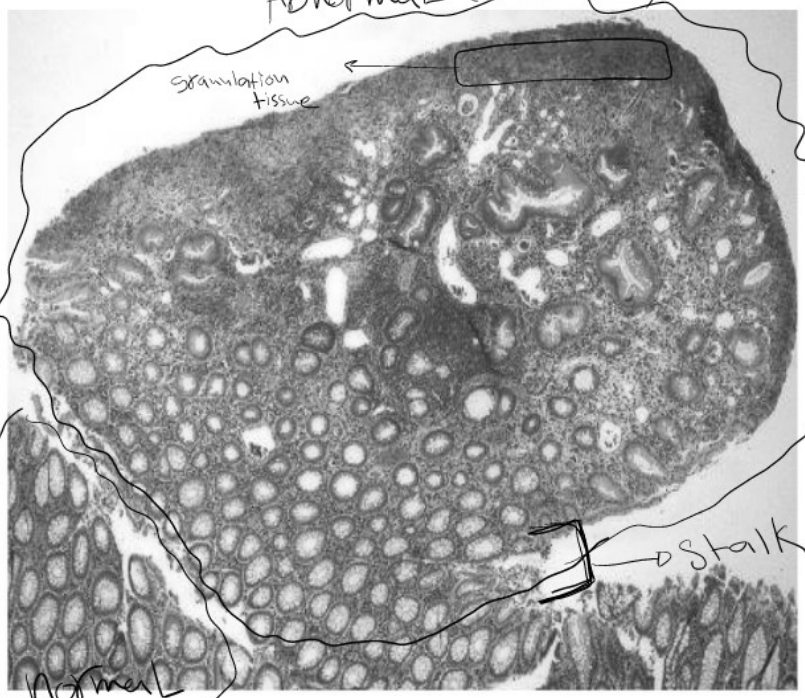
HAMARTOMAS

متعلق بـ Syndrome معناه كرش
يصيب أكثر من عضو واحد

Juvenile Polyps

- Pedunculated
- Reddish lesions
- Cystic spaces on cut sections
- Dilated glands filled with mucin and inflammatory debris.
- Granulation tissue on surface.

In The Pedunculated Polyp There is increased risk for ulcer Stool ... ←



5 Peutz-Jeghers Syndrome

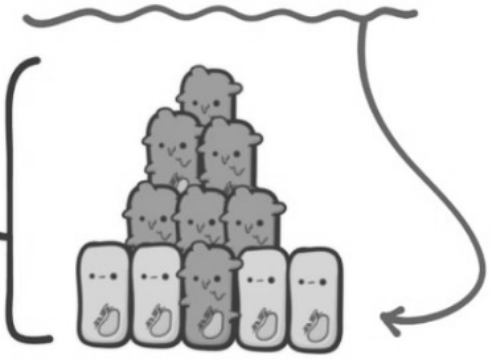
- AD. → Autosomal dominant
- Mean age: 10-15 years.
- Multiple gastrointestinal hamartomatous polyps
- Most common in the small intestine.
- Mucocutaneous hyperpigmentation
- Increased risk for several malignancies: colon, pancreas, breast, lung,
  ovaries, uterus, and testes,

- *LKB1/STK11* gene mutation.

we should scan other family members

PEUTZ-JEGHERS SYNDROME

MUTATION OF THE **STK11 GENE**



GI CELLS
1. **ACCUMULATE MUTATIONS**
&
2. DIVIDE **FASTER** THAN USUAL

POLYP

3.
* **BENIGN** OUTGROWTHS
* **MOSTLY** IN THE **SMALL INTESTINE**
* ACCUMULATE **MORE MUTATIONS**
  - K-RAS
  - P53

CANCER

* ONE **POLYP**
  ~ LOW CANCER RISK
* MANY **POLYPS**
  ~ SIGNIFICANT CANCER RISK

PEUTZ-JEGHERS SYNDROME

MUTATION OF THE **STK11 GENE**

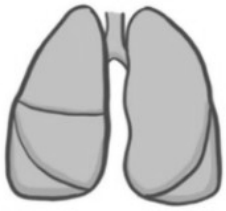
EXPRESSED IN **LOTS** OF **TISSUES**

* INCREASED RISK **CANCERS** OF *

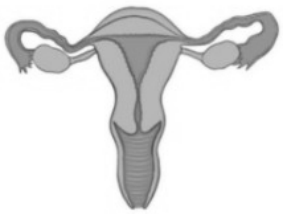
PANCREAS

BREAST

LUNGS



OVARIES AND UTERUS

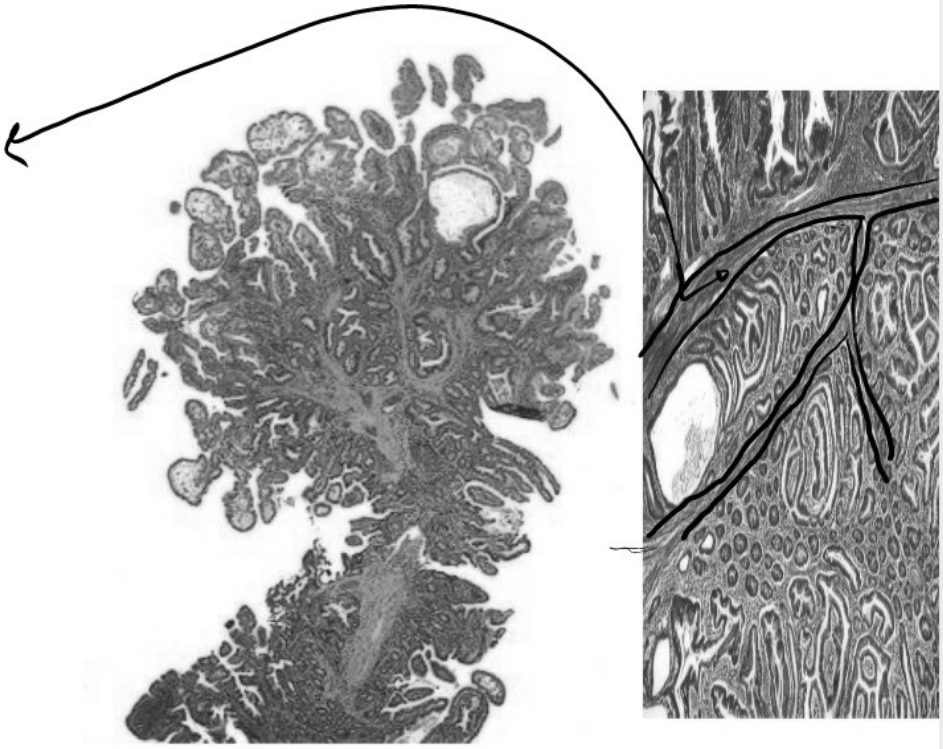


نسبتها أقل

TESTICLES

Peutz-Jeghers polyp

- Large.
- Arborizing network of connective tissue, smooth muscle, lamina propria
- Glands lined by normal-appearing intestinal epithelium
  - Christmas tree pattern.

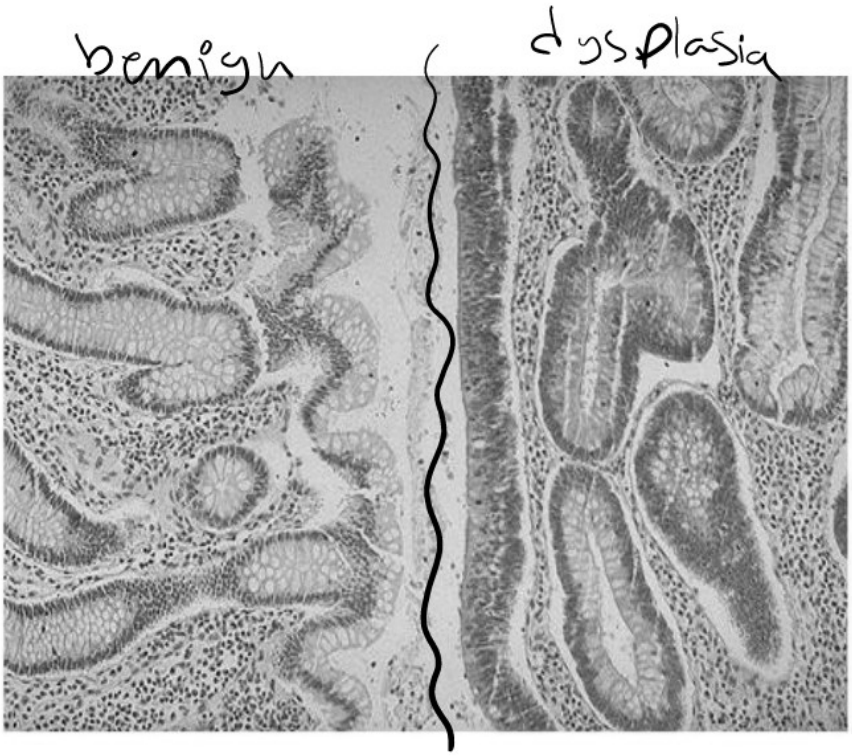


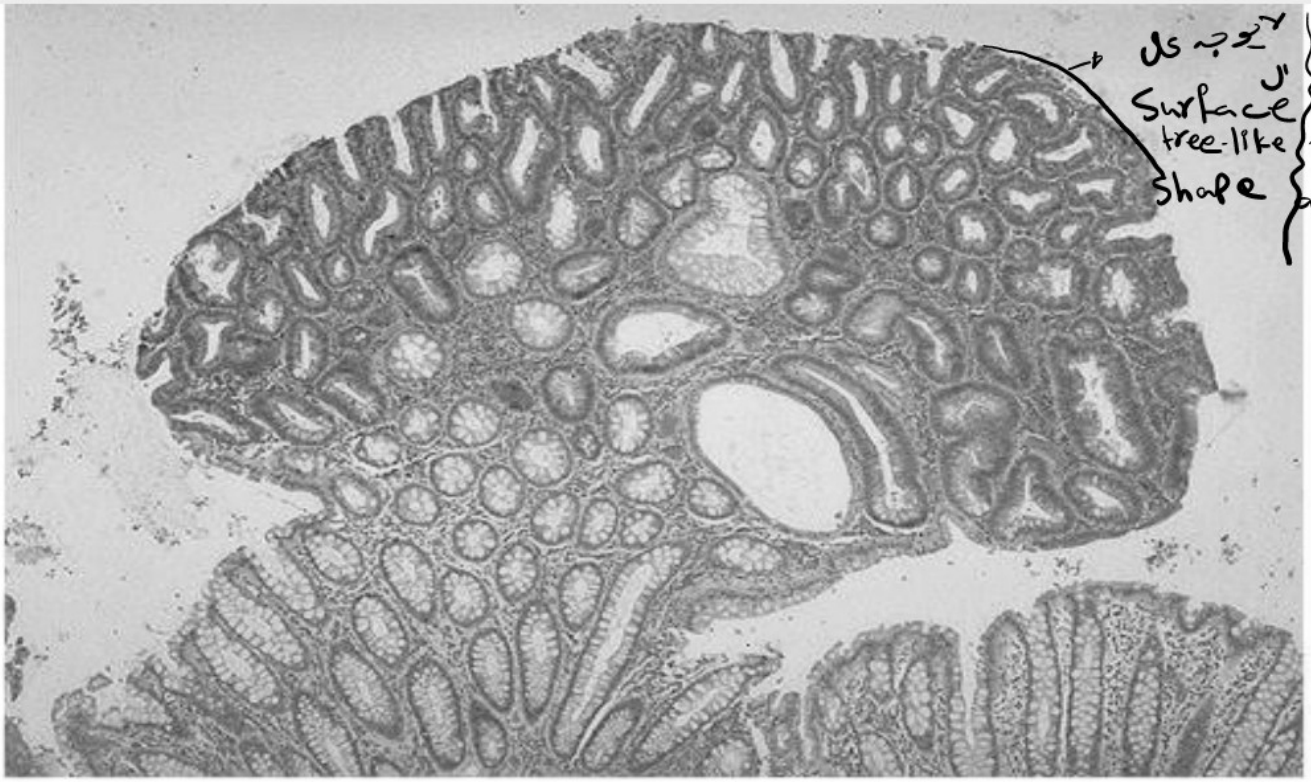
Adenomas

- Most common and clinically important
- *Increase with age.*
- *Definition: presence of epithelial dysplasia (low or high)*
- **Precursor for majority of colorectal adenocarcinomas**
- ***Most adenomas DO NOT progress to carcinoma.***
- *USA: screening colonoscopy starts at 50 yrs.*
- *Earlier screening with family history.*
- **Western diets and lifestyles increase risk.**

Colon adenoma

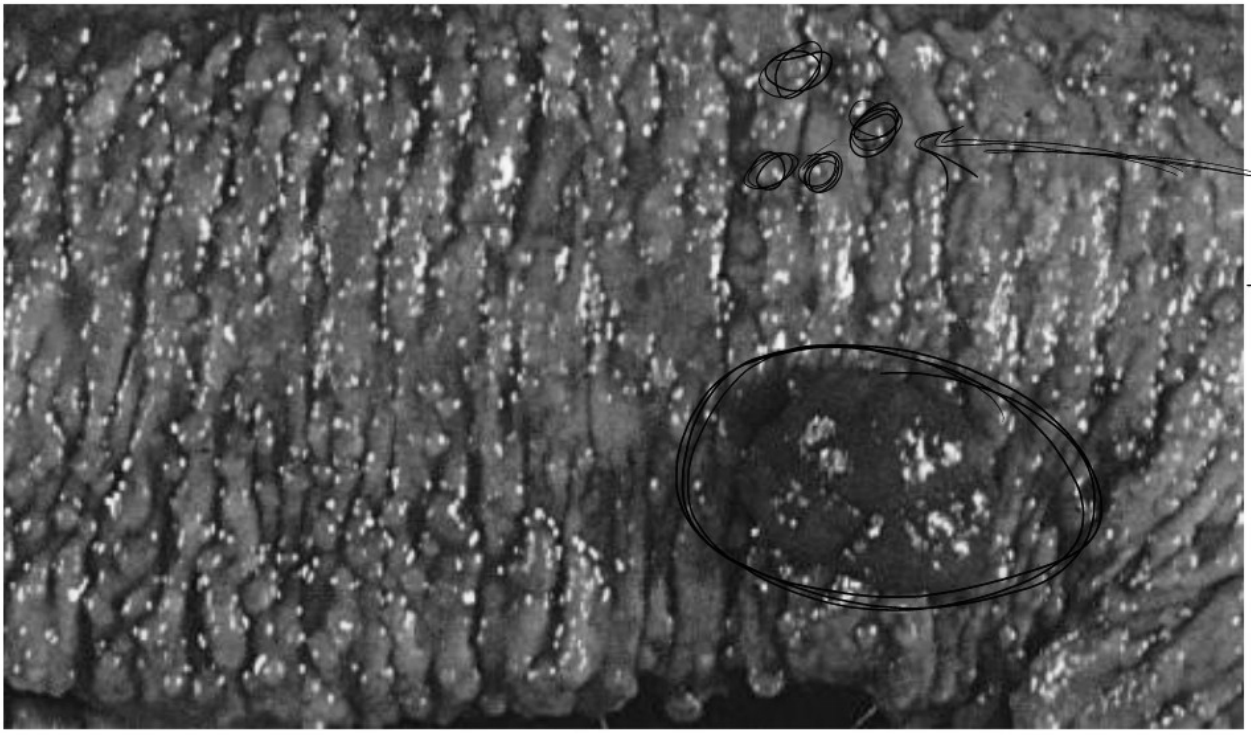
- **Hallmark: epithelial dysplasia**
- **Dysplasia**: nuclear hyperchromasia, elongation, stratification, high N/C ratio.
- **Size : most important correlate with risk for malignancy**
  more than 5 cm
- **High-grade dysplasia is the second factor**




الشوجه لل
Surface
tree-like
Shape
Tubular
adenoma

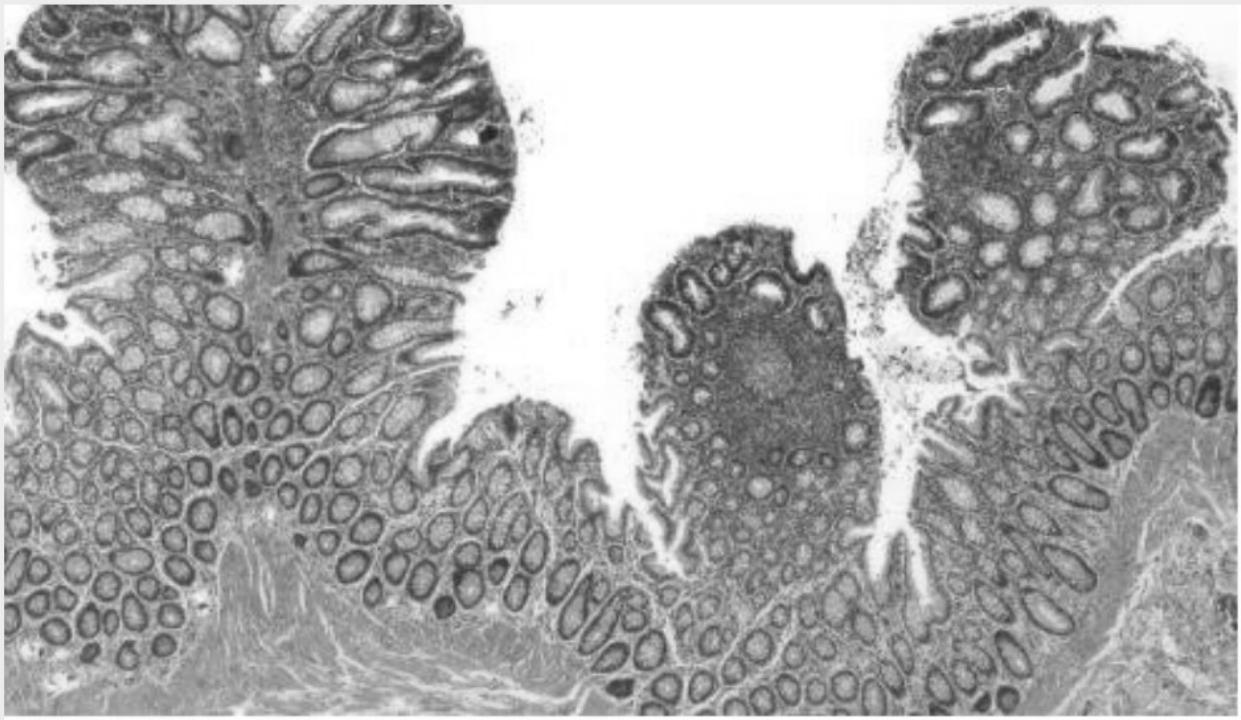
1 Familial adenomatous polyposis (FAP)

- Autosomal dominant.
- Numerous colorectal adenomas: teenage years.
- Mutation in APC gene.
- At least 100 polyps are necessary for a diagnosis of classic FAP.
- Morphologically similar to sporadic adenomas
- 100% of patients develop colorectal carcinoma, IF UNTREATED, often before age of 30.
- Standard therapy: prophylactic colectomy before 20 Year of age.
- Risk for *extraintestinal manifestations*,



- في بداية القولون
أكثر من
100
Polyp

دائمًا ال
Tumors
اللي بتكون مع
Syndrome
Prognosis ال يكون
PAD تبعها



3 Villous adenoma

2 Hereditary Nonpolyposis Colorectal Cancer

(HN*PCC*, L*ynch syndrome*)

- Clustering of tumors: **Colorectum, endometrium, stomach, ovary, ureters, brain, small bowel, hepatobiliary tract, and skin**
- Colon cancer at younger age than sporadic cancers
- Right colon with excessive mucin production .
- Adenomas are present, BUT POLYPOSIS IS NOT.

- **Inherited germ line mutations in DNA mismatch repair genes.**
- Accumulation of mutations in *microsatellite DNA (short repeating sequences)*
- Resulting in *microsatellite instability*
- Majority of cases involve either *MSH2* or *MLH1*

Colonic Adenocarcinoma

- Most common malignancy of the gastrointestinal tract
- Small intestine is uncommonly involved by neoplasia.
- Peak: 60 to 70 years
- 20% under 50 years. (familial cases)
- **Low intake of vegetable fibers and high intake of carbohydrates and fat.**
- Aspirin or other NSAIDs have a protective effect.
- Cyclooxygenase-2 (COX-2) promotes epithelial proliferation.

Pathogenesis

- Sporadic >>>> familial.
- **Two pathways:**
- **APC/β-catenin pathway >> increased WNT signaling.**
- **Microsatellite instability pathway >> defects in DNA mismatch repair.**
- Stepwise accumulation of multiple mutations.

هذا الجين كمالو ← Villous adenoma

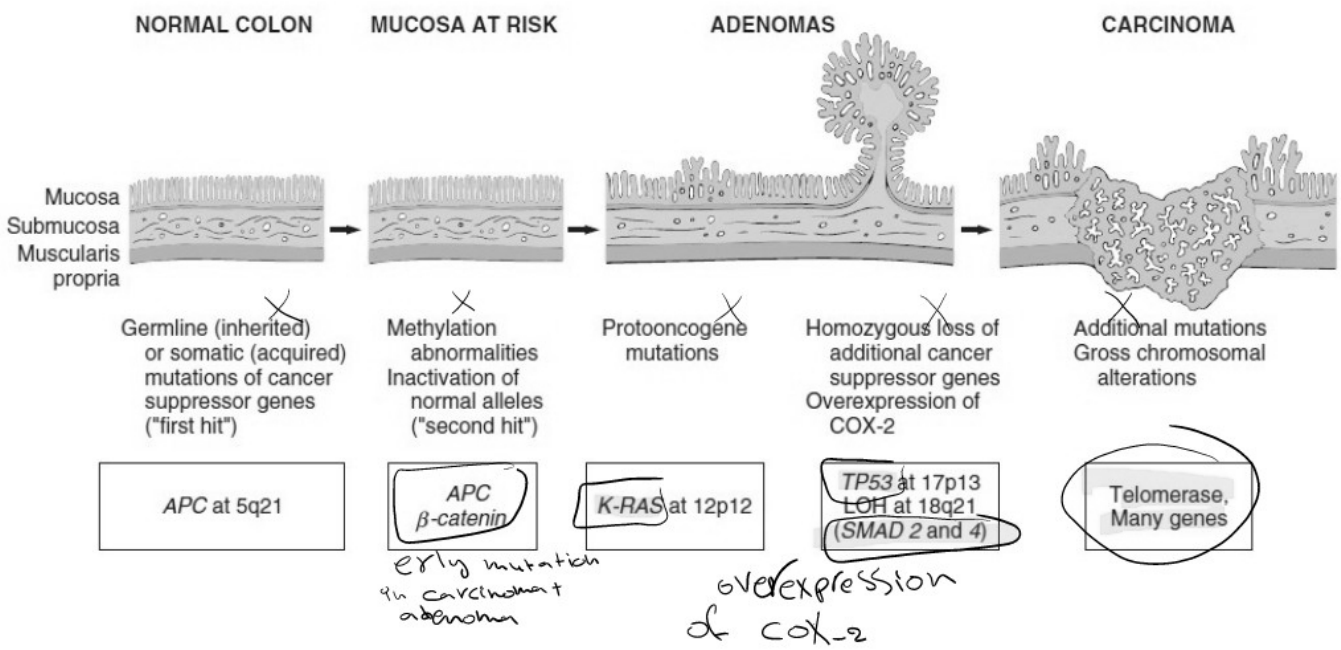
The APC/β-catenin pathway:

chromosomal instability

- **Classic *adenoma carcinoma sequence*.**
- ***80%* of sporadic colon tumors**
- Mutation of the *APC* tumor suppressor gene: EARLY EVENT
- *APC is a key negative regulator of β-catenin, a component of the WNT signaling pathway.*
- *Both copies of APC should be inactivated for adenoma to develop (1st and 2nd hits).*

sporadic 80% + familial

- *Loss of APC >>> accumulation of B-catenin >> enters nucleus >> MYC and cyclin-D1 transcription >>* promote proliferation.
- Additional mutations >> activation of KRAS *(LATE EVENT) >> inhibits apoptosis.*
- *SMAD2* and *SMAD4* *mutations (tumor suppressor genes.)*
- ***TP53* is mutated in 70% -80% of colon cancers (LATE EVENT IN INVASIVE)**
- TP53 inactivation mutation
- Expression of telomerase also increases as the tumor advances.

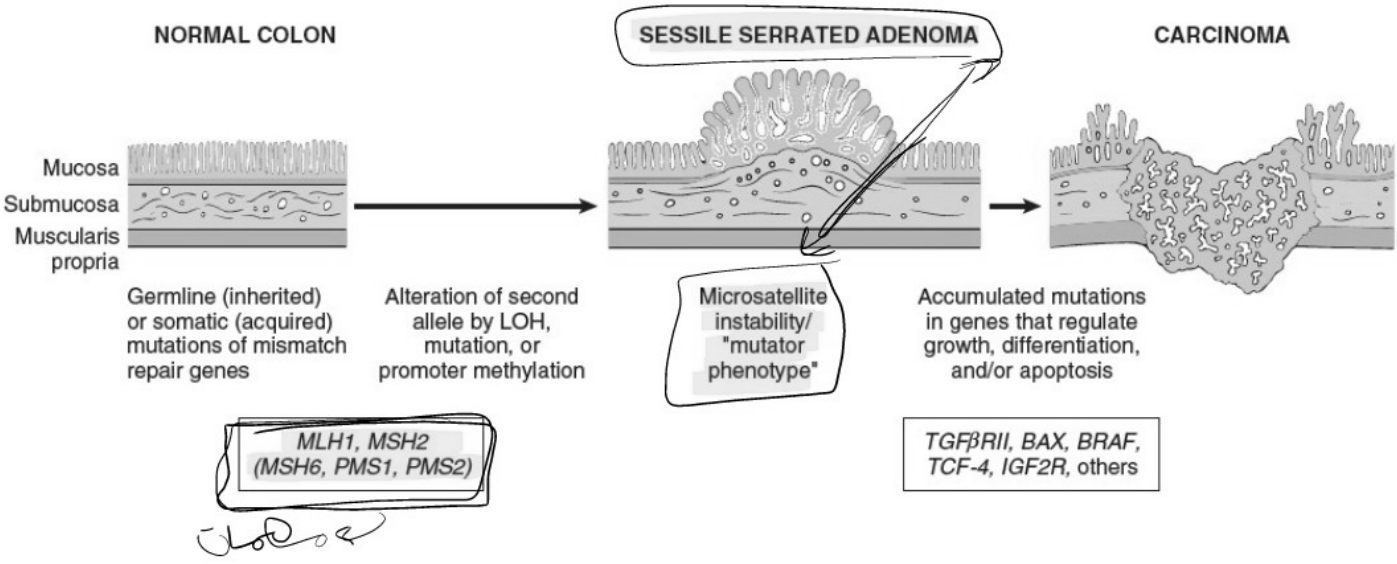

NORMAL COLON
MUCOSA AT RISK
ADENOMAS
CARCINOMA
Mucosa
Submucosa
Muscularis propria
Germline (inherited) or somatic (acquired) mutations of cancer suppressor genes ("first hit")
Methylation abnormalities
Inactivation of normal alleles ("second hit")
Protooncogene mutations
Homozygous loss of additional cancer suppressor genes
Overexpression of COX-2
Additional mutations
Gross chromosomal alterations
APC at 5q21
APC β-catenin
K-RAS at 12p12
TP53 at 17p13
LOH at 18q21
(SMAD 2 and 4)
Telomerase,
Many genes

The microsatellite instability pathway

موجودة بال Lynch Syndrome

- DNA mismatch repair deficiency
- Loss of mismatch repair genes
- Mutations accumulate in microsatellite repeats
- *Microsatellite instability*

- Silent if microsatellites located in noncoding regions
- Uncontrolled cell growth if located in coding or promoter regions of genes involved in cell growth and apoptosis (TGF-B and BAX genes)


NORMAL COLON
SESSILE SERRATED ADENOMA
CARCINOMA
Mucosa
Submucosa
Muscularis propria
Germline (inherited) or somatic (acquired) mutations of mismatch repair genes
Alteration of second allele by LOH, mutation, or promoter methylation
Microsatellite instability/ "mutator phenotype"
Accumulated mutations in genes that regulate growth, differentiation, and/or apoptosis
MLH1, MSH2 (MSH6, PMS1, PMS2)
TGFβRII, BAX, BRAF, TCF-4, IGF2R, others

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

Left side → APC/WNT Path way
right side → DNA mismatch repair

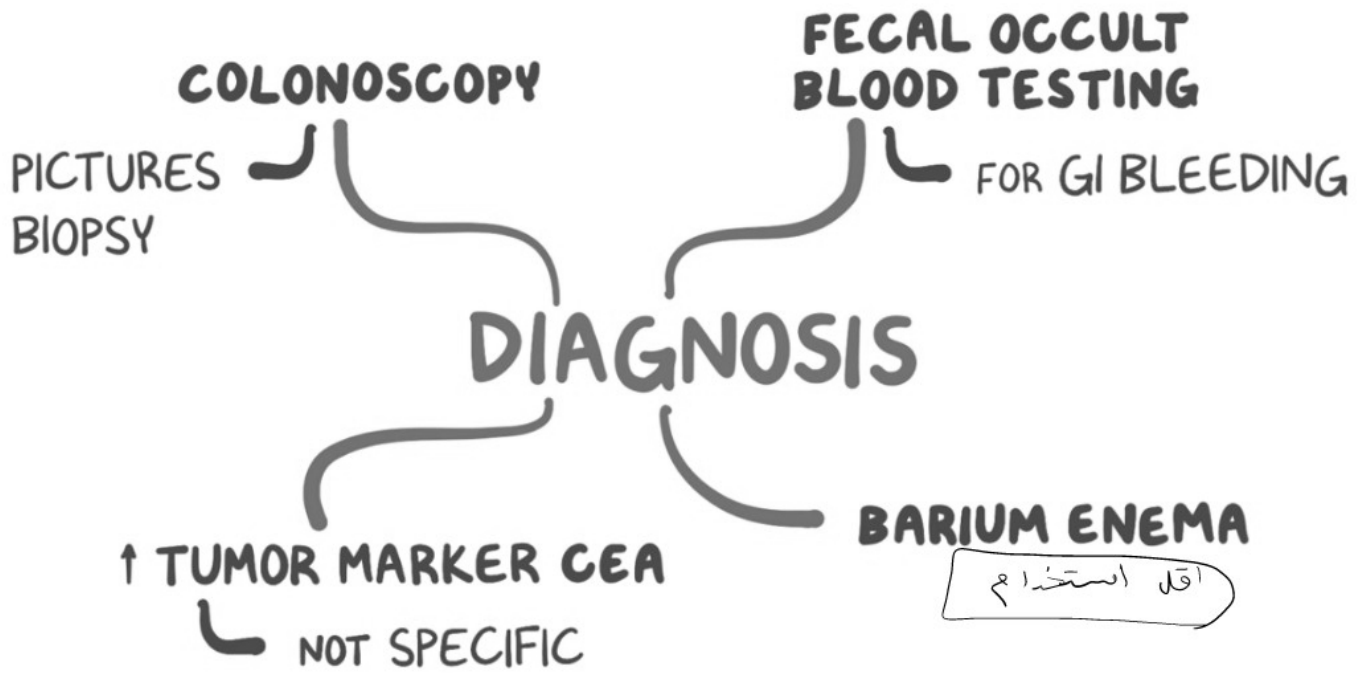
Clinical Features

- Endoscopic screening > > cancer prevention
- Early cancer is asymptomatic !!!!!!!!
- Cecal and right ~~side cancers:~~ *Fatigue and weakness (iron deficiency anemia)*
- **Iron-deficiency anemia in an older male or postmenopausal female is gastrointestinal cancer until proven otherwise.**
- *Left sided carcinomas: occult bleeding, changes in bowel habits, cramping* left lower-quadrant discomfort.

- Poor differentiation and mucinous histology > > poor prognosis

- ***Most important two prognostic factors are***
- ***Depth of invasion***
- ***Lymph node metastasis.***] → staging

- *Distant metastases (lung and liver) can be resected.*


COLONOSCOPY
PICTURES
BIOPSY
FECAL OCCULT BLOOD TESTING
FOR GI BLEEDING
DIAGNOSIS
↑ TUMOR MARKER CEA
NOT SPECIFIC
BARIUM ENEMA
اقل استخدام

ACUTE APPENDICITIS

- Most common in adolescents and young adults.
- May occur in any age.
- Difficult to confirm preoperatively
- DDx :– differential diagnosis
  - Mesenteric lymphadenitis,
  - Acute salpingitis,
  - Ectopic pregnancy,
  - Mittelschmerz (pain associated with ovulation),
  - Meckel diverticulitis.

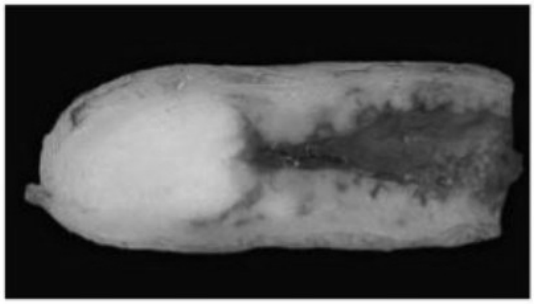

fecalith
HÔPITAL
SAINTE-JUSTINE
1 cm

TUMORS OF THE APPENDIX

- **The most common tumor: *carcinoid* (neuroendocrine tumor)**
- Incidentally found during surgery or on examination of a resected appendix
- Distal tip of the appendix
- Nodal metastases & distant spread are rare.

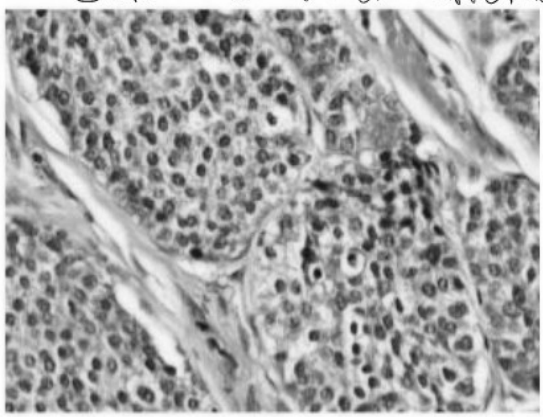
mtz is rare

Carcinoid tumor



Gross

Salt and pepper apperance



Microscopic