# Intestinal pathology, part 3

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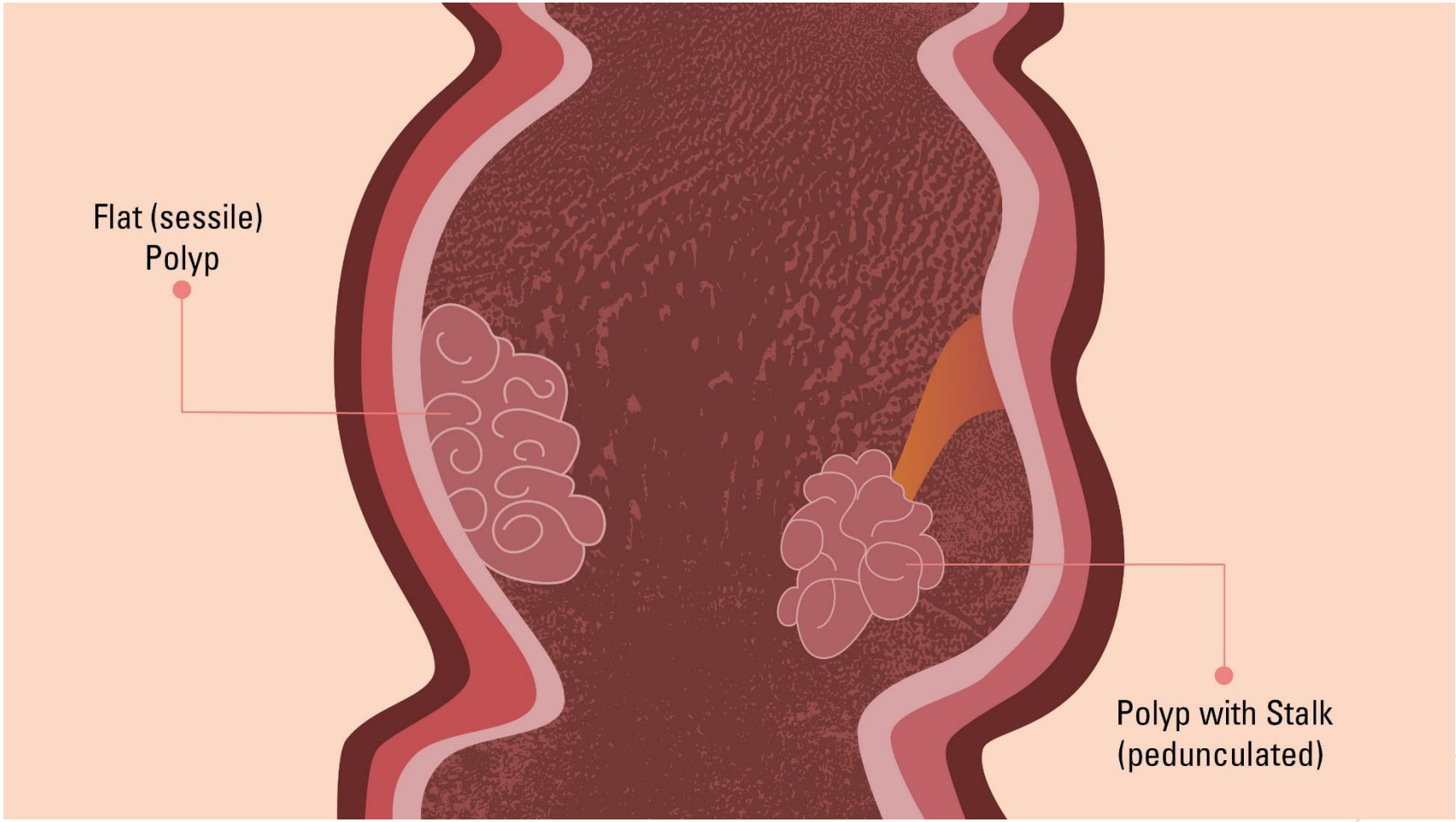
# Diseases of the intestines

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

# COLONIC POLYPS AND NEOPLASTIC DISEASE

- Colon is most common site for polyps
- ***Sessile polyp:*** no stalk (cauliflower appearance)
- ***Pedunculated polyp:*** *stalk.* *(attached to wall of bowel or intestine)*

- ***Neoplastic polyps:*** *adenoma.* *(dysplastic → considered precursors of malignancy)*
- ***Non neoplastic polyps:*** inflammatory, hamartomatous, or hyperplastic

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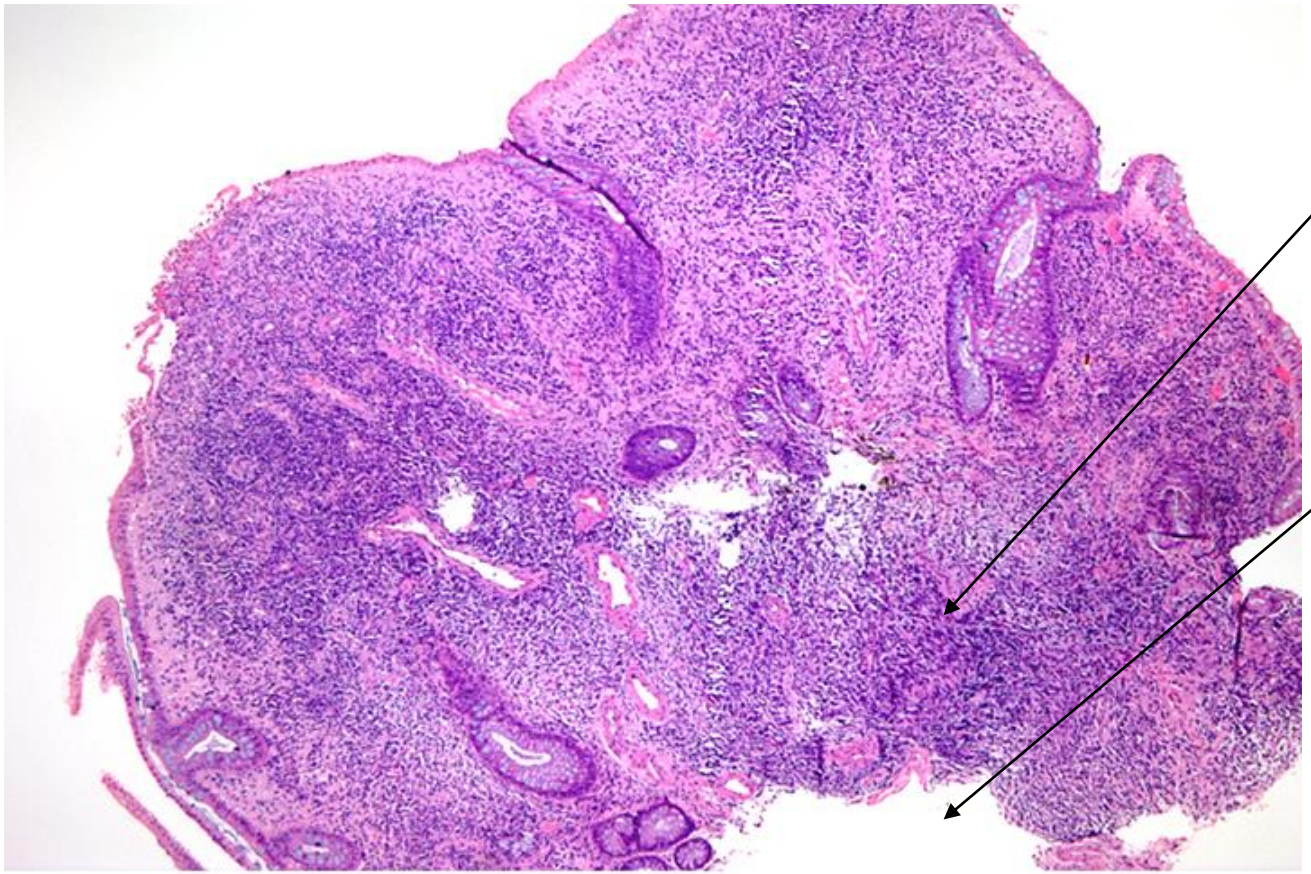
# Inflammatory Polyps

- Solitary rectal ulcer syndrome. (typical type of inflammatory polyps)
- Cause: Impaired relaxation of anorectal sphinctor.
- Leads to 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.

- Presents with: Rectal bleeding, mucus discharge and polyp.

# Inflammatory polyps



4x: low power, dense inflammation in lamina propria

Inflammatory mass filled with inflammatory cells (blue fossae, could be lymphocytes, plasma cells or neutrophils), surface of polyp here is also ulcerated and eroded. Glands are scant and only few are left because of destruction by inflammation. These glands are benign-looking.
Inflammatory polyps can also be seen in context of inflammatory bowel diseases.

Pathology Outlines

# Hamartomatous Polyps

- Sporadic or syndromic.
- Hamartomatous polyposis syndromes. (syndromic ones, same appearance as sporadic ones under microscope)
- Disorganized, tumor-like growth composed of mature cell types normally present at that site.

- Juvenile Polyps
- Peutz-Jeghers Syndrome

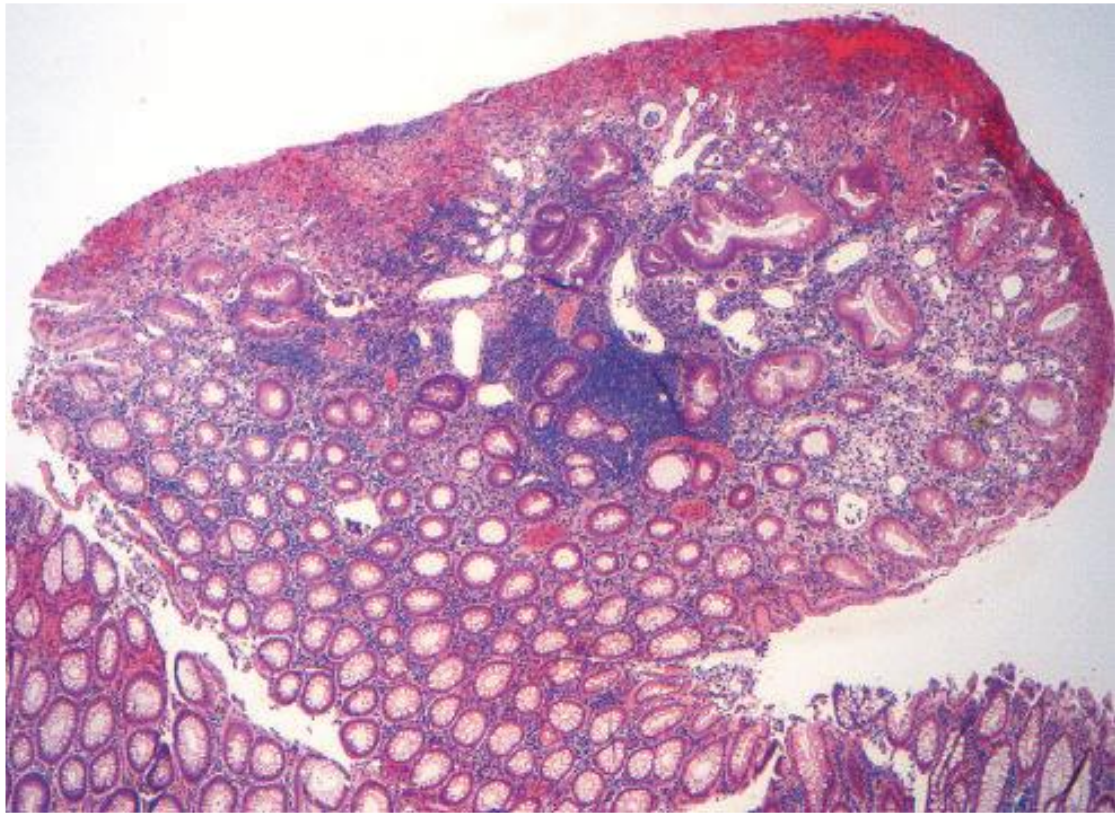
# Juvenile Polyps

- Most common hamartomatous polyp (more common than Peutz-Jeghers Syndrome)

- **Sporadic**
- Solitary. <5 years of age, this is the typical presentation
- Rectum, bleeding.

- **Syndromic (**juvenile polyposis) **.**
- Dozens. < 5 years
- Autosomal dominant.
- Transforming growth factor-β (TGF-β) signaling pathway germline mutation (SMAD4).
- Increased risk for colonic adenocarcinoma and others.

# Juvenile Polyps

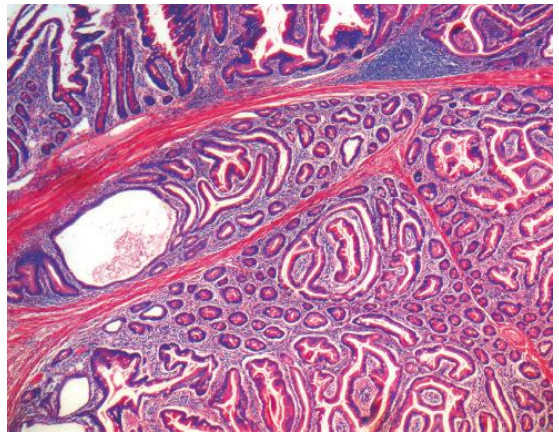


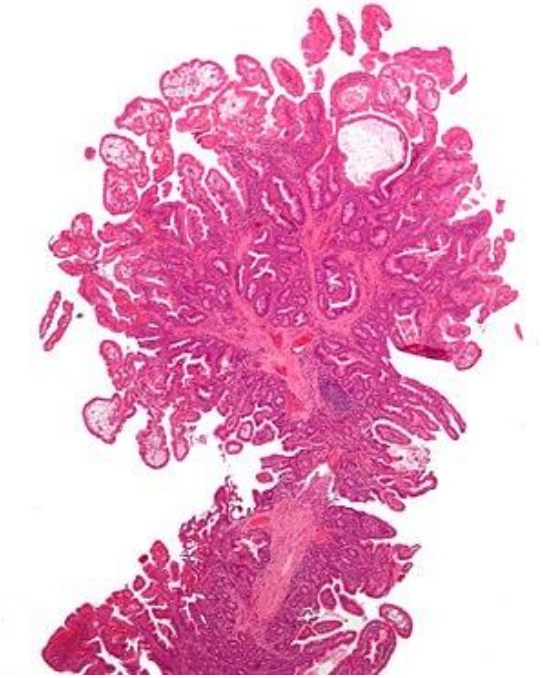
- Pedunculated (attached to bowel through stalk)
- Reddish lesions (due to presence of ulcerations, granulation tissue and new blood vessels formation)
- Cystic  spaces on cut sections
- Dilated glands filled with mucin and inflammatory debris.
- Granulation tissue on surface.
- Devoid of dysplasia and considered benign tumors but, if part of a syndrome, increase risk of malignancy

# Peutz-Jeghers Syndrome

- Autosomal dominant, rare
- **Multiple gastrointestinal hamartomatous polyps**
- **Mucocutaneous hyperpigmentation**
- **Increased risk for several malignancies: colon, pancreas, breast, lung, ovaries, uterus, and testes,**
- *LKB1/STK11* germline mutation (tumor suppressor protein).

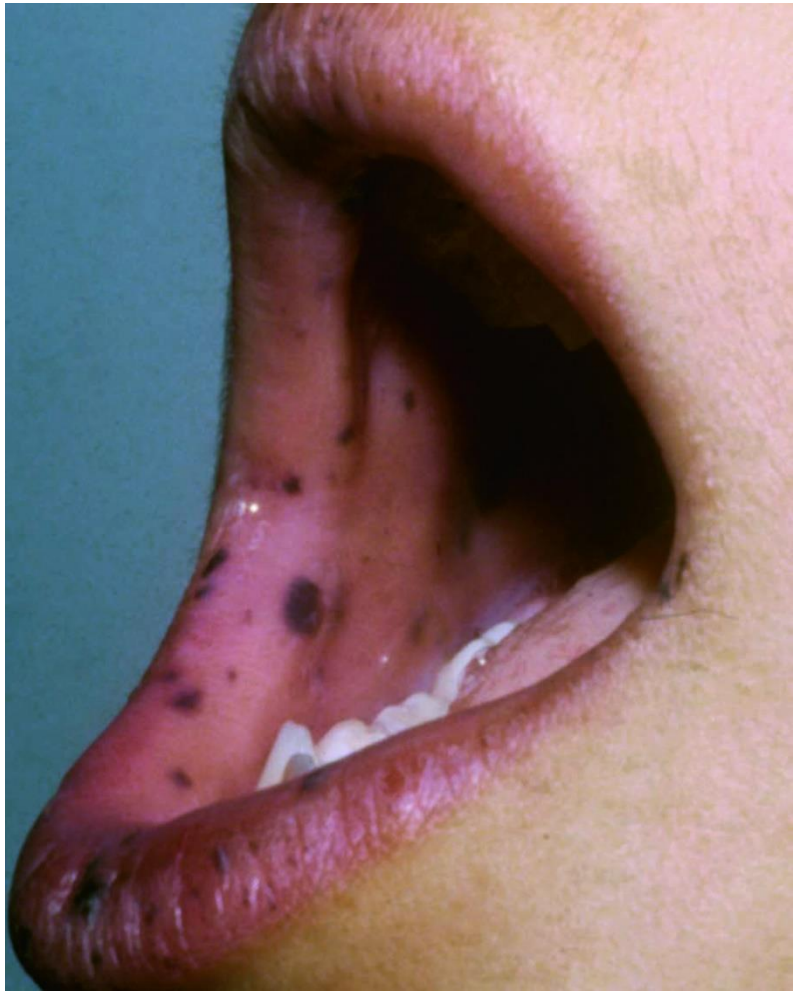
# Peutz-Jeghers polyp

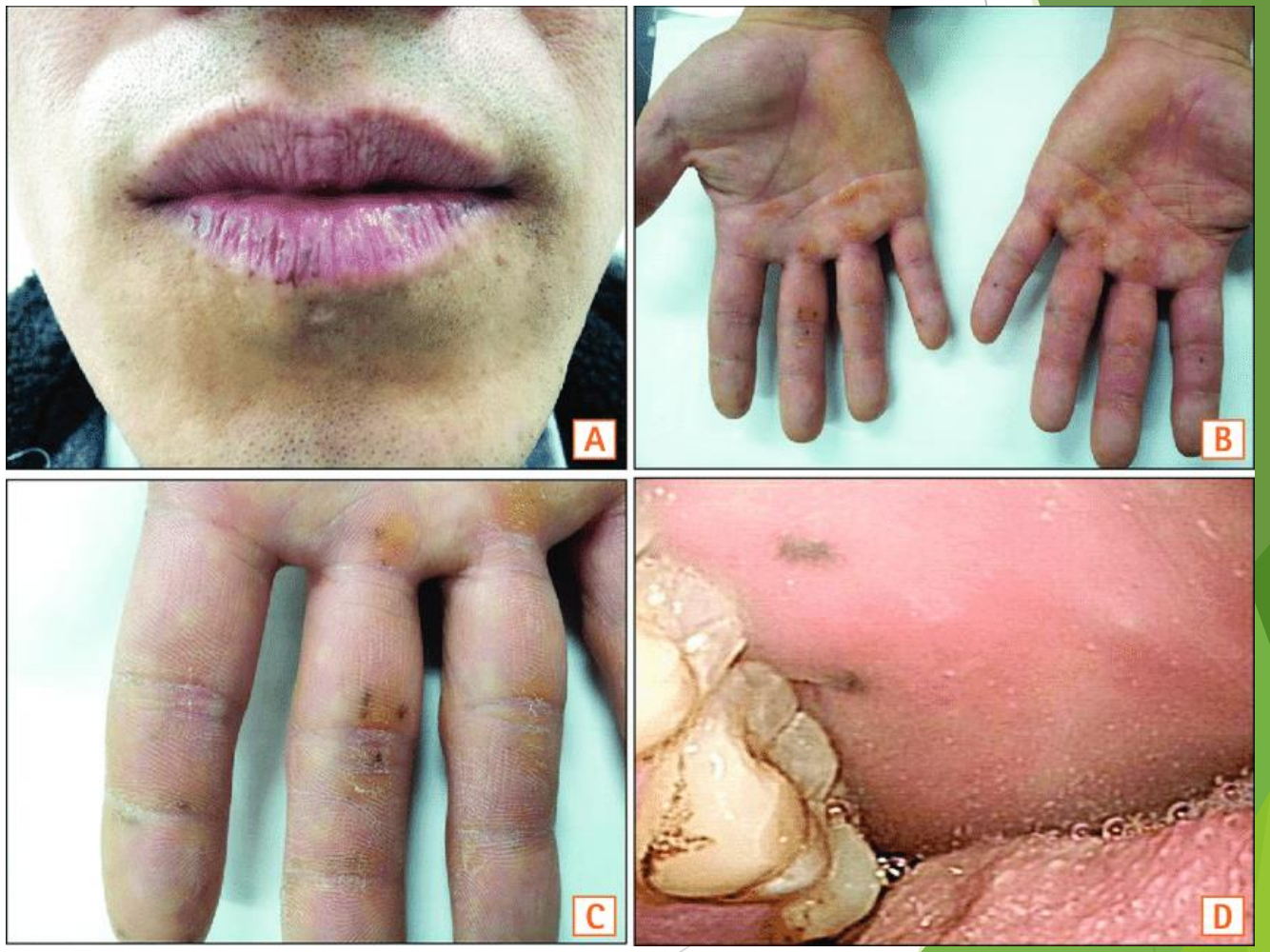




- Mostly in small intestine.
- Large, pedunculated, lobulated.
- Arborizing network of connective tissue, smooth muscle, lamina propria and glands
- Normal-appearing intestinal epithelium, no dysplasia
- Christmas tree pattern.

# Mucocutaneous pigmentation





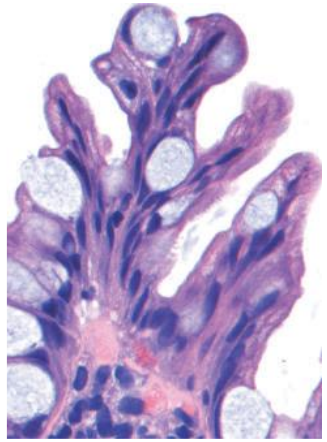
# Hyperplastic Polyps

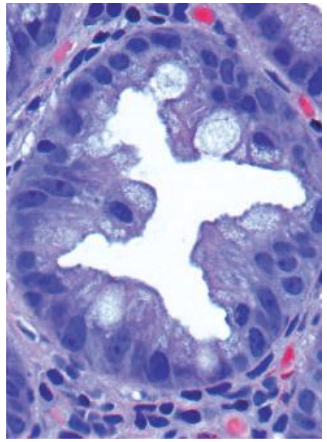
- Common
- 6-7th decades. (In advanced age)
- Decreased epithelial turnover and delayed shedding of surface epithelium >>> pileup of goblet cells & epithelial overcrowding
- **No malignant potential**
- **Biopsy is important to differentiate them from other types of polyps, in colonoscopy, they all look the same. The gold standard is the histopathologic examination to find the presence/absence of dysplasia.**

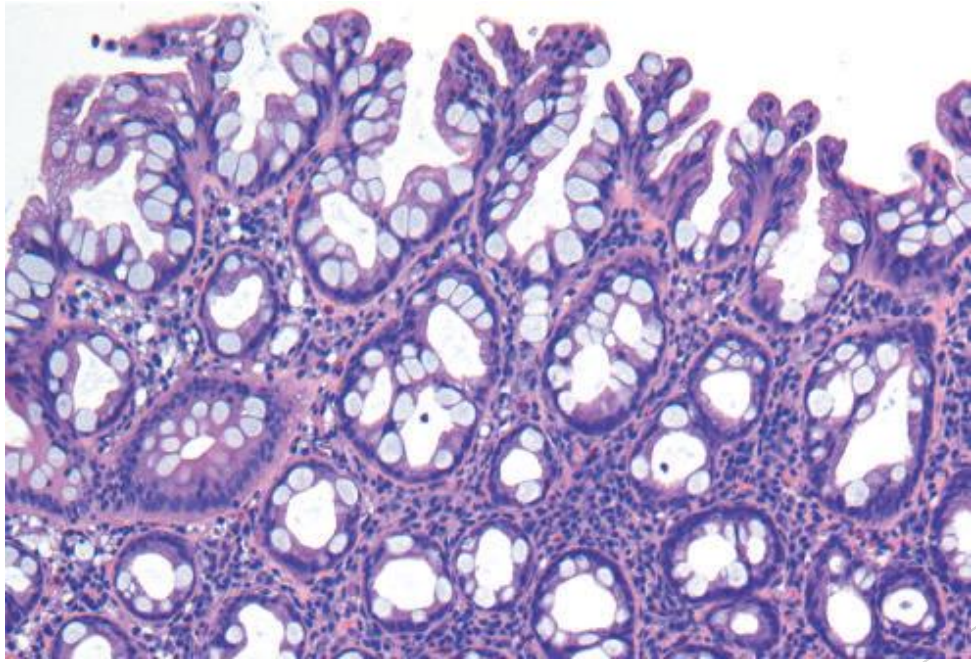
# Hyperplastic polyp

- Left colon
- Recto-sigmoid.
- Small < 5 mm
- Often multiple

- Crowding of goblet & absorptive cells.
- Serrated surface. (starry appearance in cross-sections, as in the upper right picture).





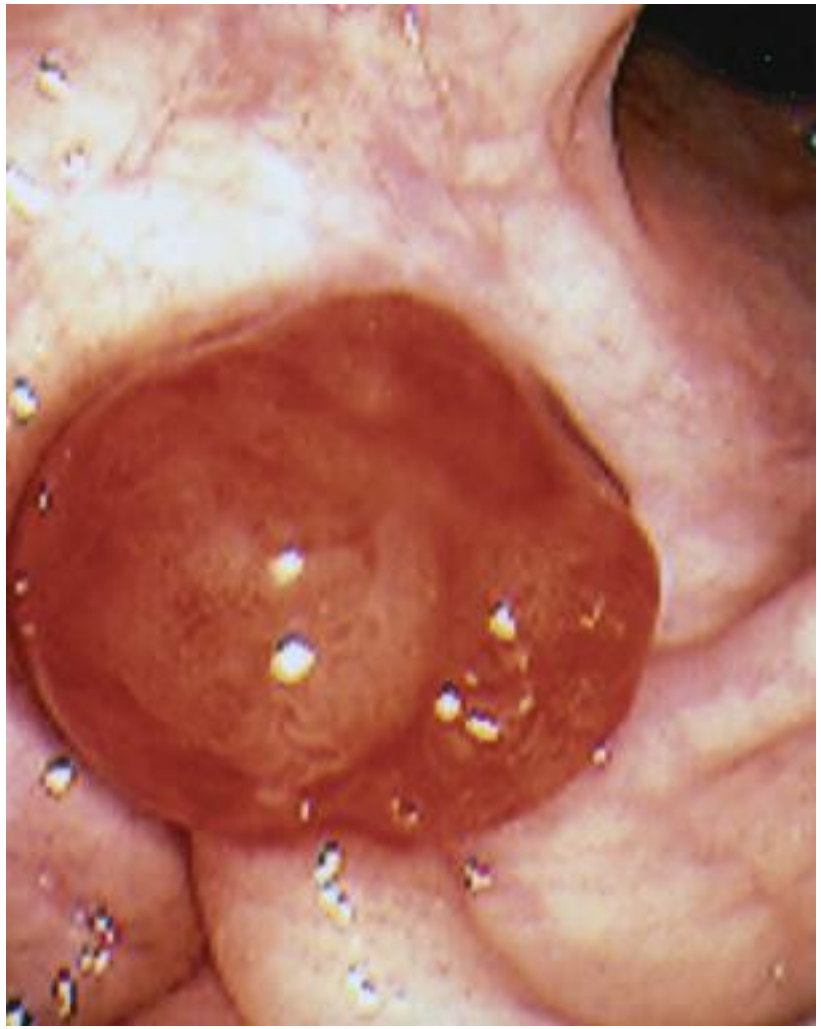


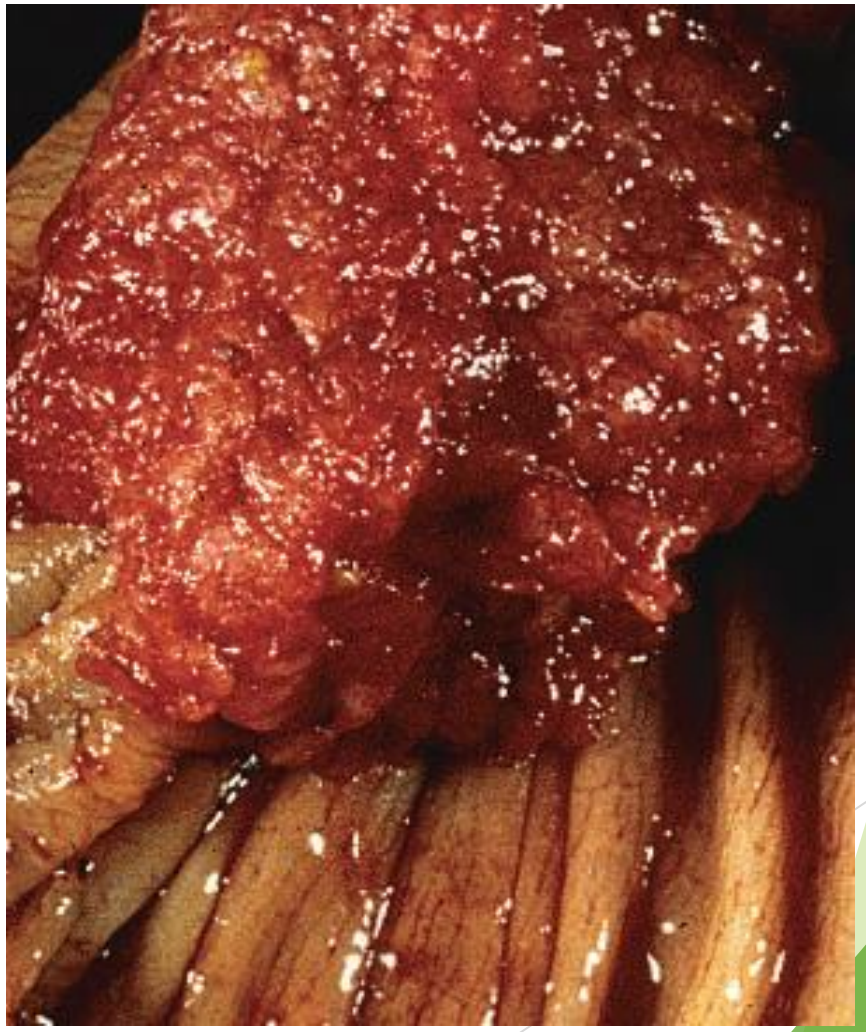
# Adenomas

- Most common and clinically important
- 50% of adults > 50 years.  (western world)
- **Precursor for majority of colorectal adenocarcinomas**
- USA: screening colonoscopy starts at 45 yrs. Because colon cancer is common
- Earlier screening with family history. (if family history present, start 10 years earlier than the youngest age in the family at which cancer was diagnosed; e.g. cancer was found at 40 for someone in the family → start screening at 30 for the patient).
- **Western diets and lifestyles (red meat availability and low-fibre diets) increase risk.**

# Pedunculated or sessile

pedunculated





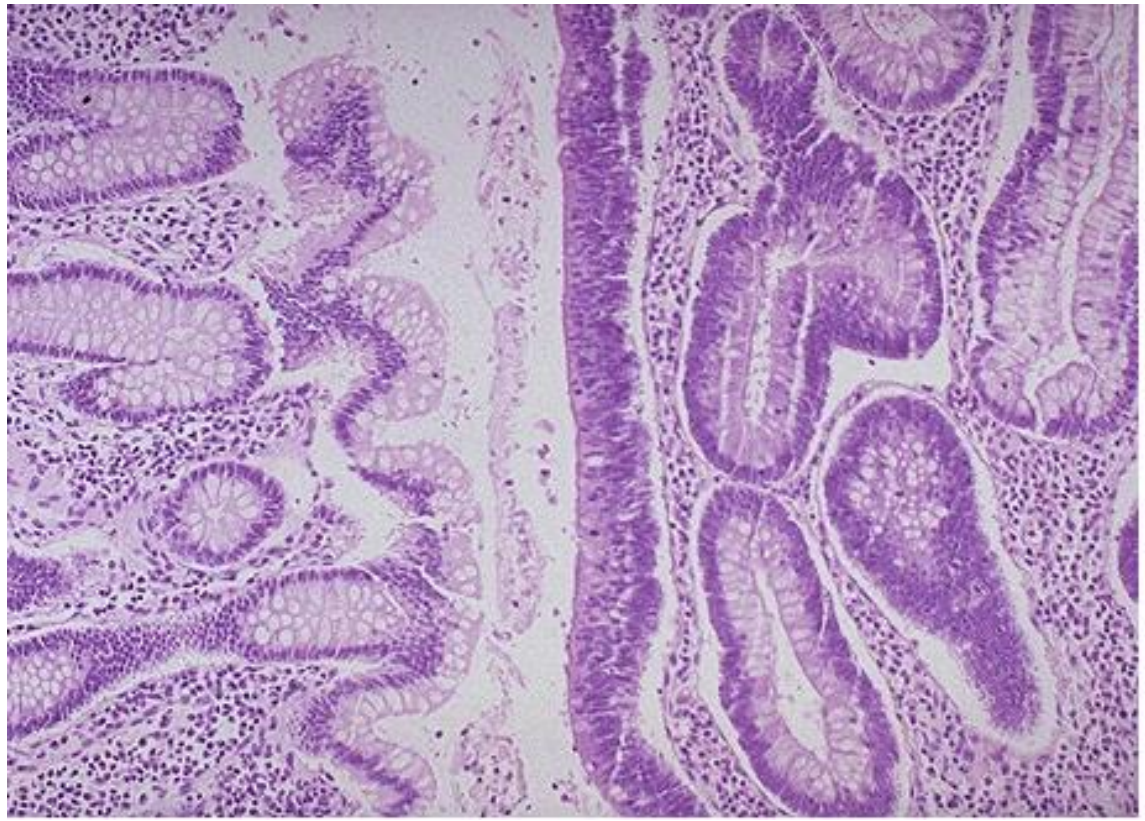
sessile

You may have noticed how similar they all look in colonoscopy, that's why histopathologic examination is the golden standard

# Colon adenoma

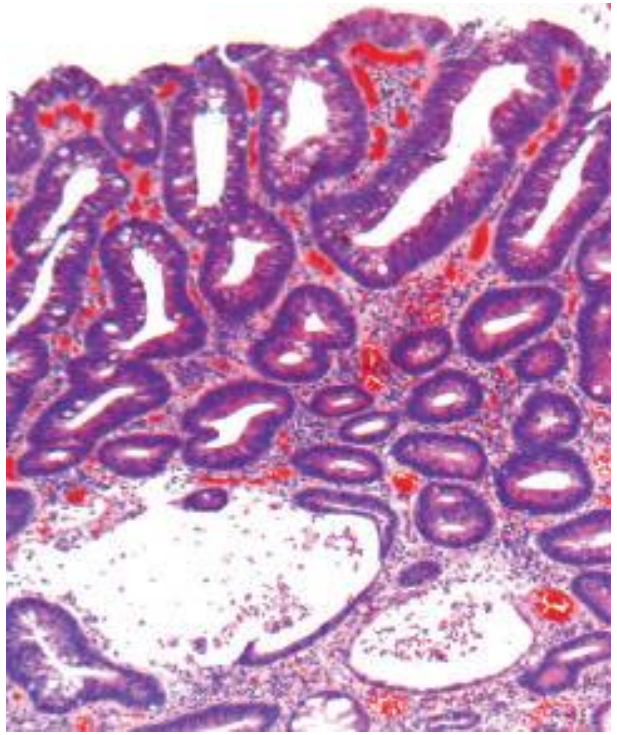
Normal intestine mucosa, nuclei small and basal

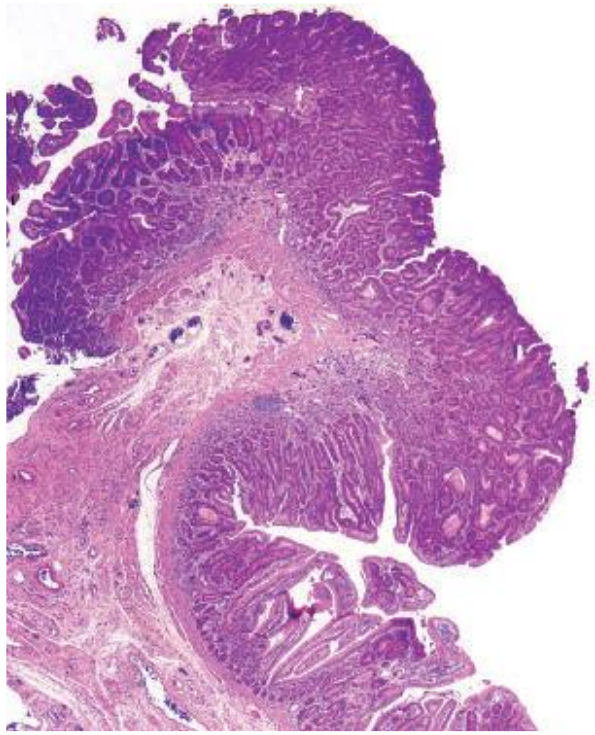
Crypts and surface nuclei are hyperchromatic and stratified → dysplastic mucosa, seen with H&E stain



- Hallmark: epithelial dysplasia differentiating feature from other types of polyps.
- Nuclear hyperchromasia, elongation, stratification (nuclei over each other), high N/C ratio.
- Size is most important correlate with risk for malignancy. (40% will have invasive focus if > 4cm)
- High-grade dysplasia is a second factor (the higher the grade, the higher the risk for invasive carcinoma)
- Architecture: Tubular, villous, tubulovillous. Pure architecture, has nothing to do with risk of malignancy

# Tubular adenoma:



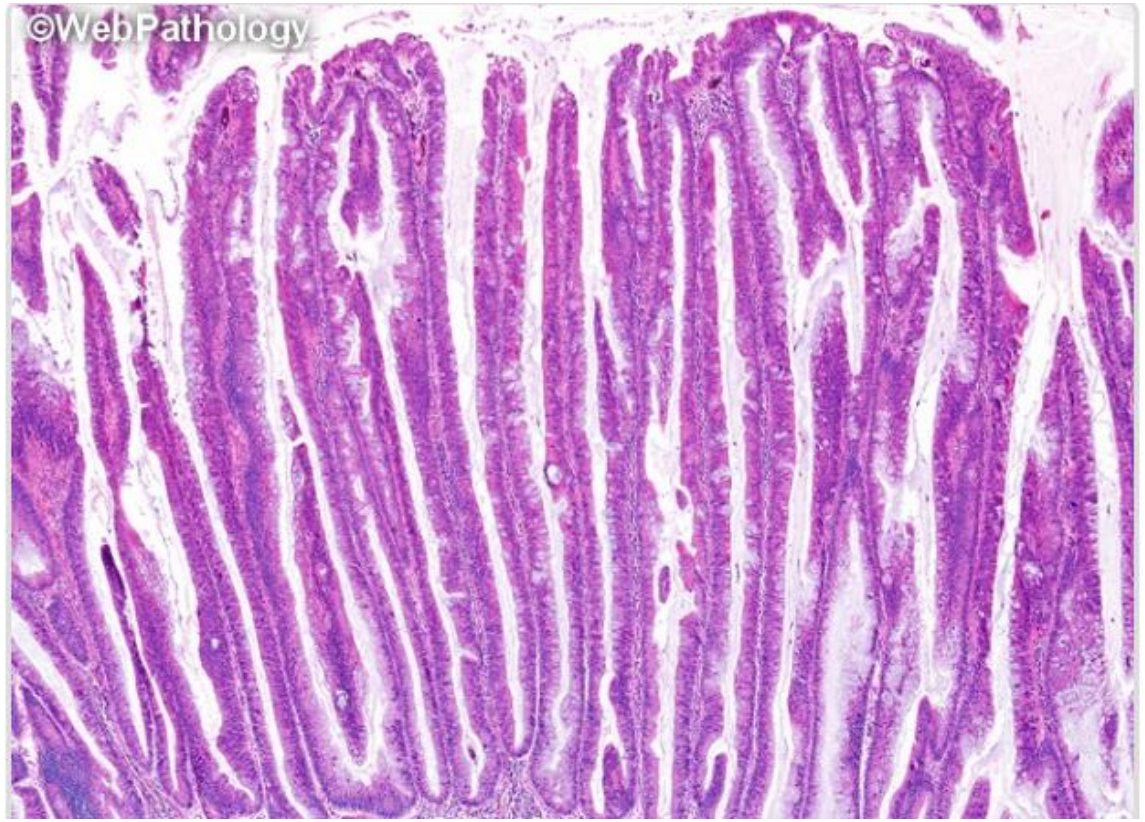


- Pedunculated
- small tubular glands

Polypoid lesion/mass where you can see hyperchromasia and stratification of nuclei reaching the surface

stalk

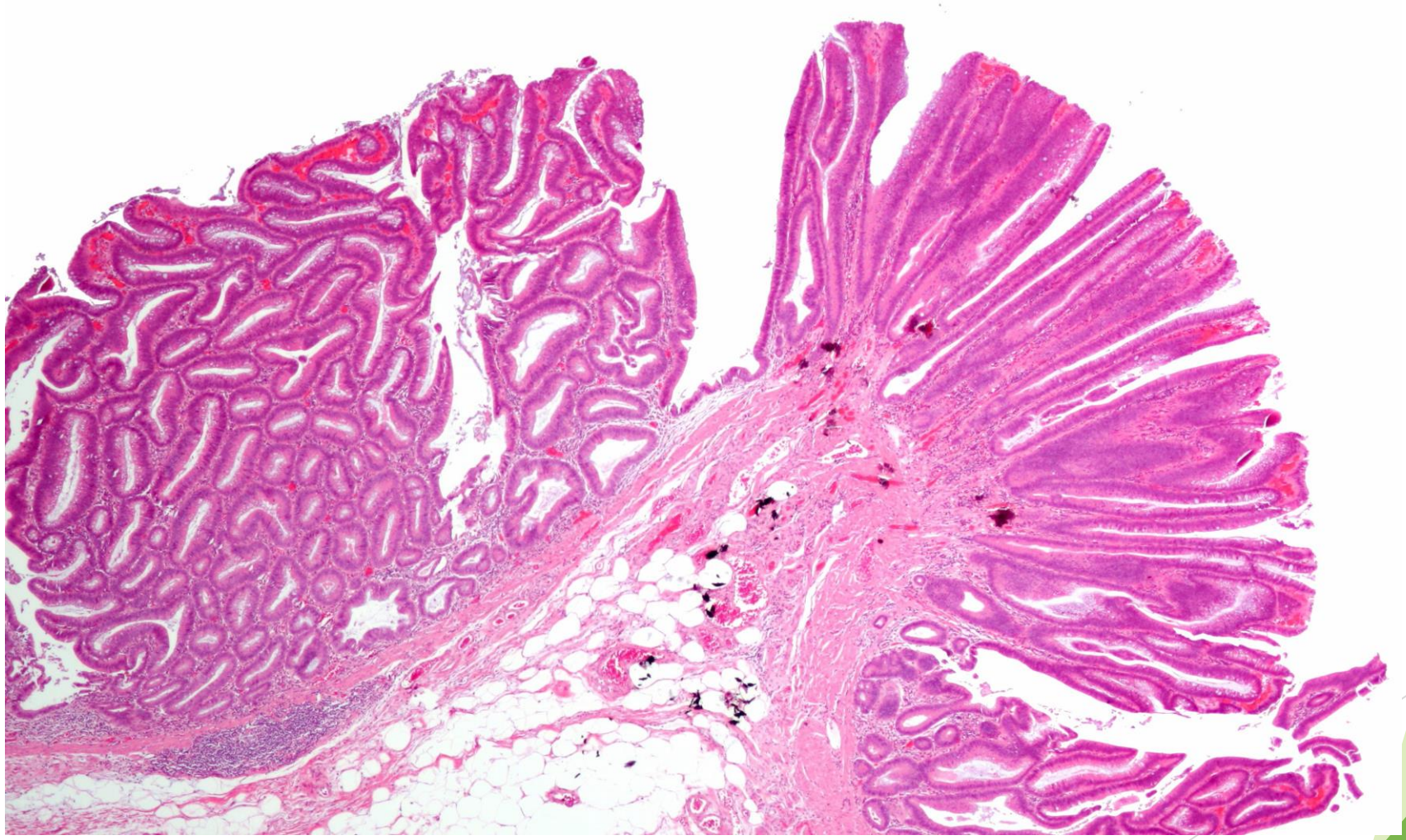
# Villous adenoma.




- Long slender villi. Like the villi of small intestine
- Large and sessile.
- More frequent invasive foci (not related to architecture here but, rather, to the size)

# Tubulovillous adenoma

Harbor both architectural components of tubular and villous adenomas.



# Sessile serrated adenoma

- Overlap with hyperplastic polyps.
- Lack dysplasia difference from classical adenoma
- Malignant potential similar to conventional adenomas.
- Serrated architecture throughout full length of glands. In hyperplastic polyps, only at surface.
- Basal crypts dilated, sometimes laterally branching

# Familial Syndromes

- Syndromes associated with colonic polyps and increased rates of colon cancer
- Genetic basis.

- **Familial Adenomatous Polyposis (FAP)**
- **Hereditary Nonpolyposis Colorectal Cancer (HNPCC), also called Lynch Syndrome**

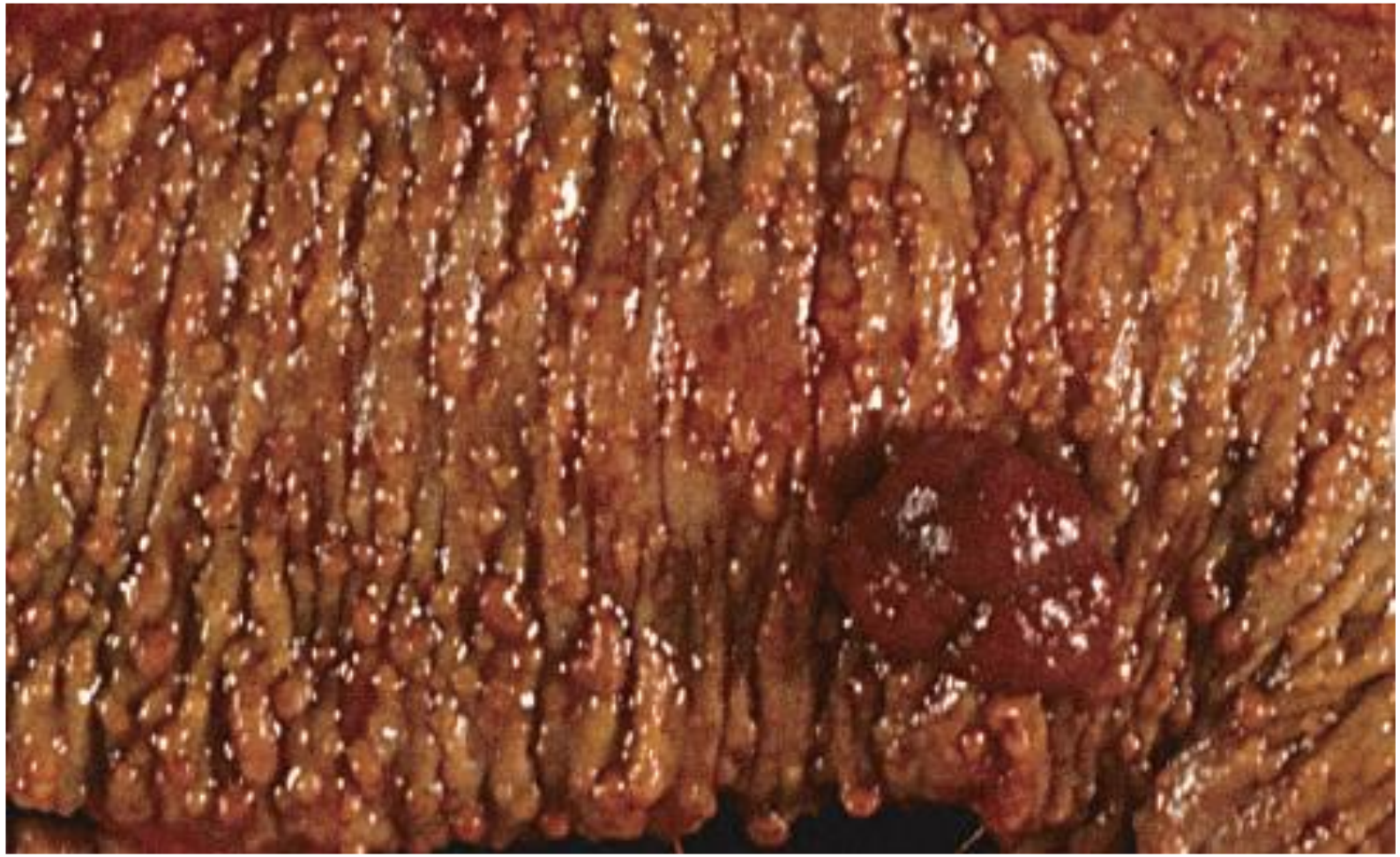
# Familial adenomatous polyposis FAP

- 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. Also, we should screen the whole family since it is an autosomal dominant gene.
- Risk for extraintestinal manifestations such as tumors.

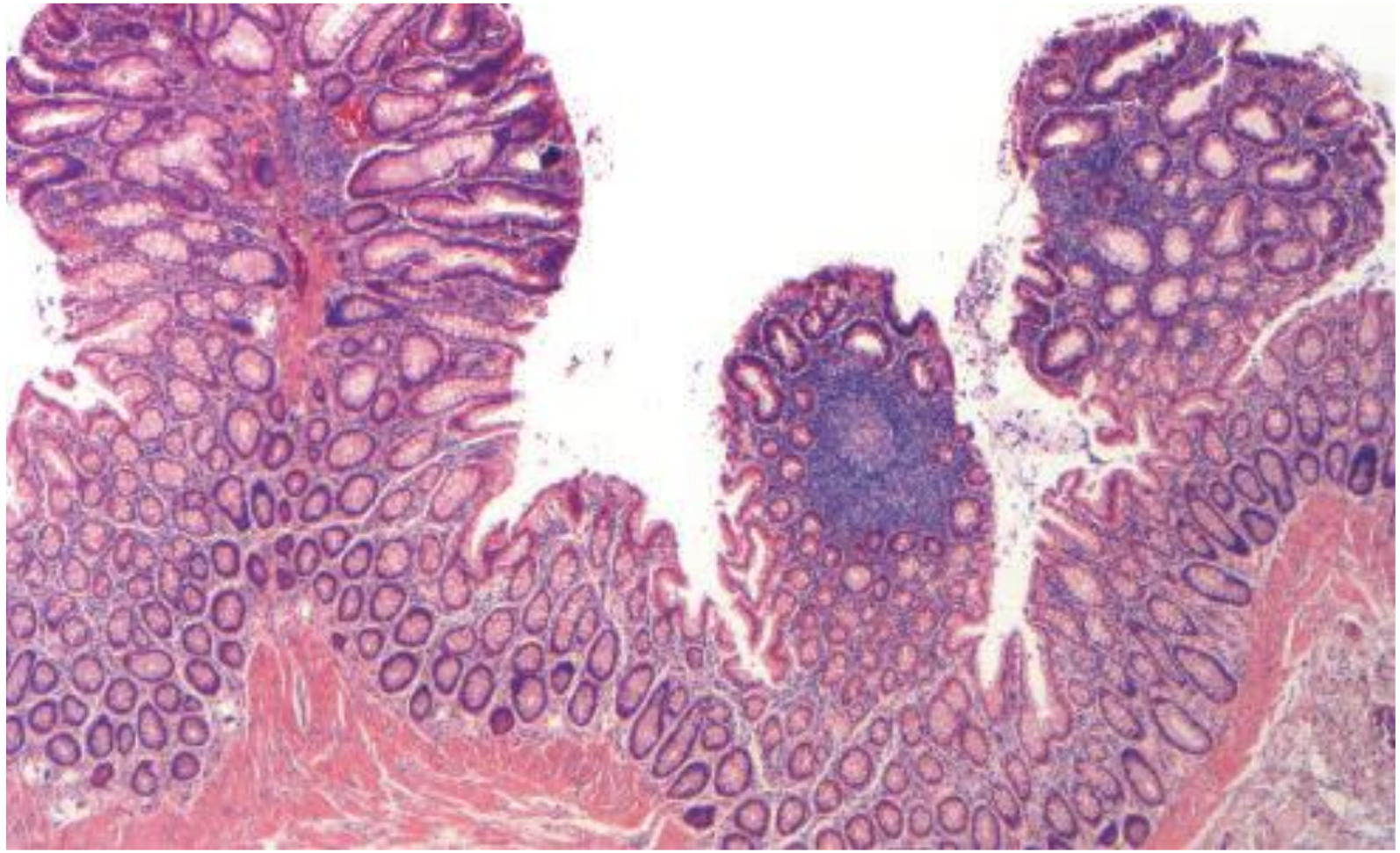
# Variants of FAP:

- Specific APC mutations.
- **Gardner syndrome**: intestinal polyps + osteomas (mandible, skull, and long bones, benign tumors); epidermal cysts; desmoid and thyroid tumors; and dental abnormalities.
- **Turcot syndrome**: intestinal adenomas and CNS tumors (medulloblastomas >> glioblastomas in 1/3 of cases)

We only need a 100 polyps to diagnose as FAP but usually they are more than a thousand (note the big polyp below on the right)



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



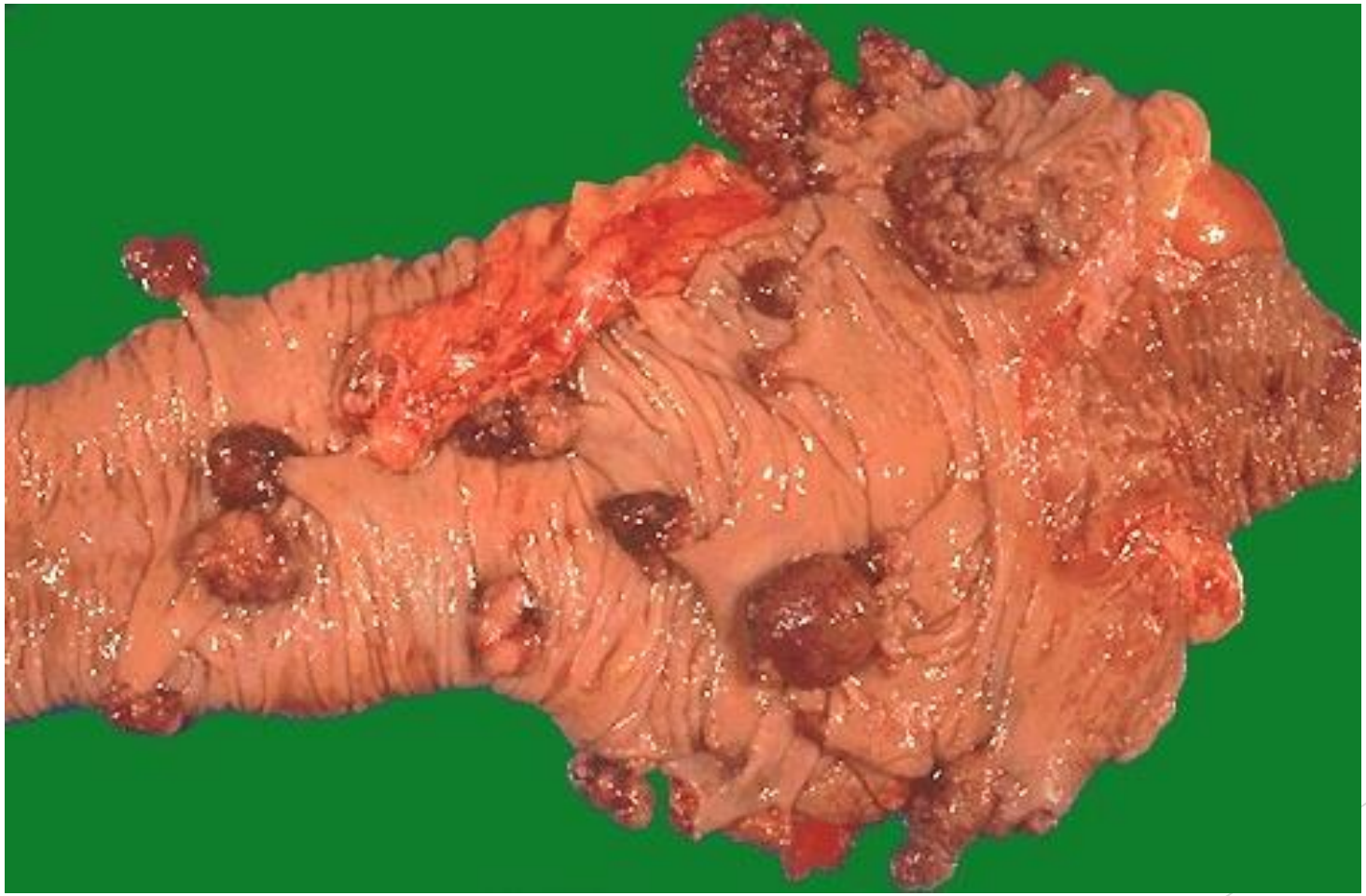
# Hereditary Nonpolyposis Colorectal Cancer: HNPCC, Lynch syndrome

- Autosomal dominant. Inherited germ-line mutations in DNA mismatch repair genes (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
- Right colon, abundant mucin.
- Only few adenomatous precursors which is why it's called nonpolyposis (typically sessile serrated adenomas).

# HNPCC, cont

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

# Cecal polyps in HNPCC.



Right side of the colon, the cecum, which is known for its broad diameter. We see many polyps but less than FAP

# Good luck!