GI

Pathology

LEC no.

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Intestinal pathology, part 3

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Key : You will find The Doctor's explanation in blue color
And the important points (in the slides) in red

Diseases of the intestines are divided into:

- Intestinal obstruction
- Vascular disorders
- Malabsorptive diseases and infections
- Inflammatory intestinal diseases.
- **Polyps and neoplastic diseases**

COLONIC POLYPS AND NEOPLASTIC DISEASE

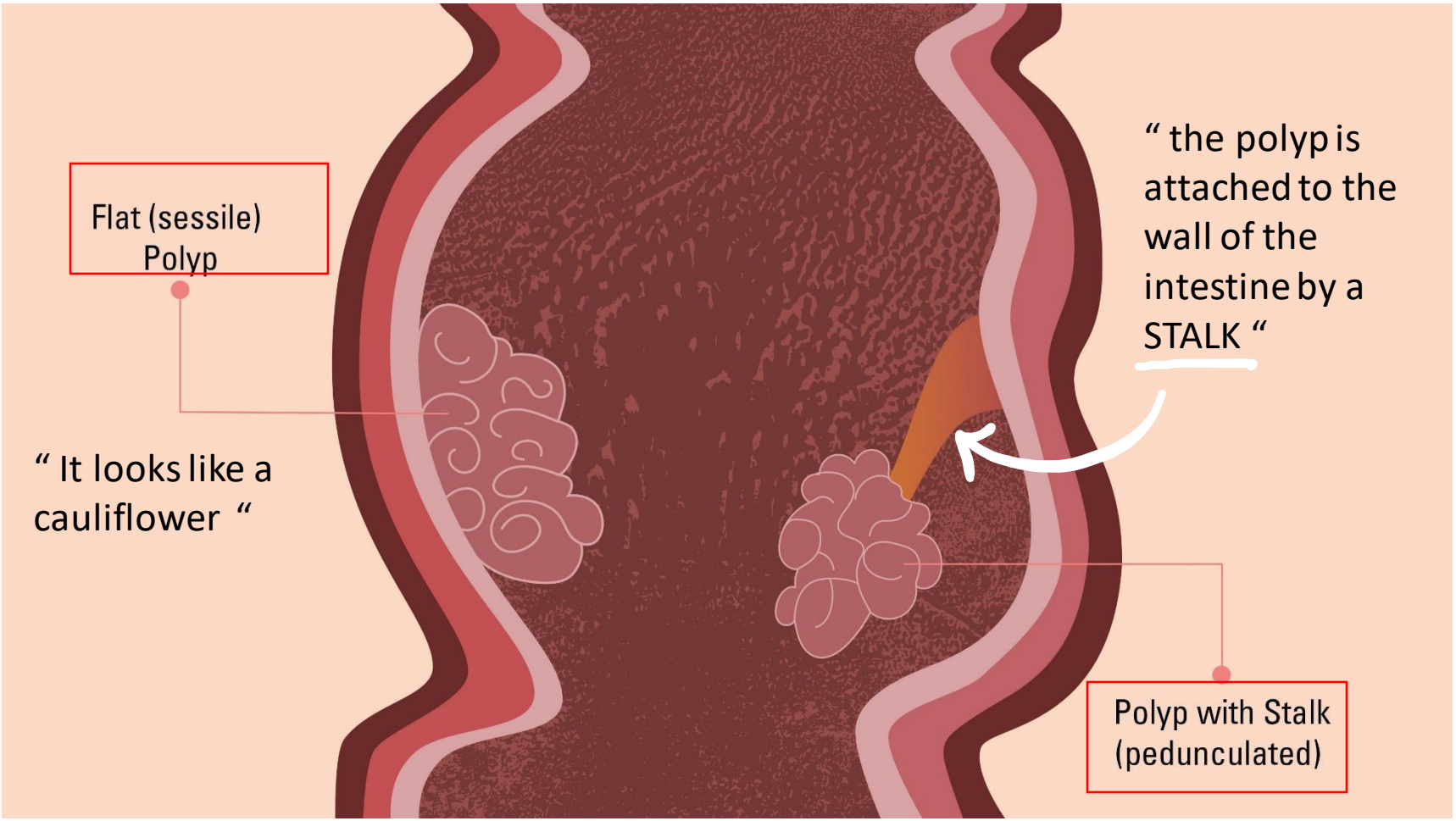
The polyps could be sessile or pedunculated according to their architecture that is seen upon colonoscopy .

- Colon is most common site for polyps
- ***Sessile polyp****:* no stalk
- ***Pedunculated polyp****: attached to the intestine by a stalk.*

Polyps can also be divided into :

- ***Neoplastic polyps****: are* ***adenomas*** *in which there is dysplasia, and are considered precursors of malignancy.*
- ***Non neoplastic polyps****: a group of polyps that are* inflammatory, hamartomatous, or hyperplastic

This picture shows the difference between sessile poly & pedunculated polyp - reminder; a polyp is any outgrowth that is above the level of mucosa.



Inflammatory Polyps

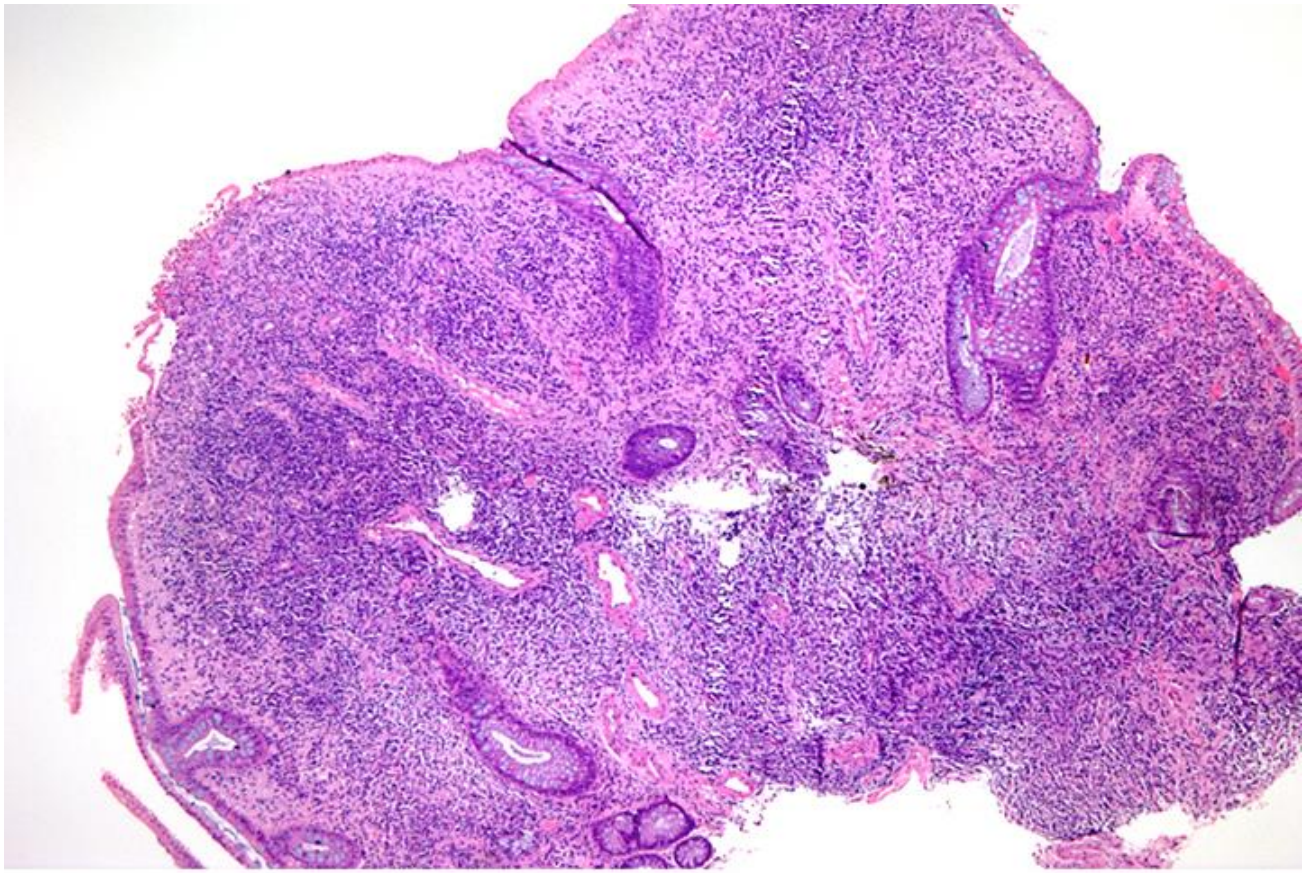
The typical type of inflammatory polyps :

- Solitary rectal ulcer syndrome.
- It is due to Impaired relaxation of anorectal sphinctor.
- This will lead to recurrent abrasion and ulceration of the overlying rectal mucosa over the sphincter.
- Chronic cycles of injury and healing give a polypoid mass of inflamed and reactive mucosal tissue.

- Rectal bleeding, mucus discharge and polyp.

The patient comes to you complaining of rectal bleeding with mucus discharge , then upon examination or colonoscopy you will find these polyps

Inflammatory polyps



4x: low power, dense inflammation in lamina propria

Histo pathological examination of the Polyp will reveal an inflammatory mass , filled with inflammatory cells . The surface of the polyp is ulcerated and eroded. The bluish fossae is due to the inflammatory cells , which could be lymphocytes,plasma cells , neutrophils. The glands are scant and only few glands are left because of the destruction by inflammation , and these glands are benign looking. Inflammatory polyps can also be seen in the inflammatory bowel diseases .

The 2nd type of non-neoplastic polyps:

Hamartomatous Polyps

If we look at the colon and find a disorganized mass which is composed of glands , smooth muscles , nerves and blood vessels, all of these tissues are native to the colon and can be found normally there , but when they form a disorganized mass then we call it a hamartomatous polyp .

The 2 types (sporadic and syndromic) look the same under the microscope

- They can be Sporadic or syndromic.
- Hamartomatous polyposis syndromes are the syndromic ones .
- Hamartoma means : a Disorganized, tumor-like growth composed of mature cell types normally present at that site.
- Hamartomatous polyps can be :
- Juvenile Polyps (more common)
- Peutz-Jeghers Syndrome

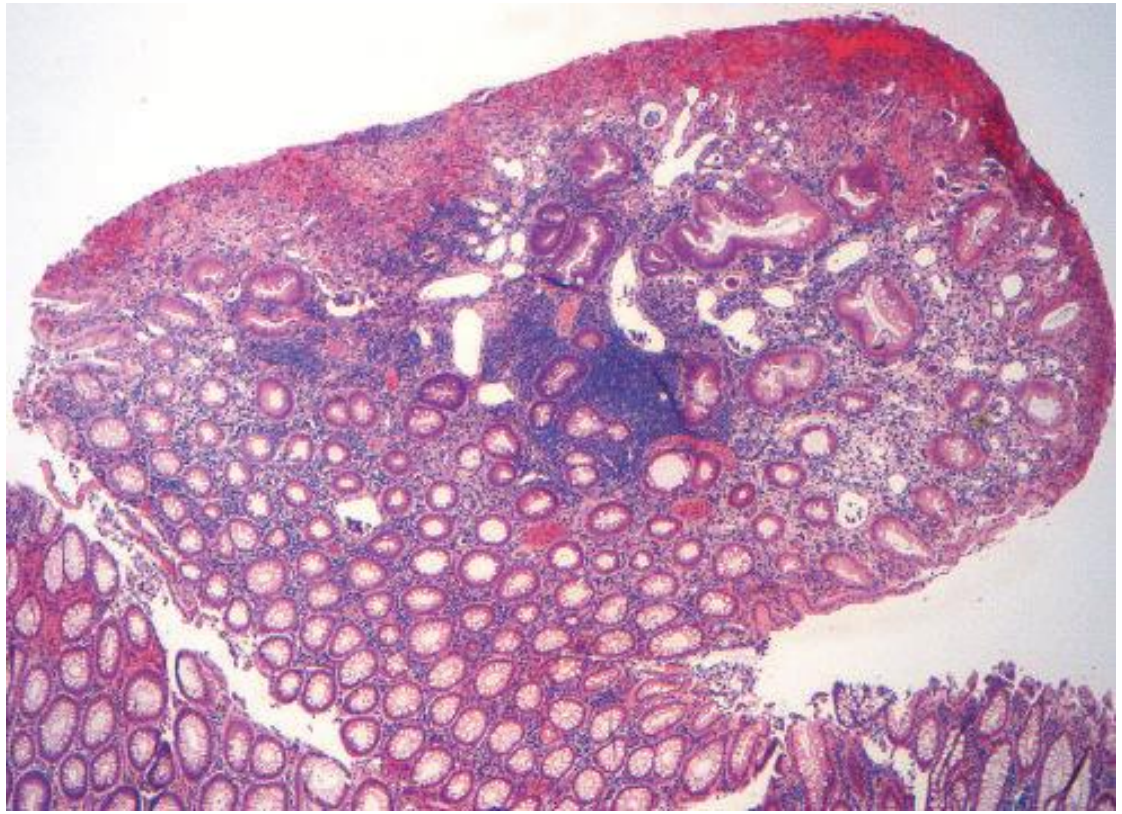
Juvenile Polyps

- Most common hamartomatous polyp
- **Sporadic**
- They are usually solitary (only one polyp)
- Solitary. <5 years of age
- Rectum, bleeding.

- **Syndromic (**juvenile polyposis) **.**
- Dozens (not a single polyp)
- . < 5 years
- Autosomal dominant.
- Transforming growth factor-β (TGF-β) signaling pathway germline mutation (SMAD4).
- Increased risk for colonic adenocarcinoma and others.

Juvenile Polyps

These polyps are devoid of dysplasia and they are considered benign polyps , but if they are part of a syndrome they offer an increased risk of malignancy



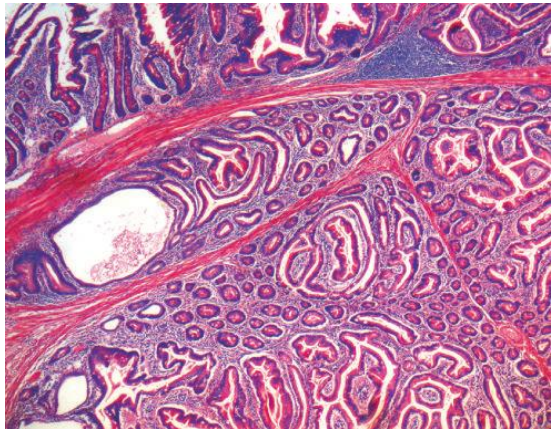
- They are usually Pedunculated (they have a stalk)
- Reddish lesions (due to surface ulcerations, granulation tissue and blood vessels formation)
- Cystic spaces on cut section , which corresponds to the Dilated glands filled with mucin and inflammatory debris.
- Granulation tissue on surface.

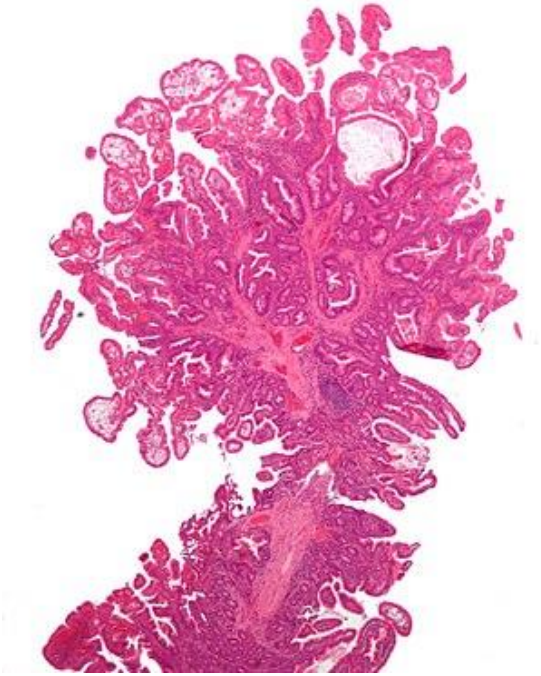
Peutz-Jeghers Syndrome

- These polyps mostly present as a syndrome, which is Autosomal dominant, rare
- This syndrome is characterized by a triad of manifestations :
- **1. Multiple gastrointestinal hamartomatous polyps**
- **2. Mucocutaneous hyperpigmentation, increased melanin pigment in skin and mucous membrane of the mouth.**
- **3. Increased risk for several malignancies: colon, pancreas, breast, lung, ovaries, uterus, and testes,**

- *LKB1/STK11* germline mutation (which encodes a tumor suppressor protein).

Peutz-Jeghers polyp

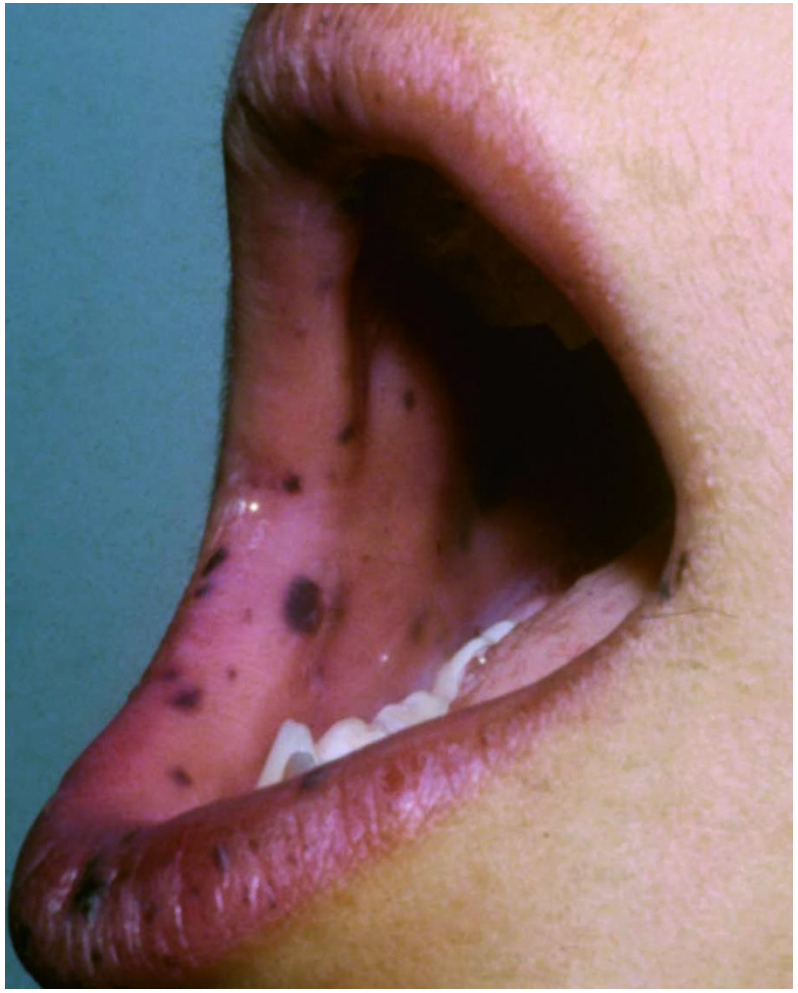


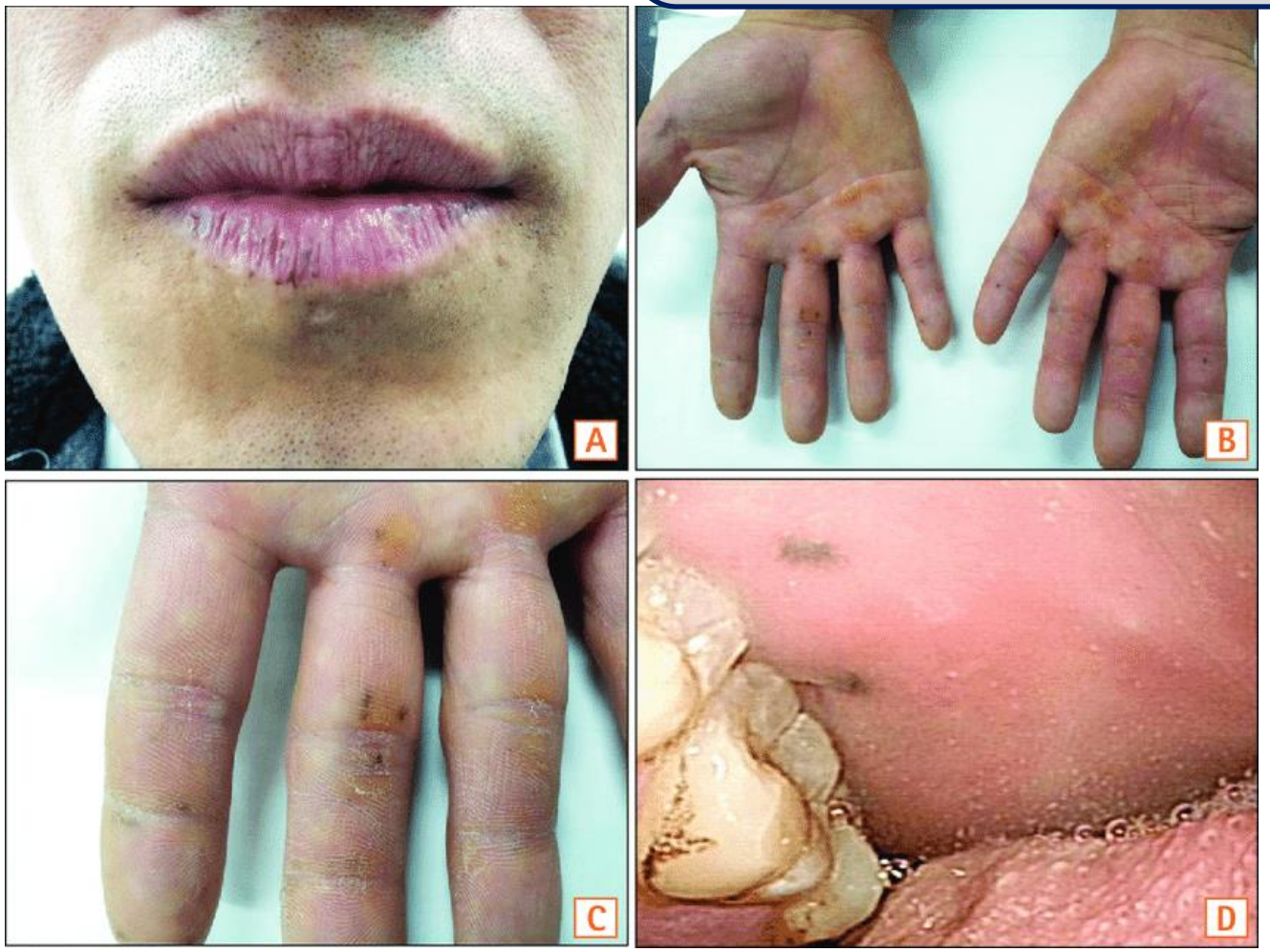


- Mostly in small intestine.
- Large, pedunculated, lobulated.
- Arborizing network of connective tissue, smooth muscle, lamina propria and glands
- The glands are lined by a Normal-appearing intestinal epithelium (no dysplasia but they offer an increased risk of malignancy as part of a syndrome) .
- Christmas tree pattern.

Mucocutaneous pigmentation

locations:
oral mucosa, over the lips, on the hands and on the roof of the mouth.

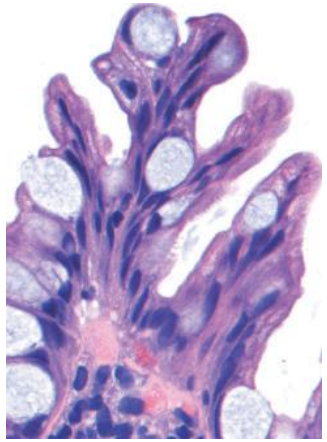


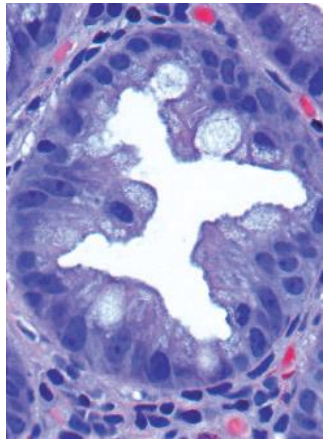


Hyperplastic Polyps (non-neoplastic)

- Common
- 6-7th decades.
- Decreased epithelial turnover and delayed shedding of surface epithelium (so cells won't die and they will accumulate) >>> pileup of goblet cells & epithelial overcrowding
- **No malignant potential**
- **Biopsy is important to differentiate them from other types of polyps , because all polyps will look the same upon colonoscopy, but the gold standard method to differentiate them is the histo pathological appearance and the presence or absence of dysplasia .**

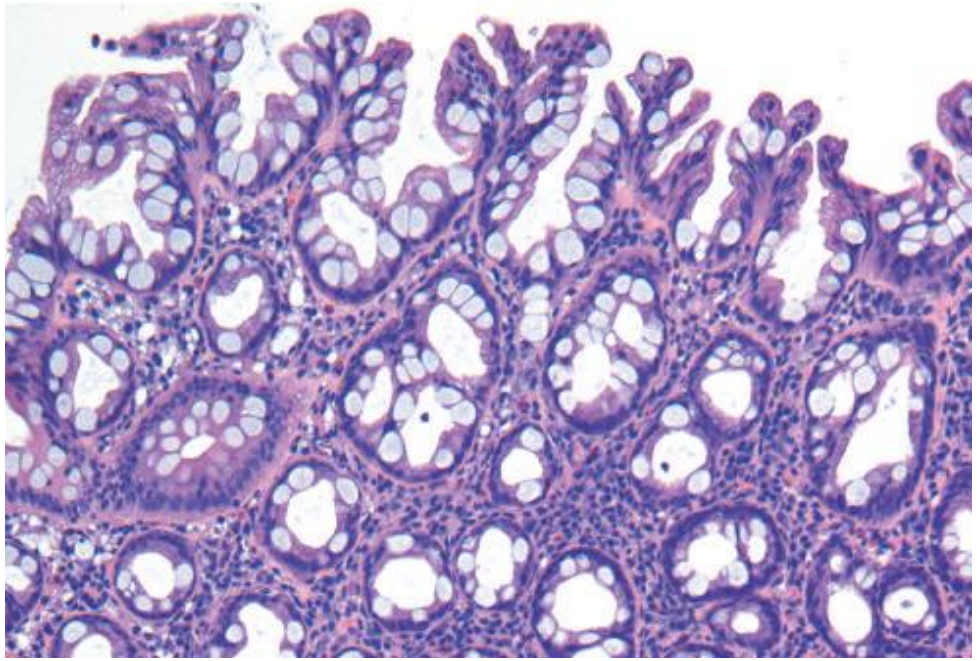
Hyperplastic polyp





Crypts have a star appearance in a cut section

- Mostly seen in the left colon
- Especially in the Recto-sigmoid.
- Small < 5 mm
- Often multiple

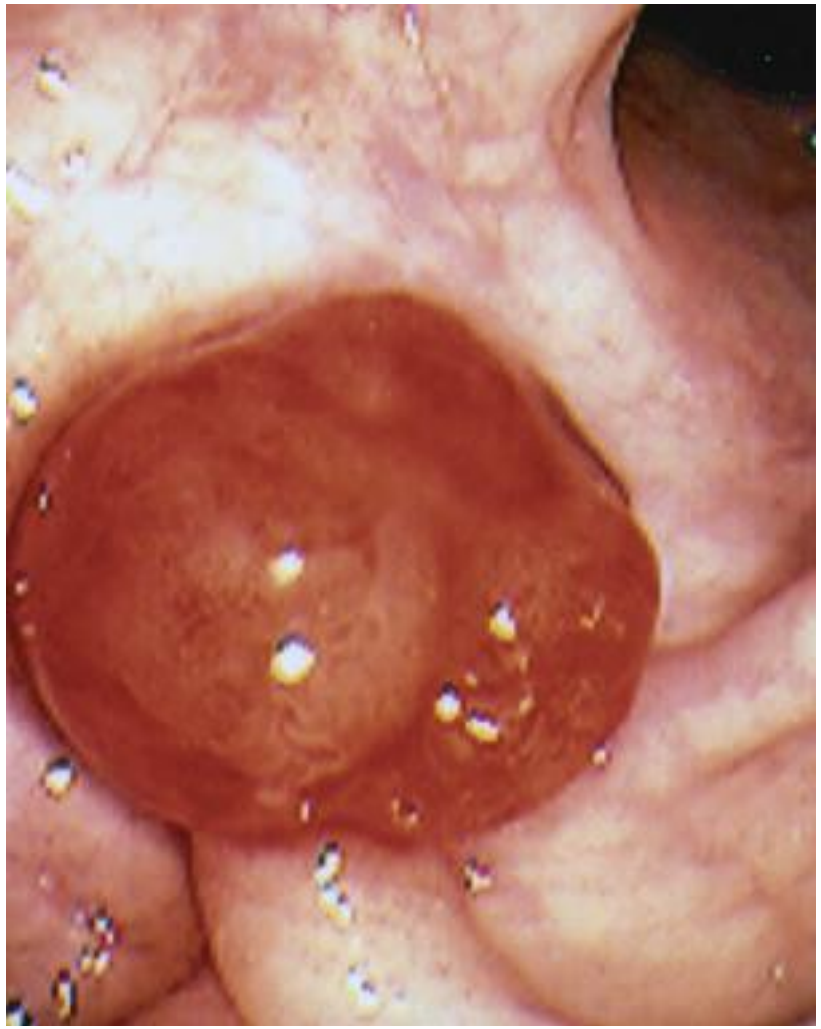


- Crowding of goblet & absorptive cells.
- The surface of the polyp has a **Serrated** appearance (only seen on the surface)(like a saw tooth مثل أسنان المشط).

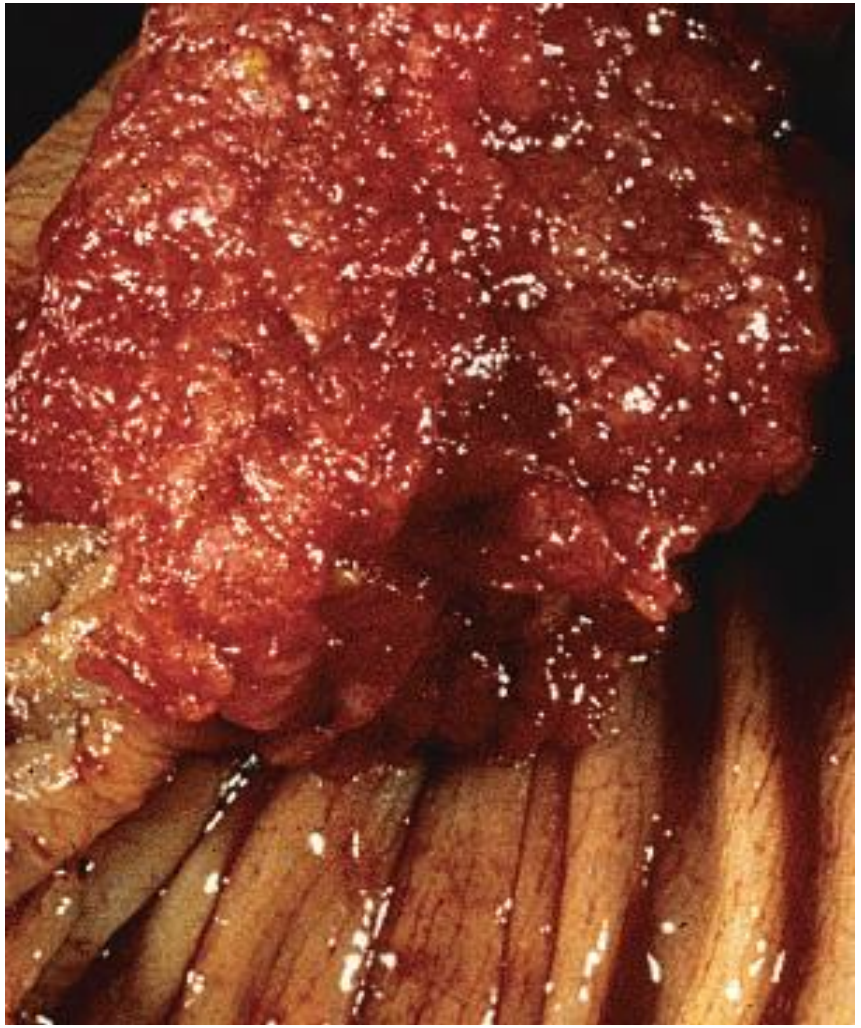
Adenomas

- Most common and clinically important colonic polyps
- 50% of adults > 50 years. (western world)
- **Precursor for majority of colorectal adenocarcinomas**
- USA: screening colonoscopy starts at 45 yrs.
- Earlier screening is applied when there is a family history.
- **Western diets (red meat + long fiber diet) and lifestyles increase risk.**

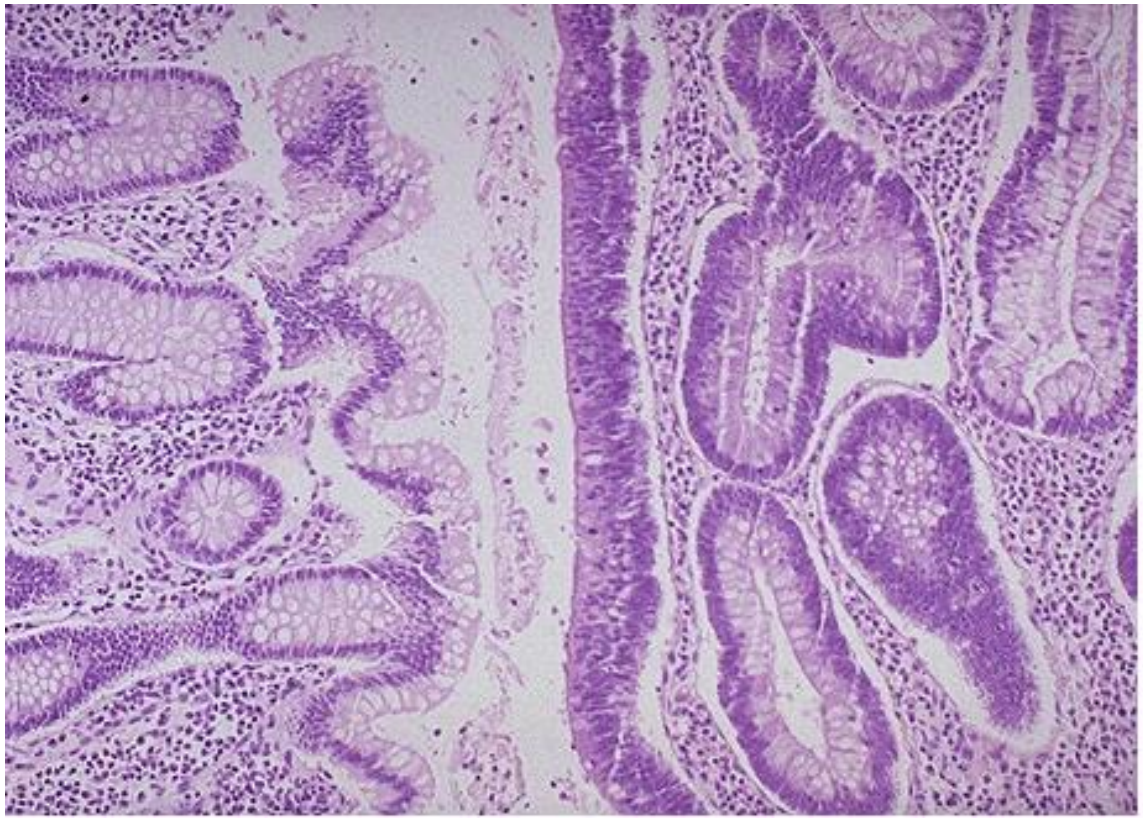
Pedunculated or sessile



The Gold standard way to differentiate between the polyps is the histopathologic examination, because all of them will look the same upon colonoscopy.



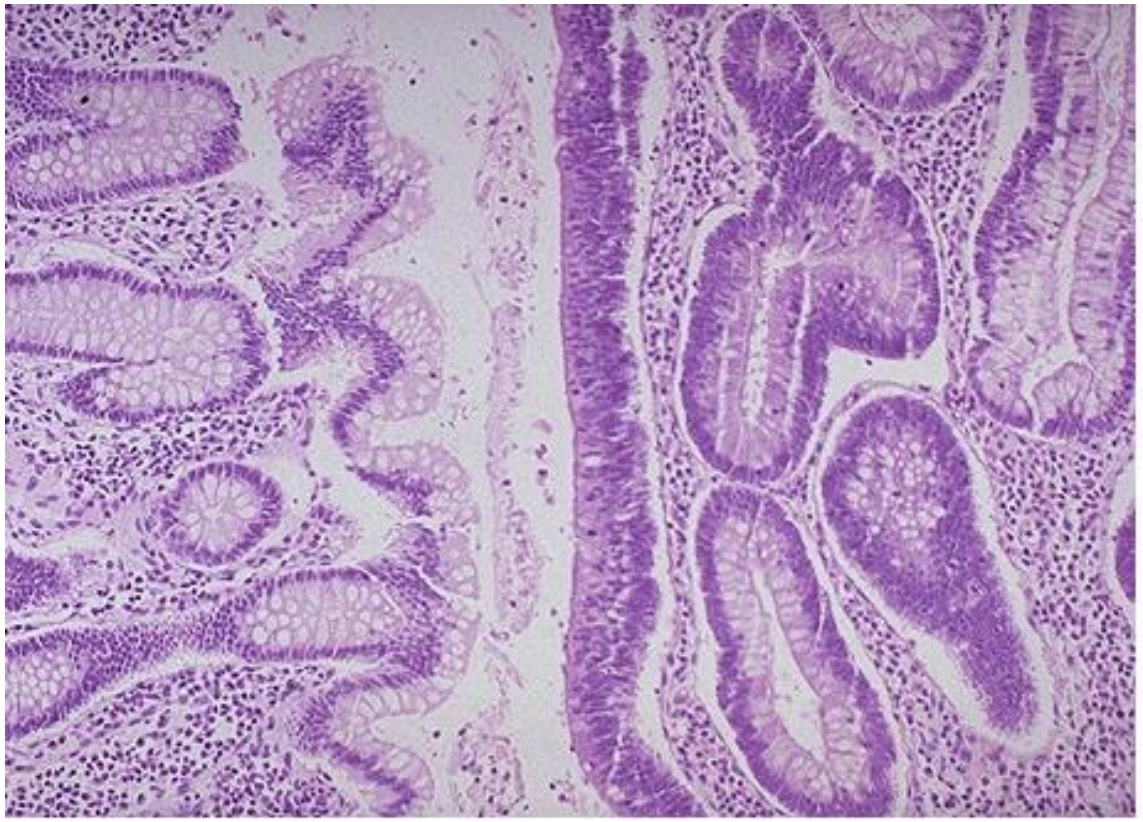
Colon adenoma



- **Hallmark : epithelial dysplasia**
- Dysplasia is defined as : Nuclear hyperchromasia, elongation, stratification of the nuclei (over each other) , high N/C ratio.
- Size is most important correlate with risk for malignancy. (if the adenoma's size is > 4cm , 40% of them will have an invasive focus)
- The second most important factor is the presence of High-grade dysplasia
- The higher the grade the higher the risk of developing carcinoma .
- Architecture: Tubular, villous, tubulovillous. (They are divided according to their architecture NOT according to the risk of malignancy)

Normal mucosa

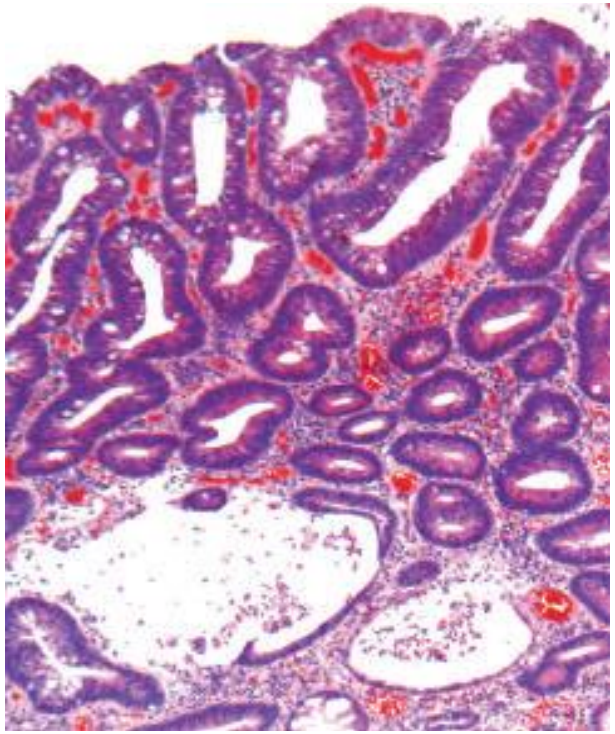
Dysplastic mucosa

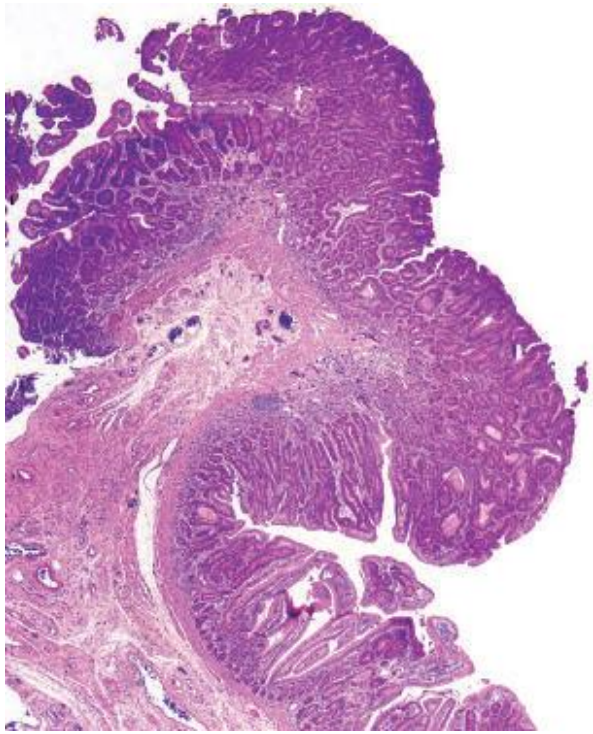


In the left side of the picture we can see the normal intestinal mucosa , in which the nuclei are basally located and small in size. On the right side, the nuclei of Crypts and surface are hyperchromatic and stratified , their color is deeply blue seen in H&E stain with high nuclear to cytoplasmic ratio (N/C ratio).

Tubular adenoma:

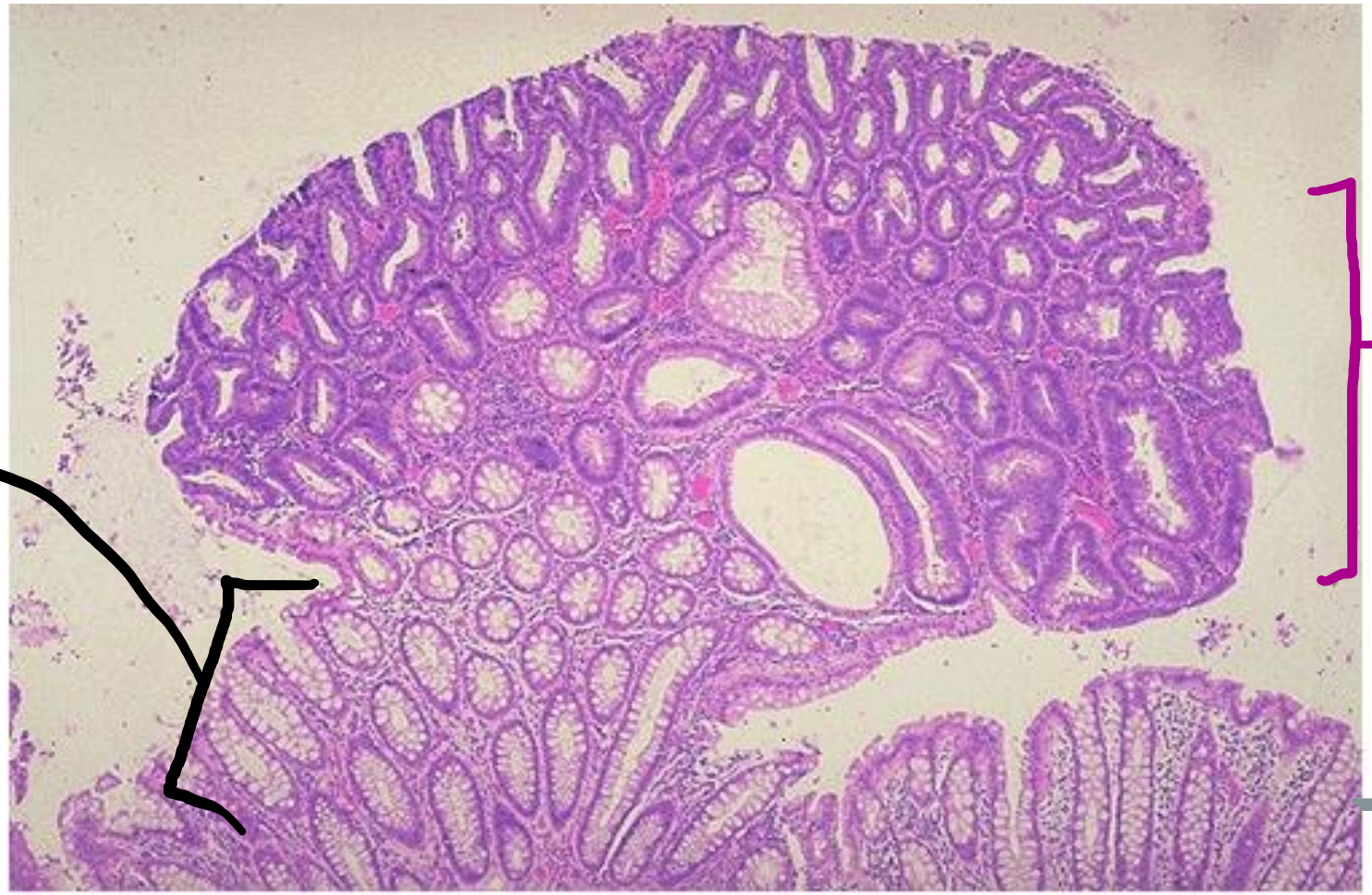
They’re named so because of the presence of small tubular glands on the surface





- **Pedunculated**
- **small tubular glands**

This is a colonic tubular adenoma,



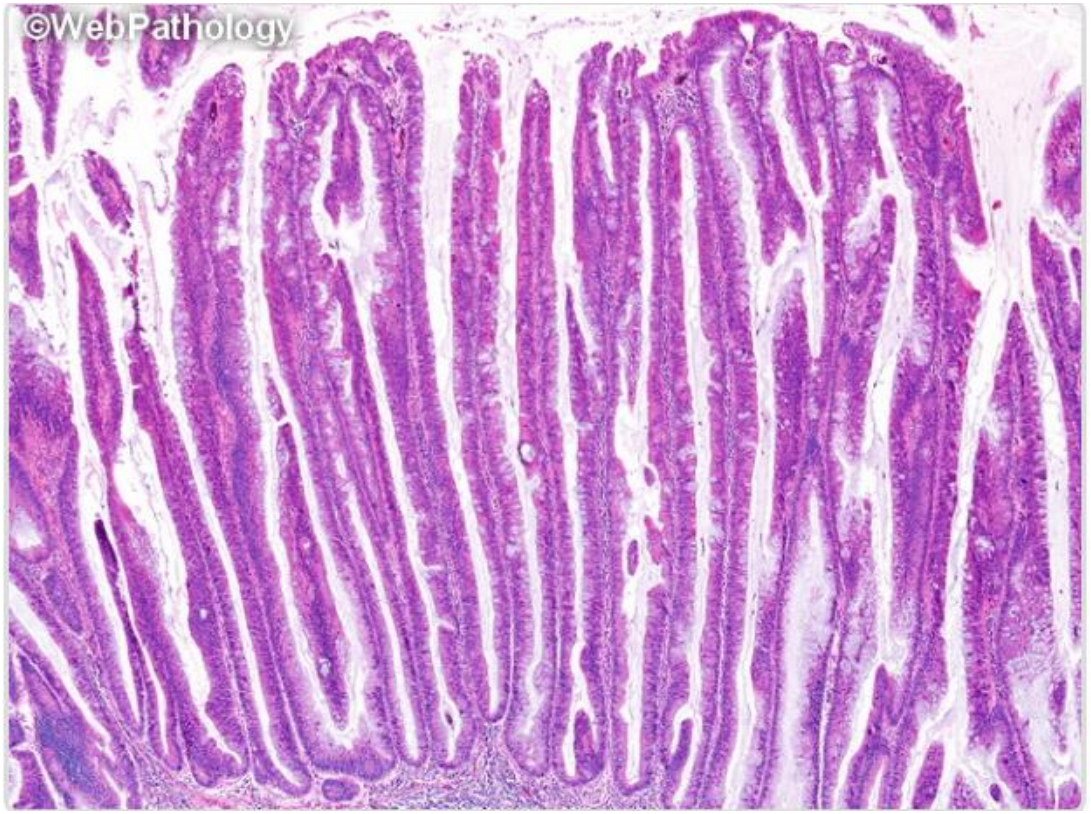
Polyploid lesion (polyp)

You can see the hyperchromasia, and the stratification of the nuclei

Stalk

Normal mucosa

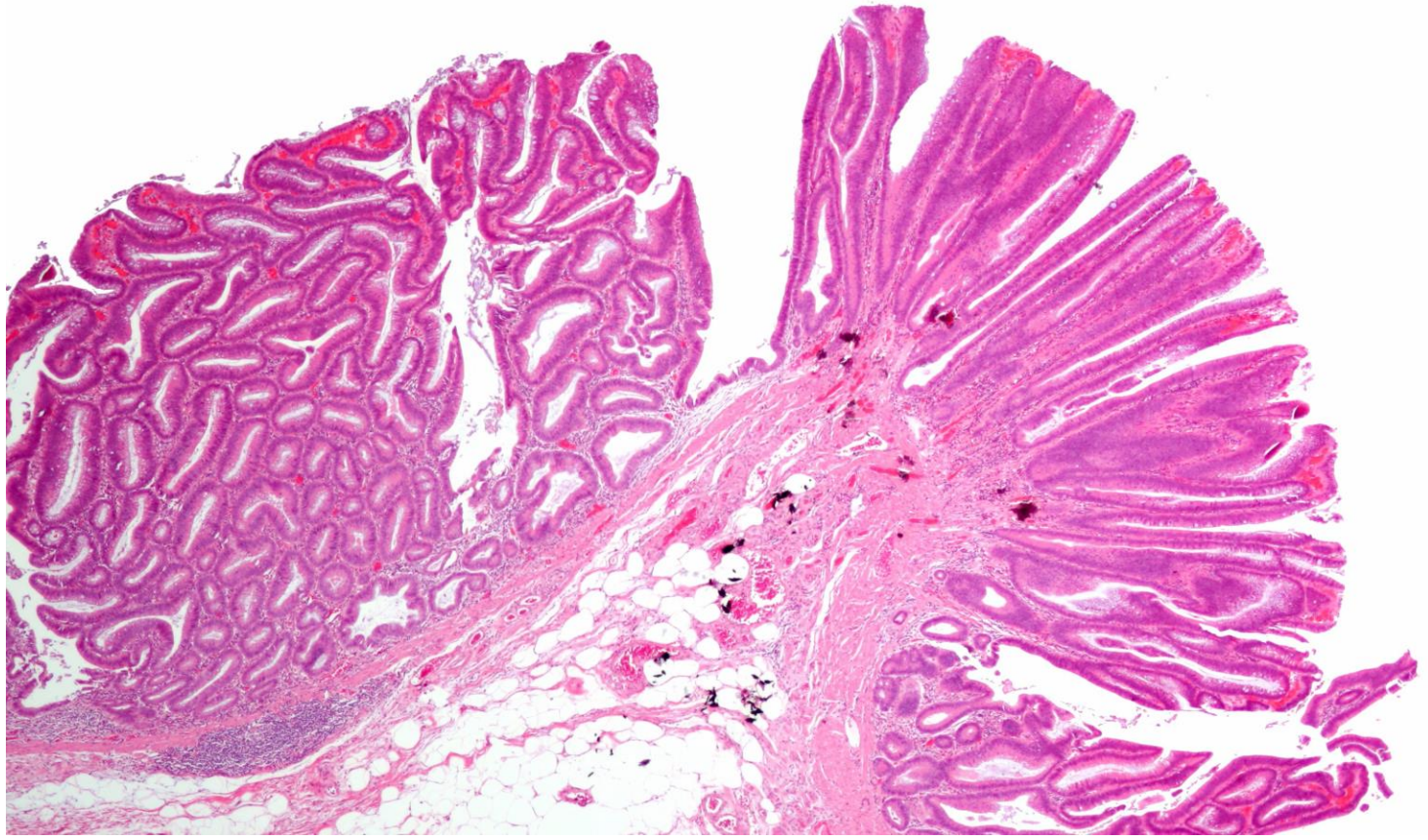
Villous adenoma.



- Long slender villi (finger like projections) .
- Large and sessile.
- More frequent invasive foci
- **Note : the risk of invasive carcinoma is not related to the architecture , but to the size of these adenomas.**

Tubulovillous adenoma

It harbors both architectural features of tubular component and villous component



Sessile serrated adenoma

- Overlap with hyperplastic polyps.
- **Lack dysplasia (unlike other adenomas).**
- Malignant potential similar to conventional adenomas (although they lack dysplasia).
- Serrated architecture throughout full length of glands (not only on the surface like the hyperplastic polyps) .
- Basal crypts dilated + sometimes laterally branching

The typical appearance of sessile serrated adenoma . You can notice that the serrations (SAW TOOTH appearance) reach the full area of the crypts not only the surfaces .

Familial Syndromes

- Syndromes associated with colonic polyps and increased rates of colon cancer
- These syndromes have Genetic basis.
- The most important syndromes are :
- **Familial Adenomatous Polyposis (FAP)**
- **Hereditary Nonpolyposis Colorectal Cancer (HNPCC) , sometimes called: Lynch syndrome**

Familial adenomatous polyposis FAP

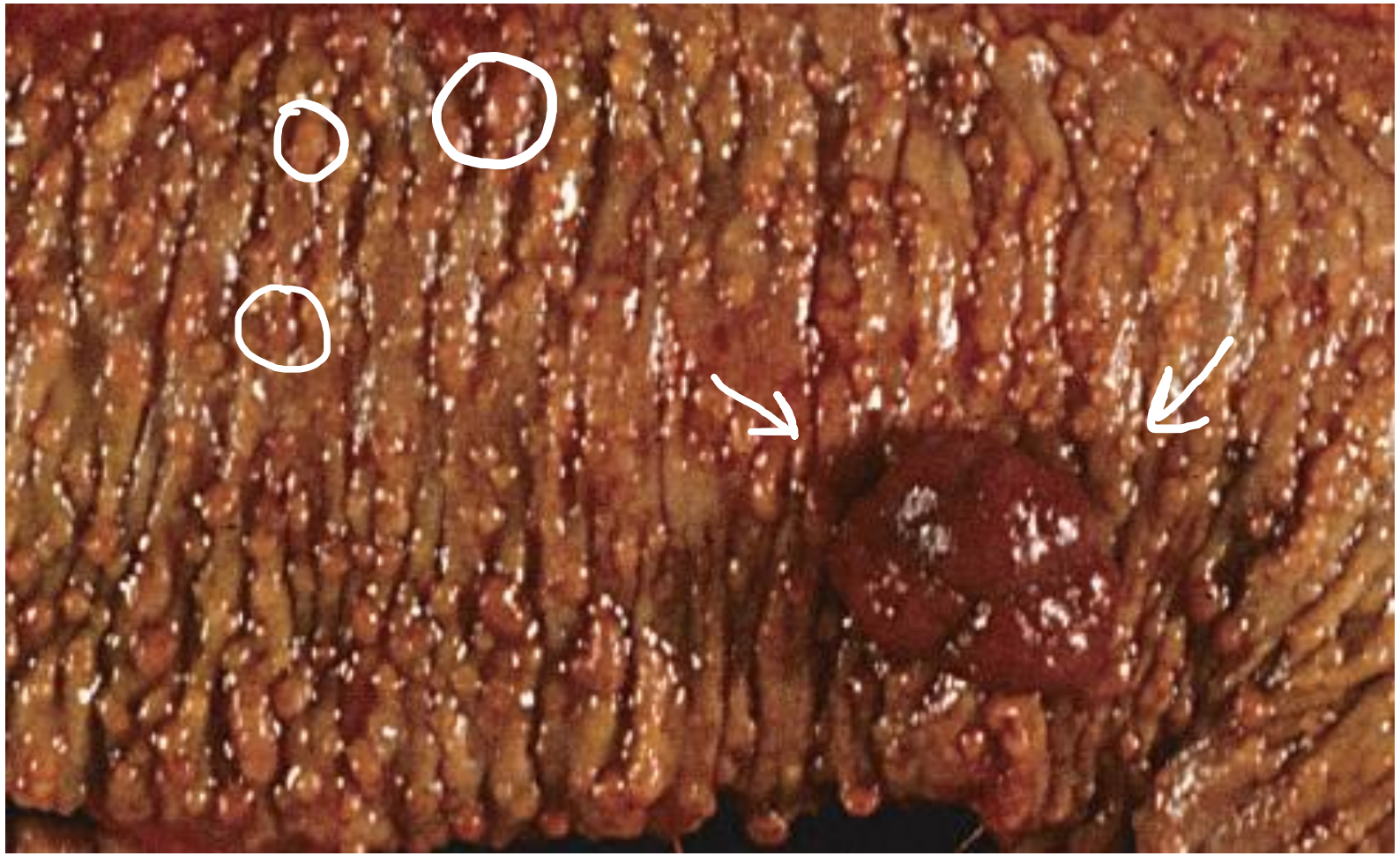
- Autosomal dominant (when there's a member of the family affected by FAP we should screen all the family members , because it's inherited).
- Numerous colorectal adenomas: teenage years.
- Mutation in APC (adenomatous polyposis coli) gene.
- At least 100 polyps are necessary for a diagnosis of classic FAP.
- Morphologically similar to sporadic adenomas (they are adenomas and they both harbor dysplasia weather low grade or high grade) .
- 100% of patients develop colorectal carcinoma, IF UNTREATED, often before age of 30.
- Standard therapy: prophylactic colectomy.
- Risk for extraintestinal manifestations , sometimes extraintestinal tumors (in addition to the risk of colorectal carcinoma)

Variants of FAP:

- Classified according to Specific APC mutations.
- **1- Gardner syndrome**: intestinal polyps + osteomas (mandible, skull, and long bones); epidermal cysts(skin related cyst) + desmoid and thyroid tumors + and dental abnormalities.
- **2- Turcot syndrome**: intestinal adenomas and CNS tumors (medulloblastomas >> in 1/3 of the cases it could be glioblastomas)

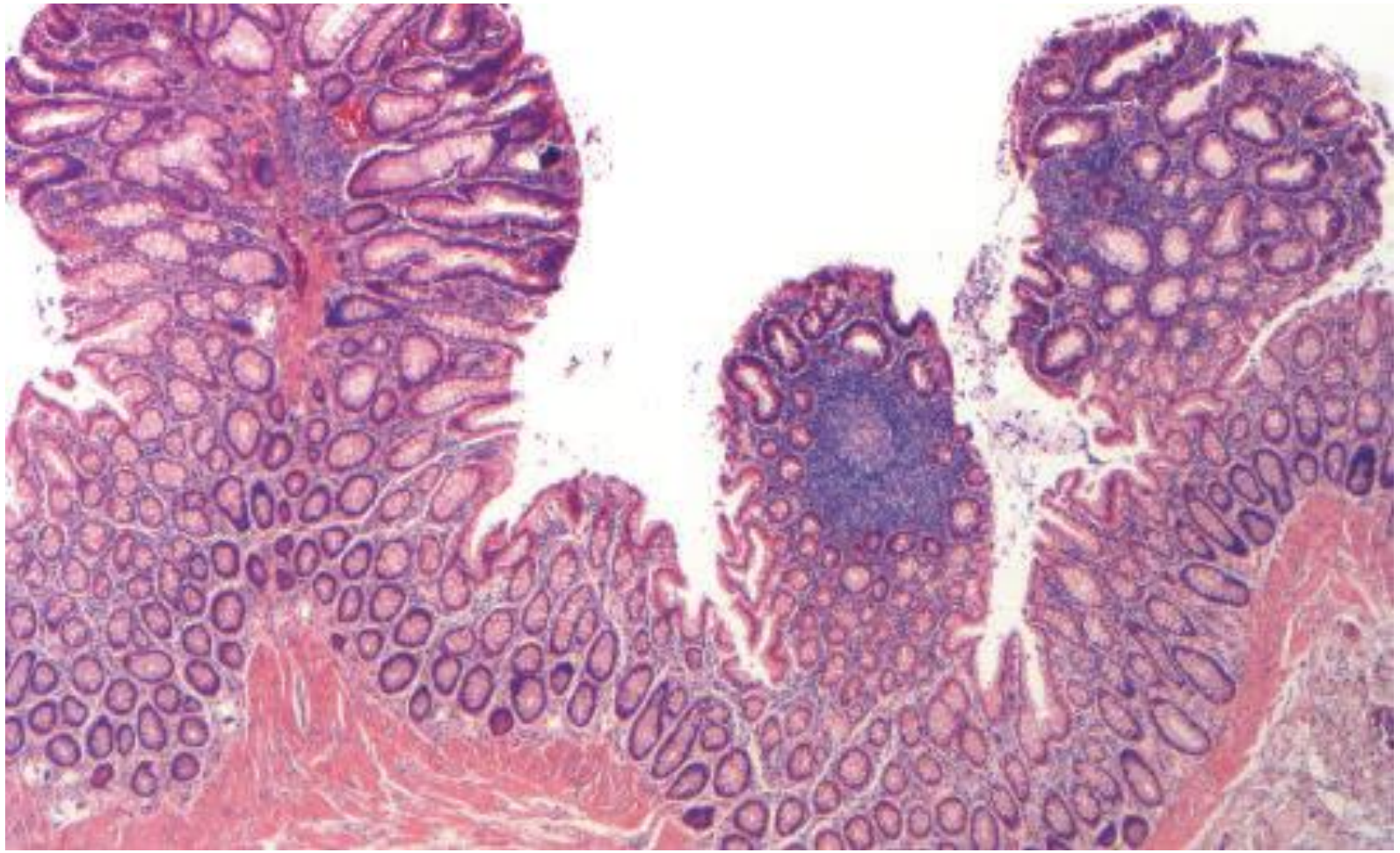
We need at least 100 polyp to diagnose the classic FAP . However, most of the time patients have 1000 or more polyps with variable sizes (Like a carpet of polyps).

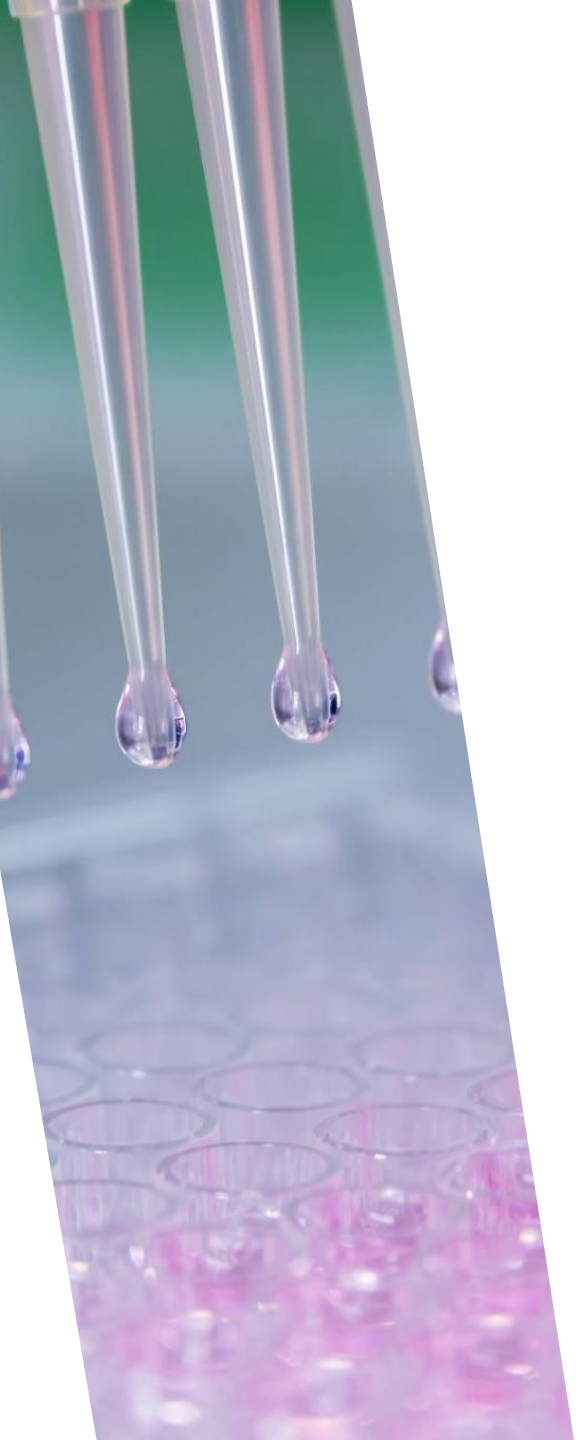
Many small polyps



One large polyp

Similar to classical/conve-ntional sporadic adenomas under the microscope, we can see 3 polyps here in the same picture





Hereditary Nonpolyposis Colorectal Cancer: HNPCC, Lynch syndrome

- Autosomal dominant. Inherited germ-line mutations in DNA mismatch repair genes which are important in (detection, resection and repair of errors in DNA replication).
- Increased risk of: Colorectum, endometrium, stomach, ovary, ureters, brain, small bowel, hepatobiliary tract, and skin cancers.
- Colon cancer at younger age than sporadic cancers(before 50 yrs)
- Right colon, abundant mucin.
- Only few adenomatous precursors (typically sessile serrated adenomas).

It's called " nonpolyposis " because we don't see as many polyps as we see in FAP , however, there is definitely a polyp precursor lesion for the development of colorectal cancer .

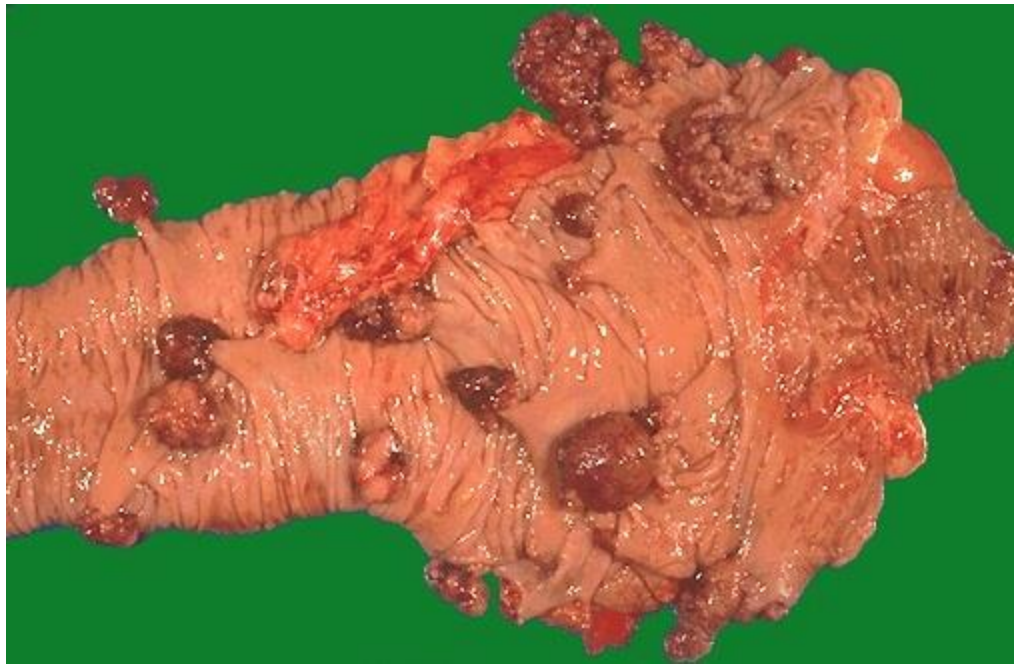
HNPCC, cont

- Accumulation of mutations at 1000x higher rates in microsatellite DNA (which are short repeating sequences where most of the mutations occur)
- Resulting in microsatellite instability which will lead to high incidence of cancers including the colorectal.
- 5 genes identified but Majority of cases involve either MSH2 or MLH1.

Mutations in the DNA mismatch repair genes >> micro satellite instability.

Cecal polyps in HNPCC.

This is the right side of the colon , the cecum, which is known for its broad diameter.we can see here many polyps but still less in number than those in FAP.



اللهمّ أعزّ جباهًا ما ركعت إلّا إليك

و سدّد سيوفًا شُرّعت في سبيلك

و اجعَل النّصر مؤزّرًا على أياديهم

اللهمّ إنّهم أعدّوا استجابةً لقولك " و أعدّوا "

فمكّن لهم يا من قلتَ و قولك الحقّ :

" و كان حقًّا علينا نصر المؤمنين"