Intestinal pathology, part 3

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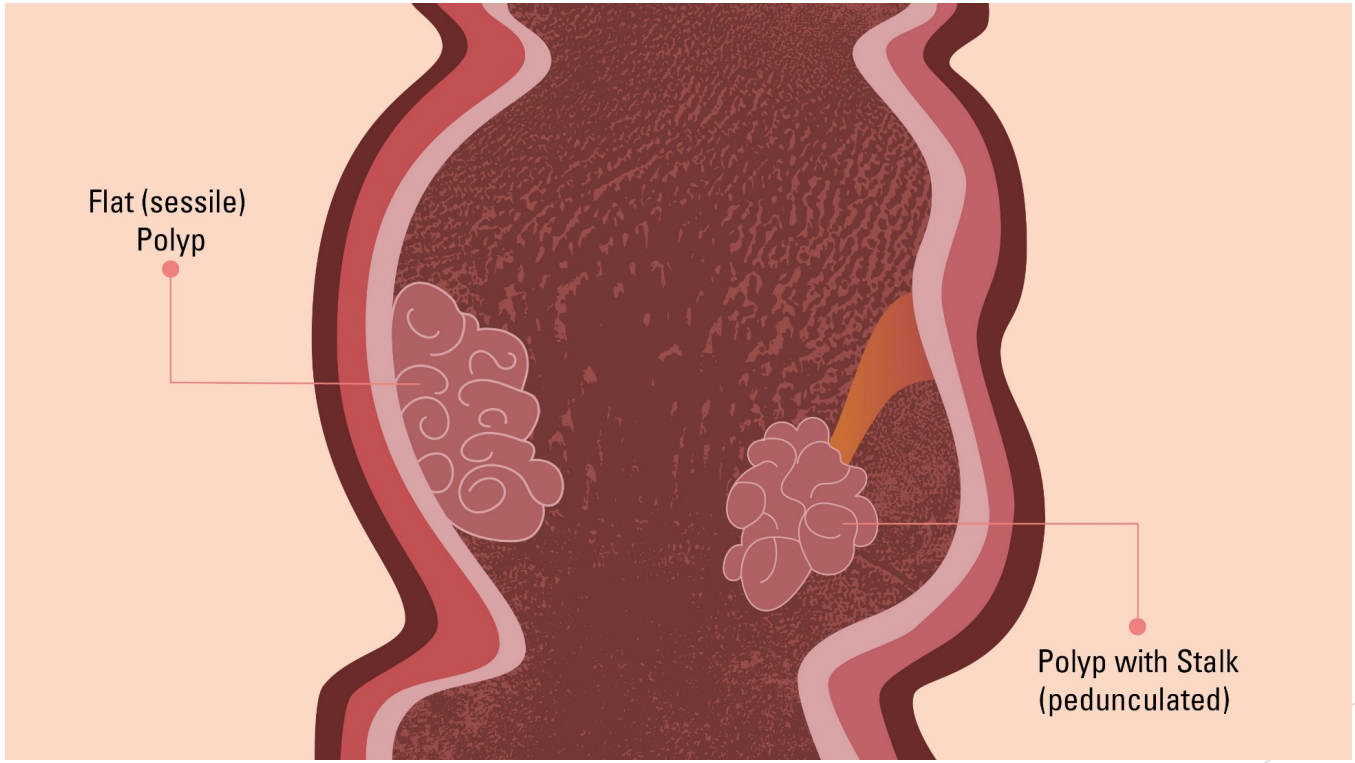
Diseases of the intestines

- 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
- ***Pedunculated polyp:*** *stalk.*

- ***Neoplastic polyps:*** *adenoma.*
- ***Non neoplastic polyps:*** inflammatory, hamartomatous, or hyperplastic



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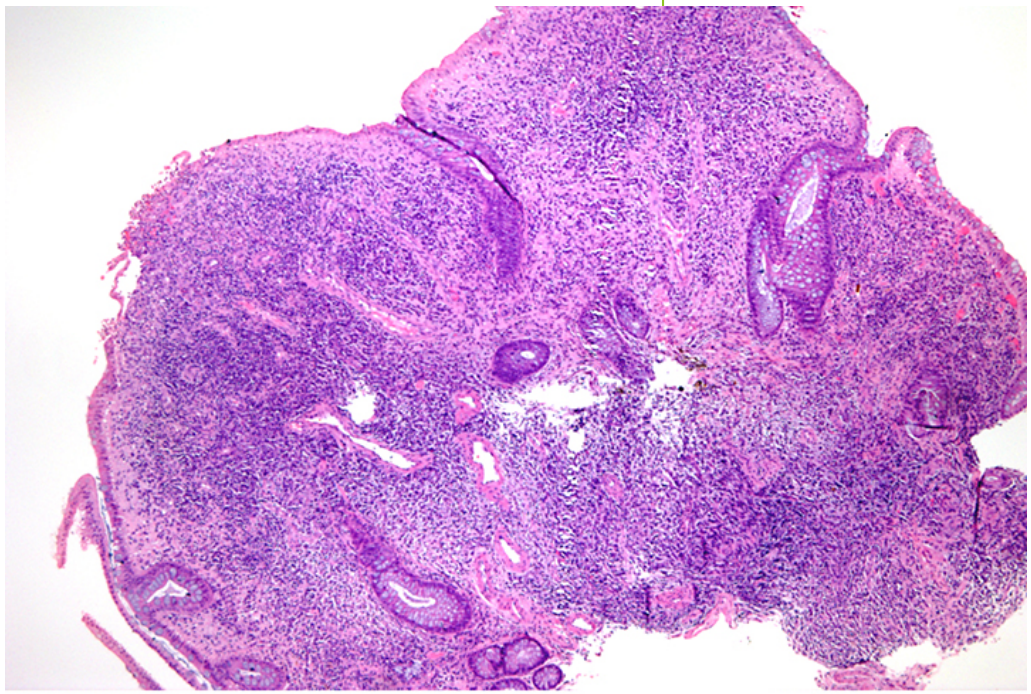
Inflammatory Polyps

- Solitary rectal ulcer syndrome.
- Impaired relaxation of anorectal sphinctor.
- 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.

- Rectal bleeding, mucus discharge and polyp.

Inflammatory polyps



4x: low power, dense inflammation in lamina propria

Pathology Outlines

Hamartomatous Polyps

- Sporadic or syndromic.
- Hamartomatous polyposis syndromes.
- Disorganized, tumor-like growth composed of mature cell types normally present at that site.

- Juvenile Polyps
- Peutz-Jeghers Syndrome

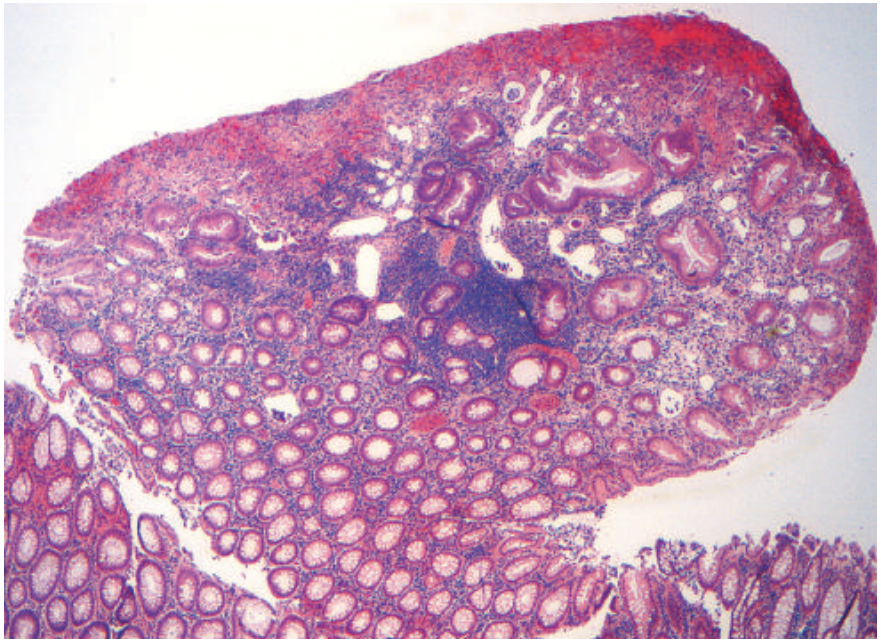
Juvenile Polyps

- Most common hamartomatous polyp

- **Sporadic**
- Solitary. <5 years of age
- 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

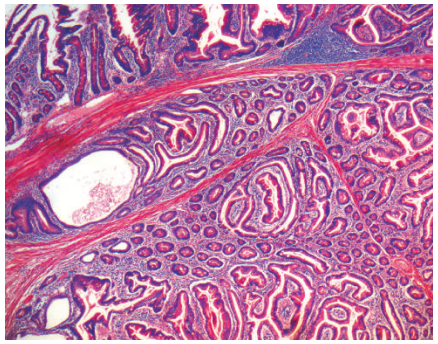


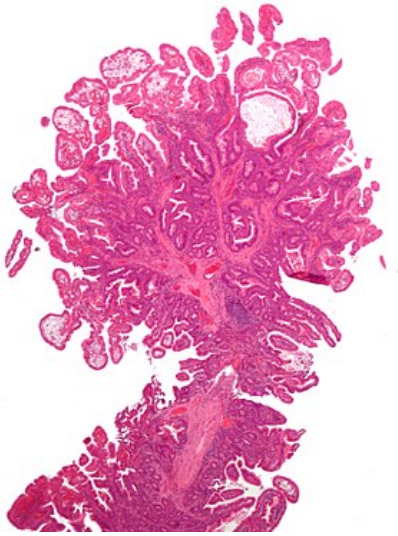
- Pedunculated
- Reddish lesions
- Cystic spaces on cut sections
- Dilated glands filled with mucin and inflammatory debris.
- Granulation tissue on surface.

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).

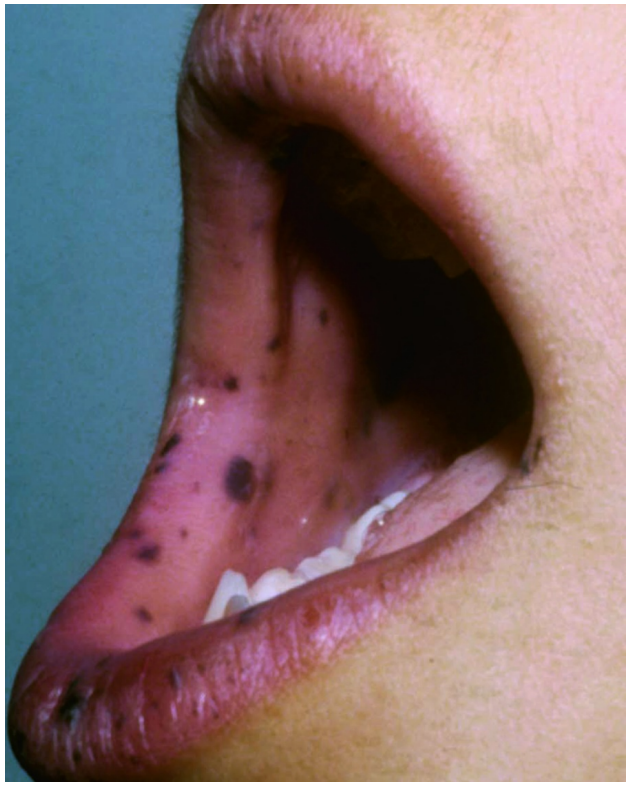
Peutz-Jeghers polyp

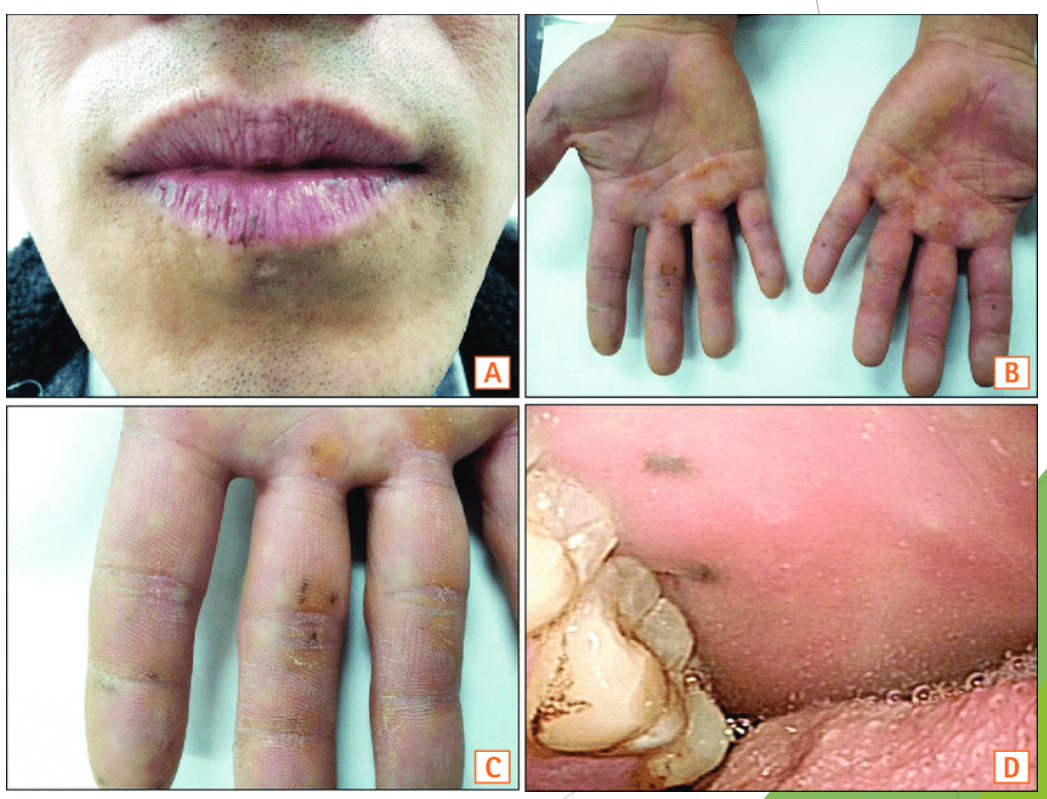




- Mostly in small intestine.
- Large, pedunculated, lobulated.
- Arborizing network of connective tissue, smooth muscle, lamina propria and glands
- Normal-appearing intestinal epithelium
- Christmas tree pattern.

Mucocutaneous pigmentation





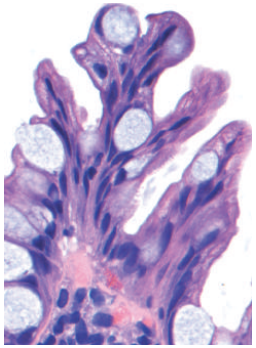
Hyperplastic Polyps

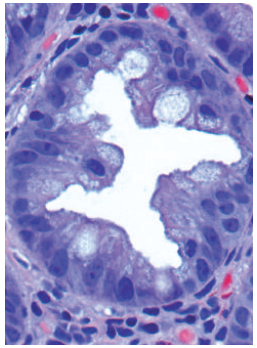
- Common
- 6-7th decades.
- Decreased epithelial turnover and delayed shedding of surface epithelium >>> pileup of goblet cells & epithelial overcrowding
- **No malignant potential**
- **Biopsy is important.**

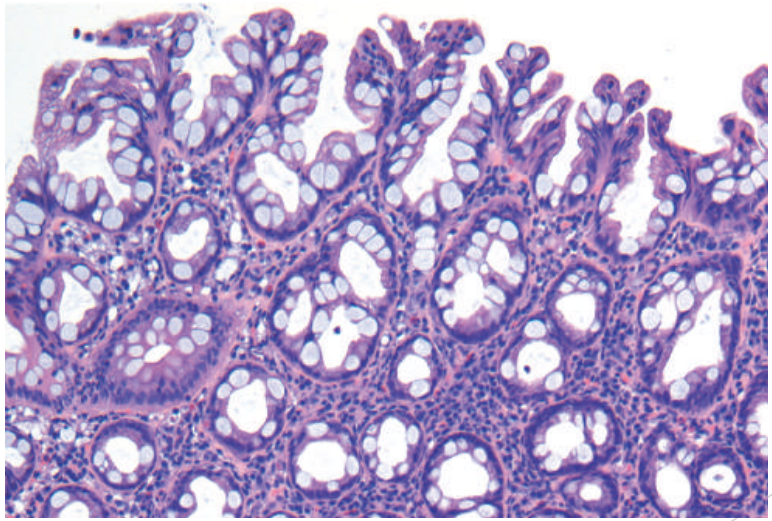
Hyperplastic polyp

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

- Crowding of goblet & absorptive cells.
- Serrated surface.



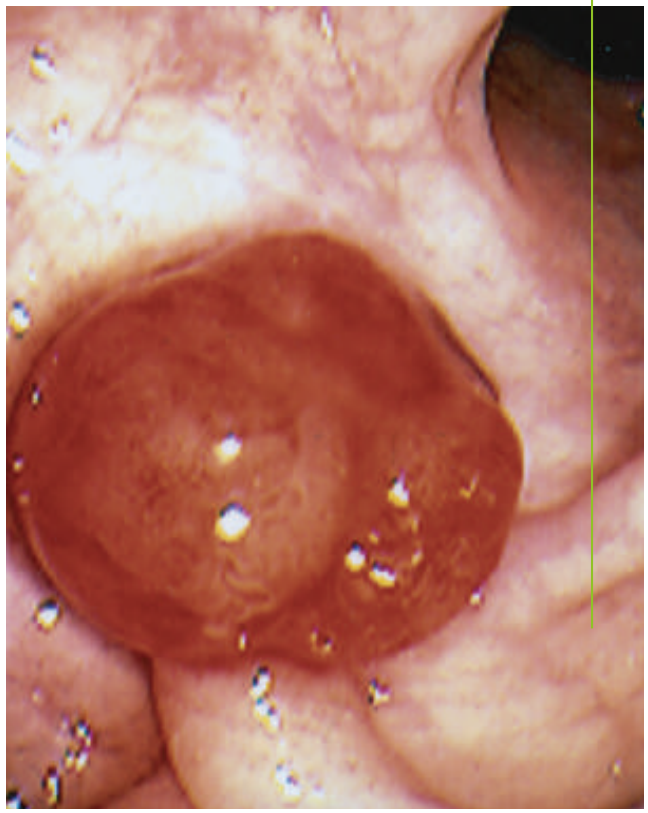


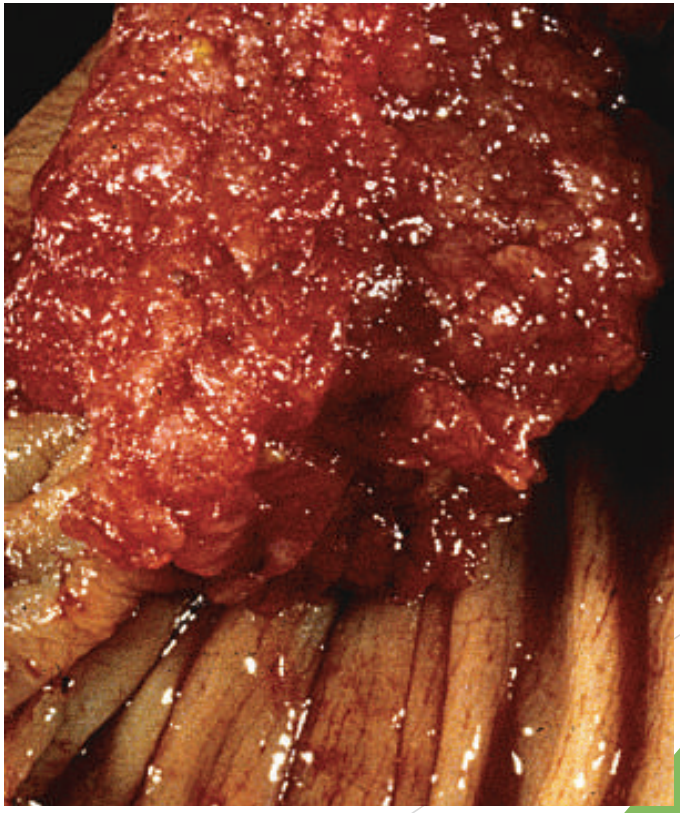


Adenomas

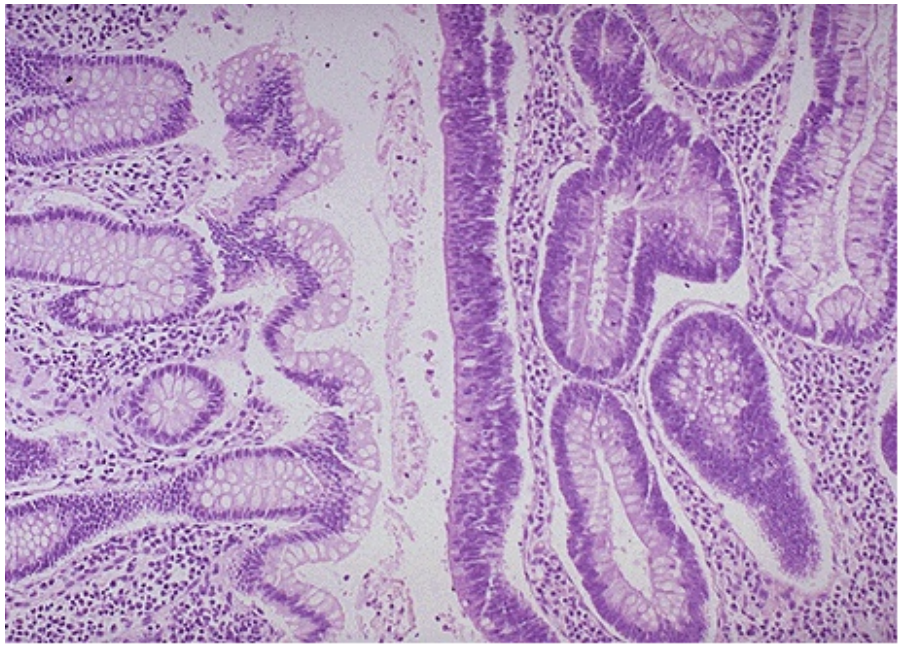
- Most common and clinically important
- 50% of adults > 50 years. (western world)
- **Precursor for majority of colorectal adenocarcinomas**
- USA: screening colonoscopy starts at 45 yrs.
- Earlier screening with family history.
- **Western diets and lifestyles increase risk.**

Pedunculated or sessile



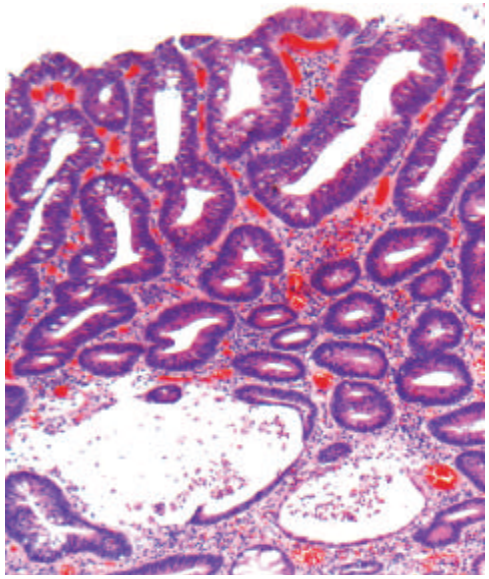


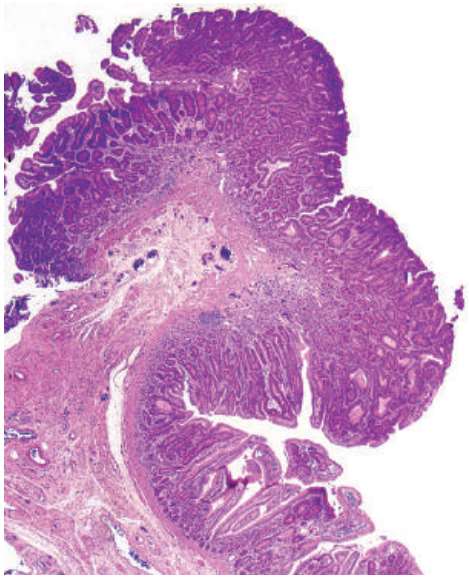
Colon adenoma



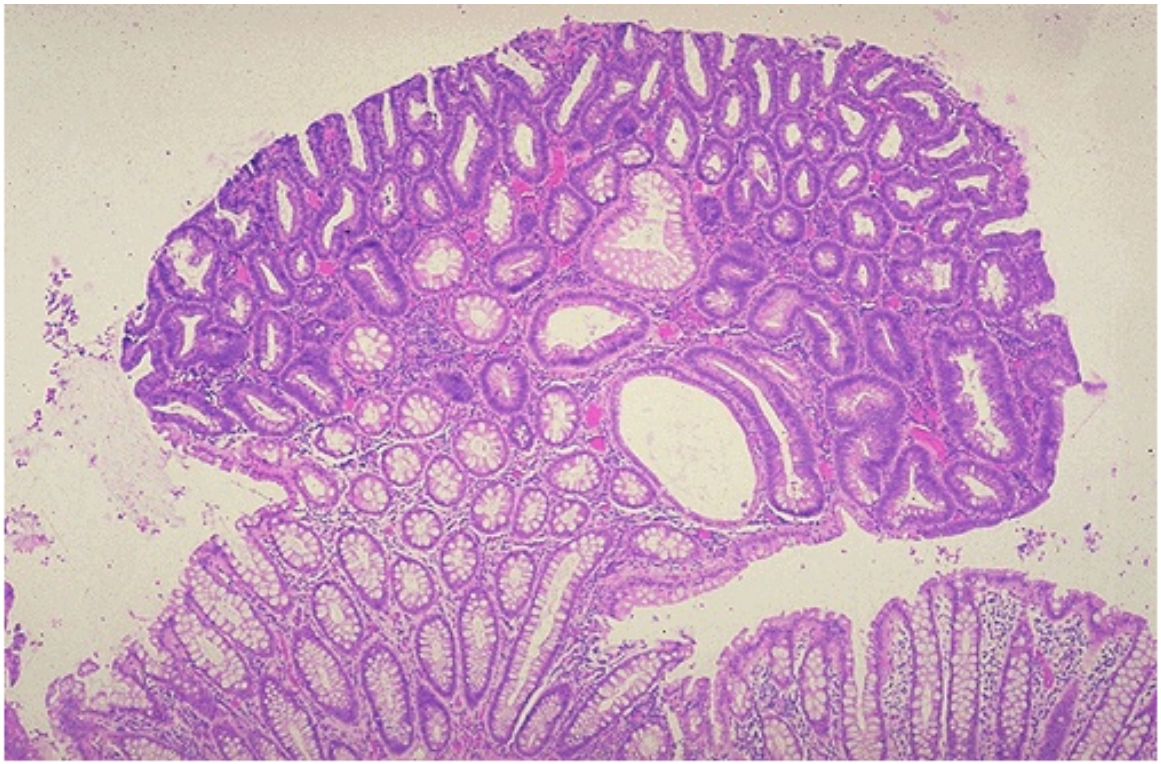
- Hallmark: epithelial dysplasia
- Nuclear hyperchromasia, elongation, stratification, high N/C ratio.
- Size is most important correlate with risk for malignancy. (40% if > 4cm)
- High-grade dysplasia is a second factor
- Architecture: Tubular, villous, tubulovillous.

Tubular adenoma:

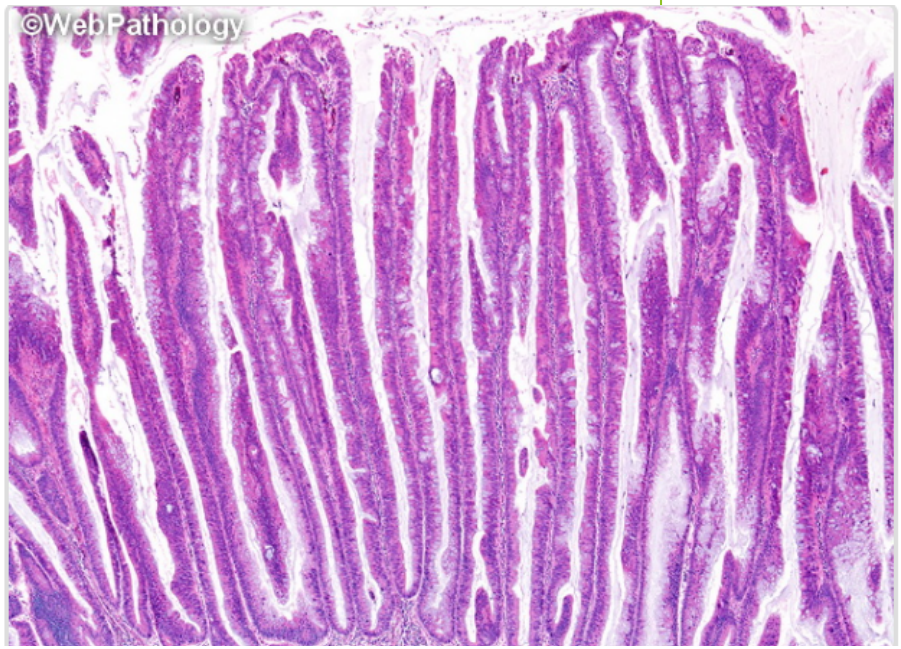




- Pedunculated
- small tubular glands

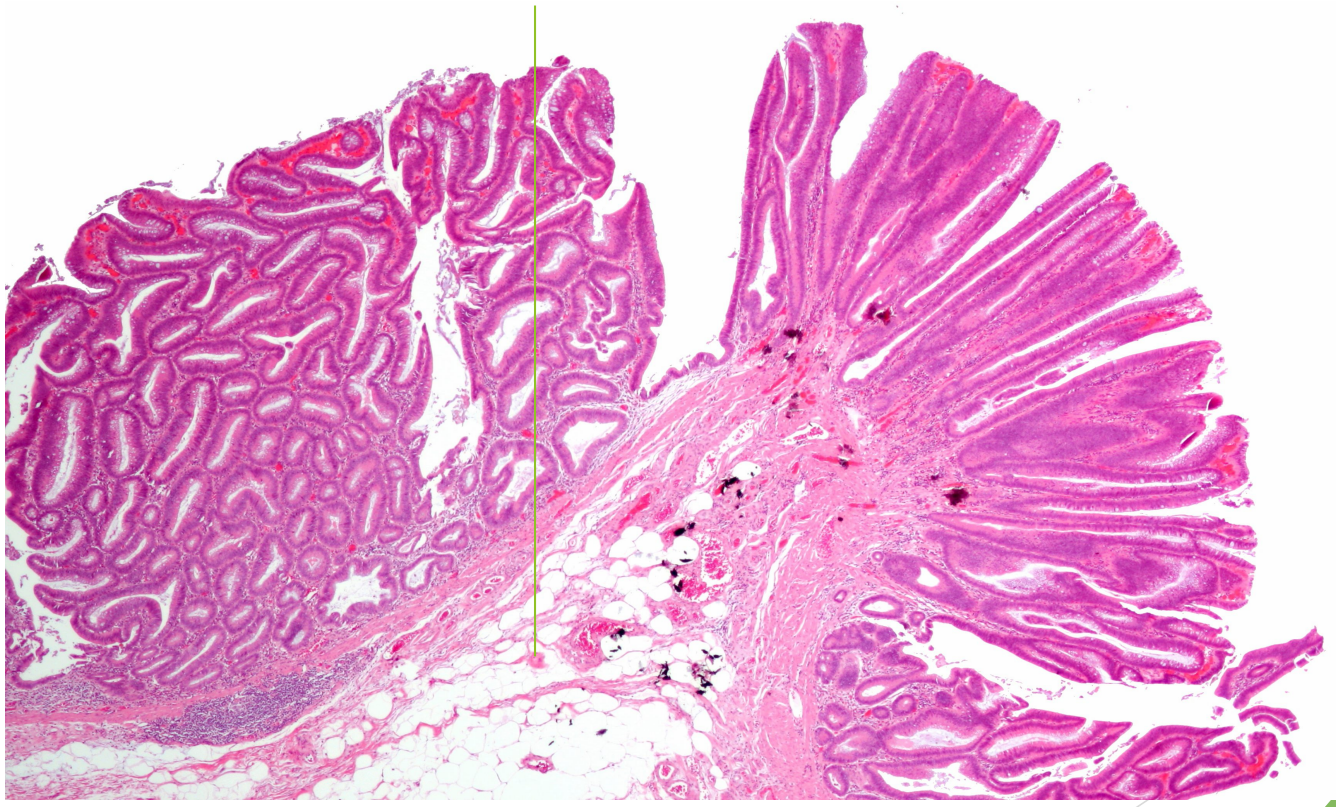


Villous adenoma.



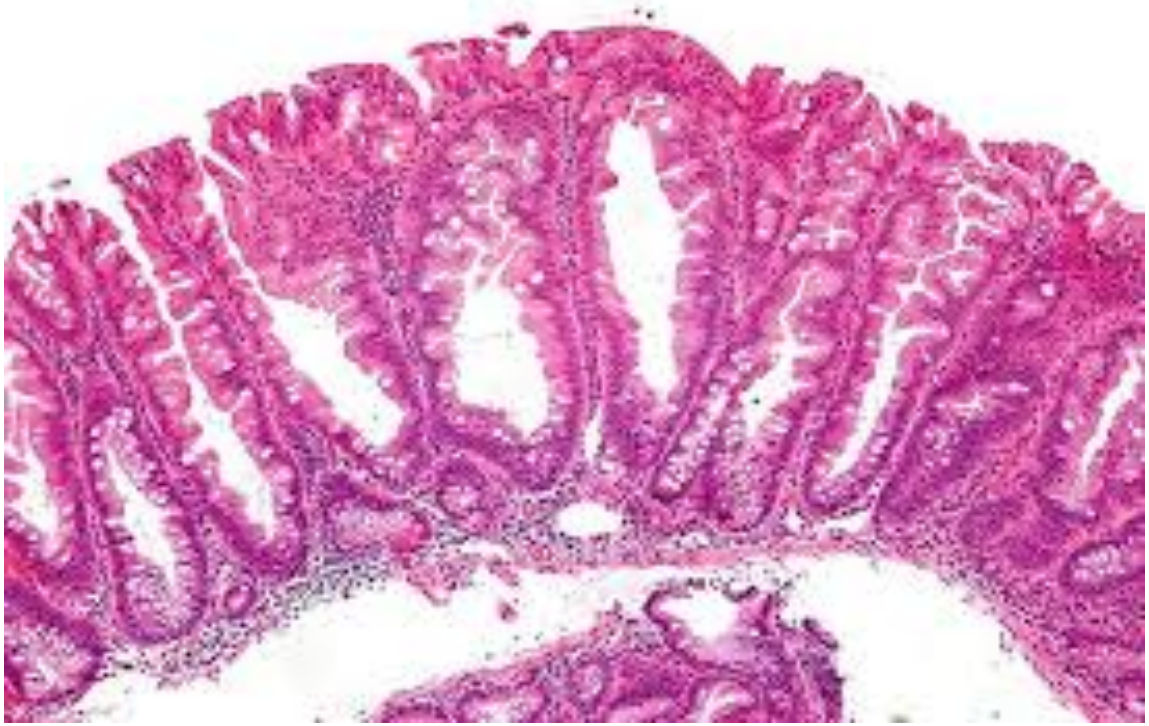
- Long slender villi.
- Large and sessile.
- More frequent invasive foci

Tubulovillous adenoma



Sessile serrated adenoma

- Overlap with hyperplastic polyps.
- Lack dysplasia
- Malignant potential similar to conventional adenomas.
- Serrated architecture throughout full length of glands.
- Basal crypts dilated.



Familial Syndromes

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

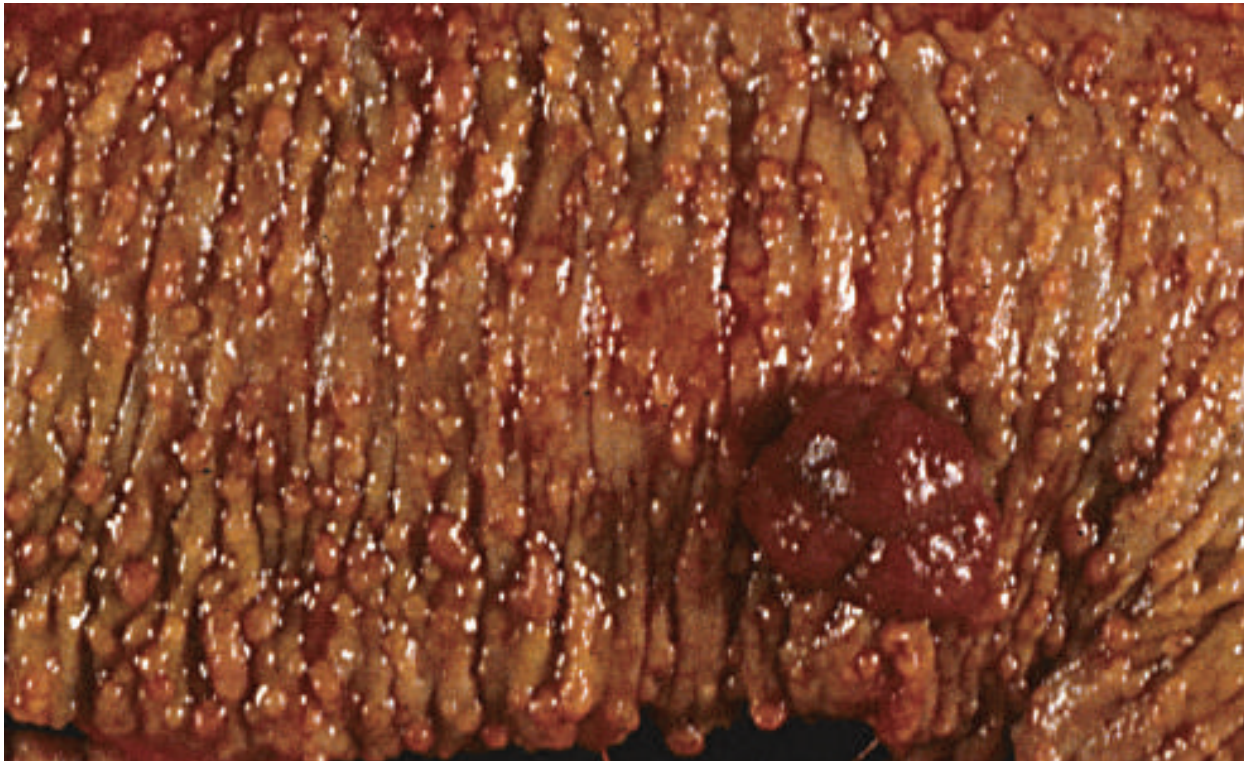
- **Familial Adenomatous Polyposis (FAP)**
- **Hereditary Nonpolyposis Colorectal Cancer (HNPCC)**

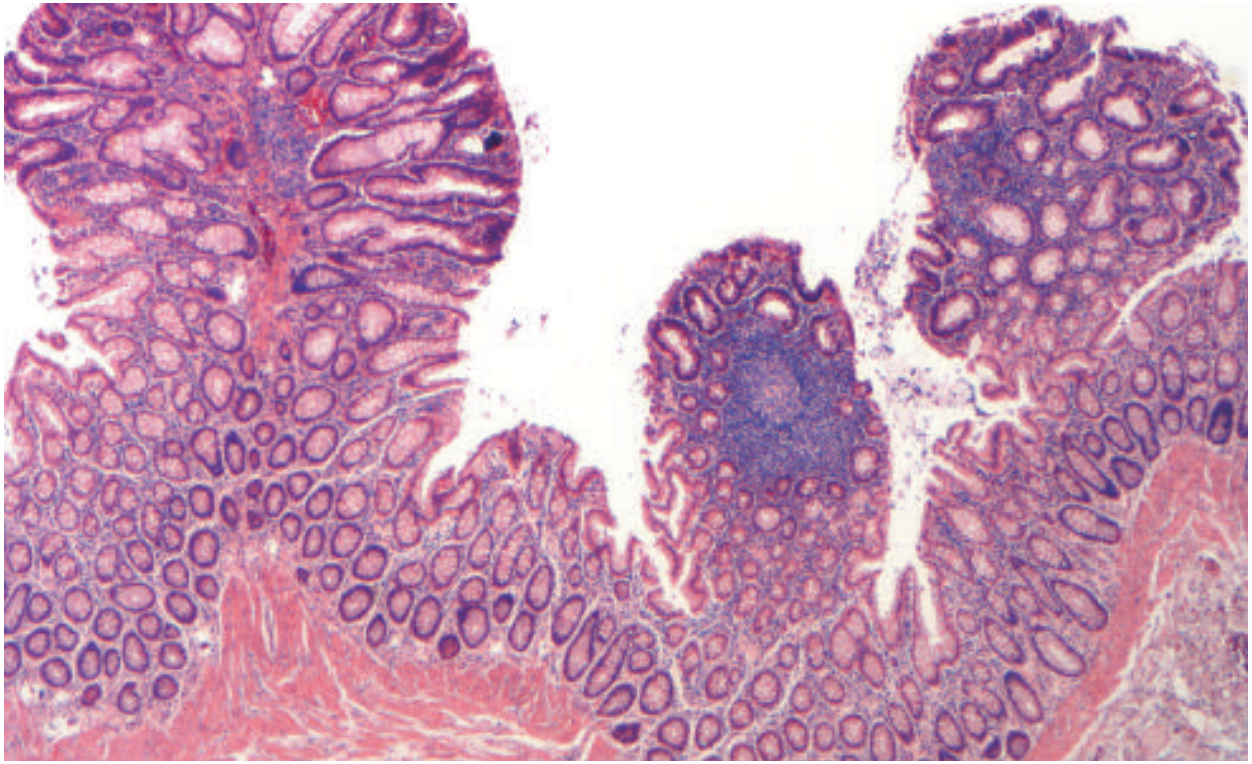
Familial adenomatous polyposis FAP

- 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.
- Risk for extraintestinal manifestations

Variants of FAP:

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





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 (typically sessile serrated adenomas).

HNPCC, cont

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

Cecal polyps in HNPCC.