GNT
Pathology

Benign Tumors of Intestine

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Learning Objectives

- Know the classification of intestinal tumors (small intestine and colon)
- Know the definition of a polyp.
- Compare adenomatous/neoplastic polyps and non neoplastic polyps (hyperplastic polyps, inflammatory polyp and hamartomatous polyp) with respect to pathology (gross and microscopic features).
- Know the three subtypes of adenomatous polyps, eg, tubular adenoma, villous adenoma, tubulovillous adenoma.
- Describe the adenomatous polyp-cancer sequence and the features associated with risk of malignancy, eg, polyp size, histologic architecture, and severity of epithelial dysplasia.
- Describe the classification of the hereditary syndromes involving the GI tract and the syndromes associated with an increased risk of cancer (Peutz-Jeghers syndrome, familial adenomatous polyposis, and hereditary nonpolyposis colorectal carcinoma)

Tumors of the small and large intestines

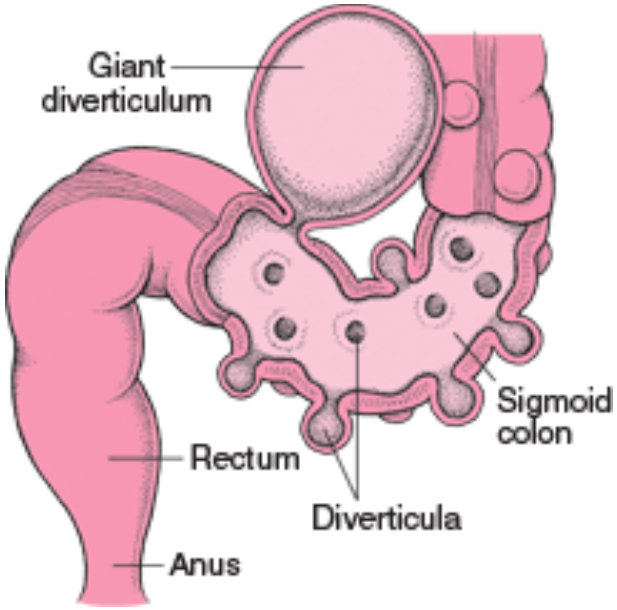
Polyps

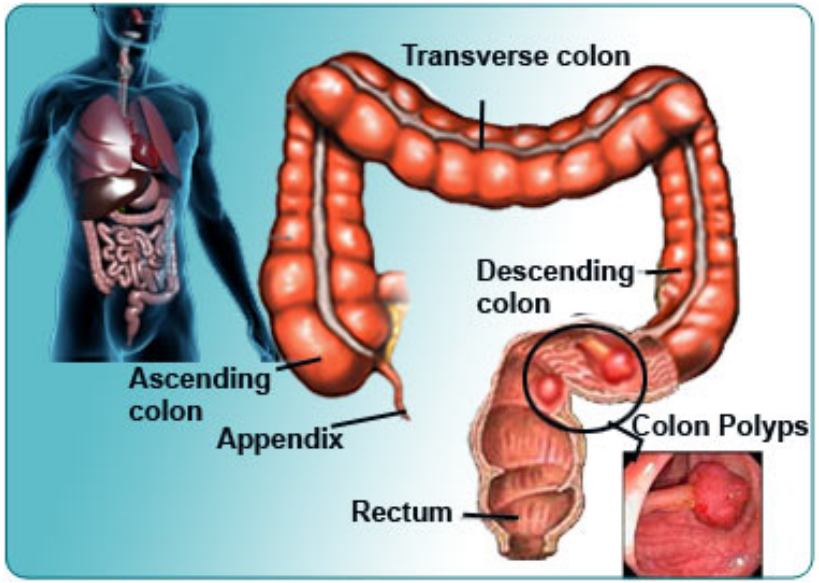
Carcinoma

Carcinoid tumor

Lymphoma

- Sigmoid colon: Most common site GI polyps, diverticula and cancer



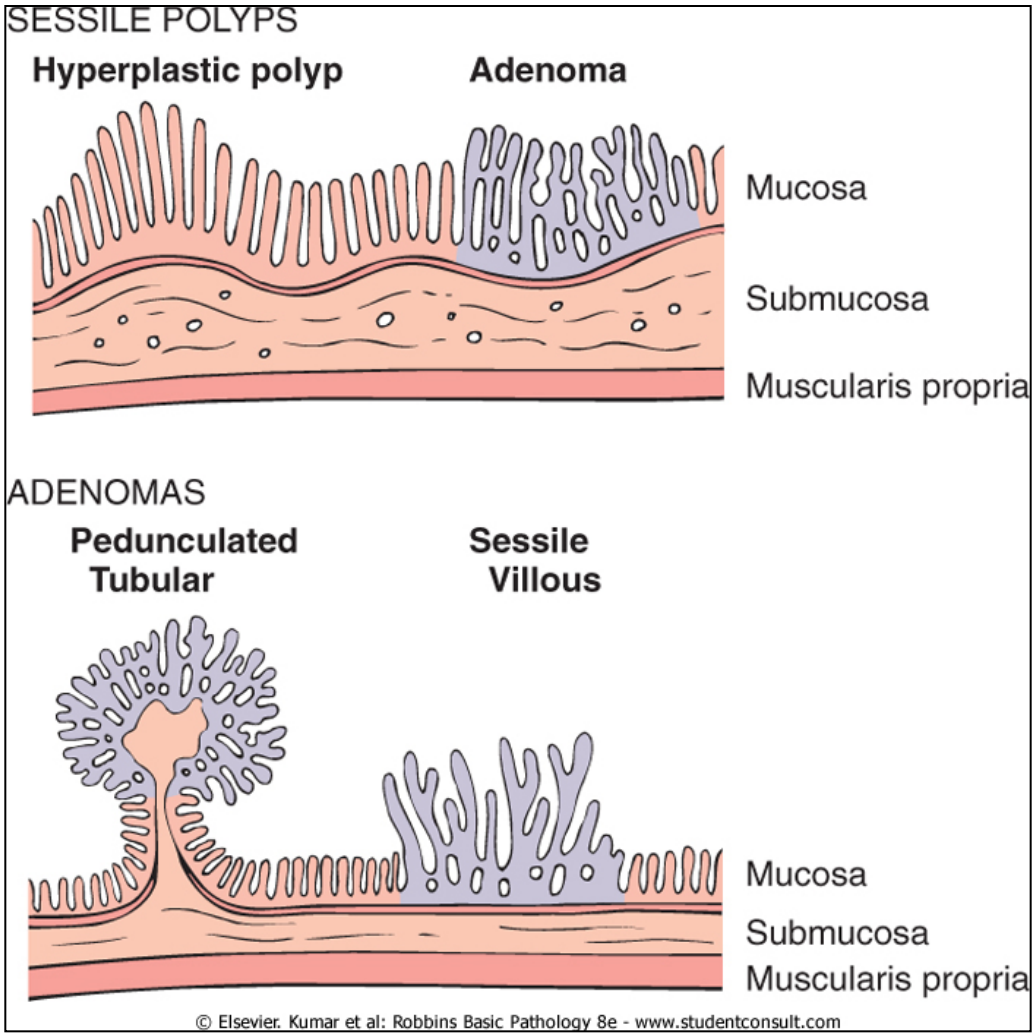


Polyps

- ***Non-neoplastic polyps*** **90%**
  - Hyperplastic polyps
  - Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps)
  - Inflammatory polyps
  - Lymphoid polyps

- ***Neoplastic polyps*** **10%**
  - Adenoma

Polyps


SESSILE POLYPS
Hyperplastic polyp
Adenoma
Mucosa
Submucosa
Muscularis propria
ADENOMAS
Pedunculated
Tubular
Sessile
Villous
Mucosa
Submucosa
Muscularis propria
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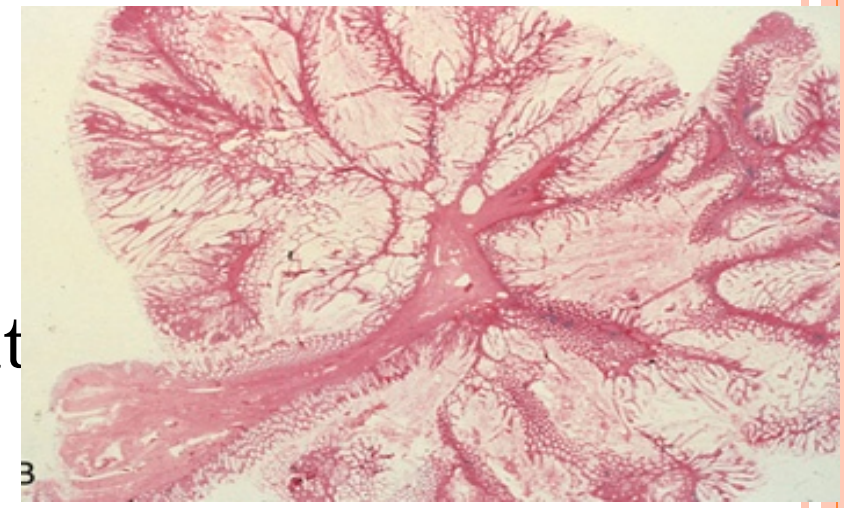
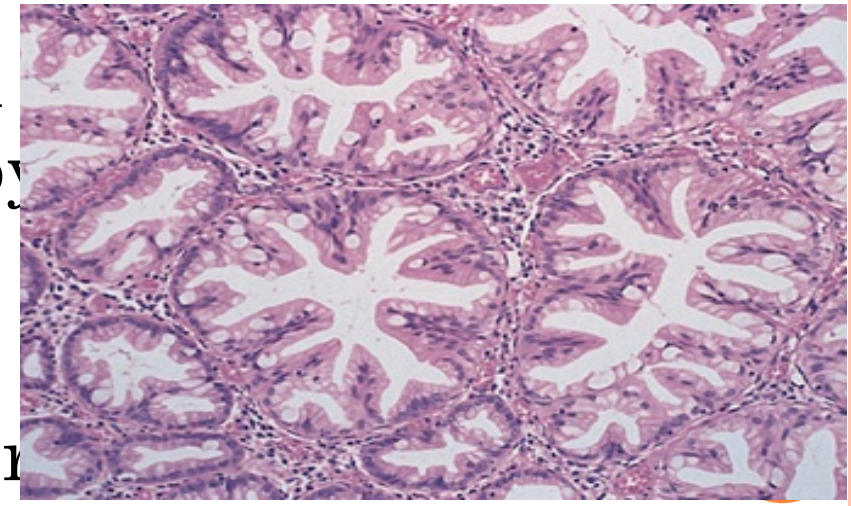
Hyperplastic Polyp

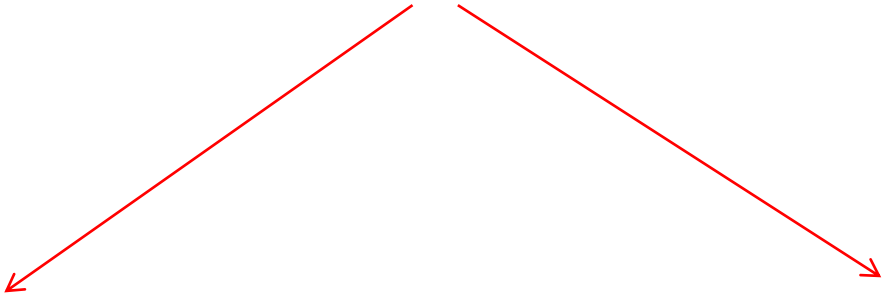
- Asymtomatic
- > 50% are located in the rectosigmoid
- Most common type in adult
- Sawtooth surface
- Star shaped crypts
- Composed of well-formed glands and crypts lined by differentiated goblet or absorptive cells.
- No malignant potential or polyposis syndromes





Non-Neoplastic Polyp

Hamartomatous polyps



Juvenile polyps
Retention polyp

Peutz-Jeghers polyps

HAMARTOMATOUS POLYP

Juvenile Polyps (retention polyp)

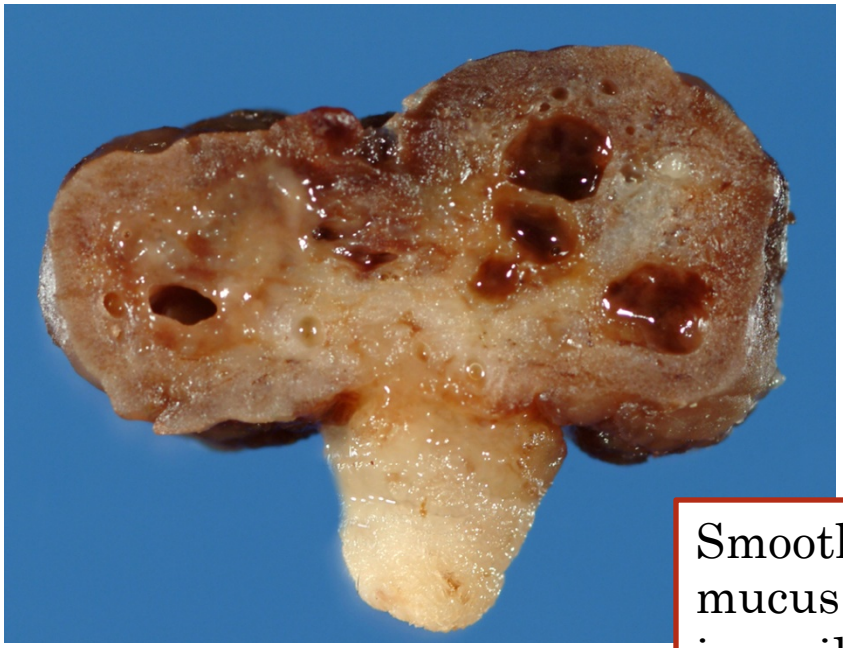
- Developmental malformations affecting the glands and lamina propria
- Commonly occur in children under 5 years old in the rectum.
- In adult called retention polyp.
- no malignant potential

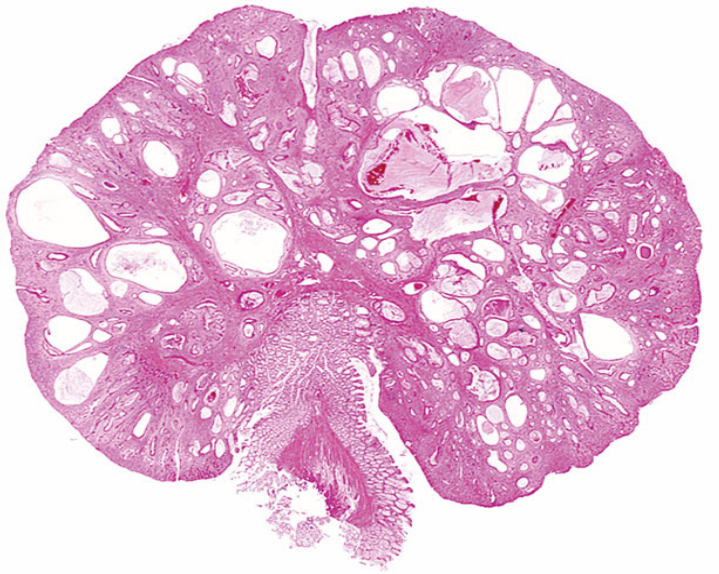
Juvenile polyposis

- Autosomal dominant
  - **TGF-β signaling pathway abnormalitides**
  - **Juvenile polyps; risk of gastric, small intestinal, colonic, and pancreatic adenocarcinoma**
- Cowden syndrome
  - **Abnormality in PTEN**
  - **Hamartomatous polyps, lipomas, ganglioneuromas, inflammatory polyps; increased risk for colon cancer and cancer of thyroid and breast**
- Cronkhite-Canada syndrome
  - Nonhereditary polyposis syndrome
  - Polyps plus ectodermal abnormalities (Nail atrophy, hair loss, abnormal skin pigmentation) cachexia, and anemia

HAMARTOMATOUS POLYP

Juvenile Polyps (retention polyp)



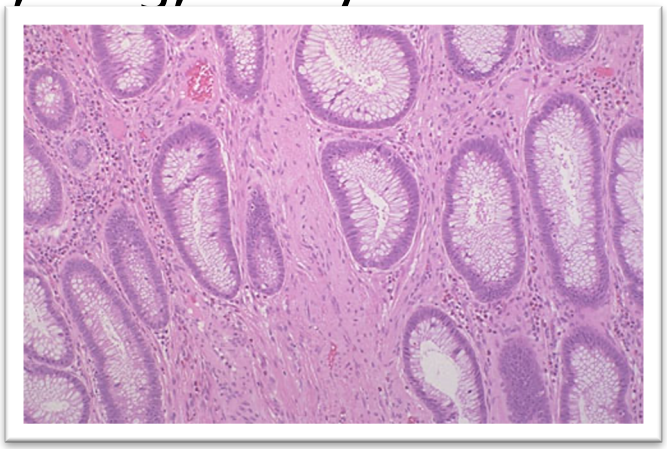


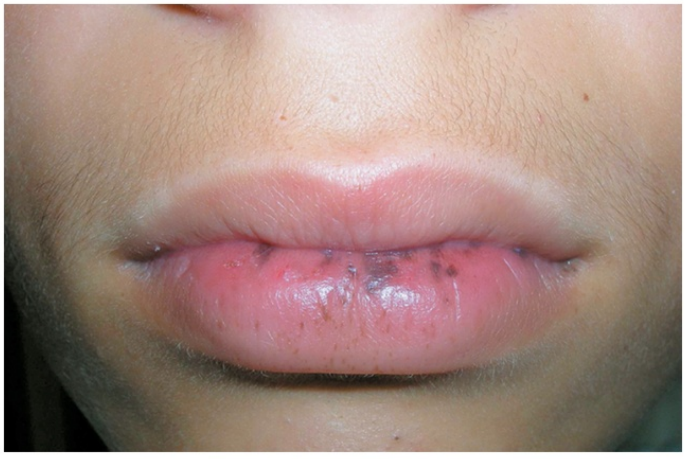
Smooth eroded surface with numerous mucus retention cysts, typical of sporadic juvenile polyps.

Hamartomatous Polyps

Peutz-Jehgers syndrome

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





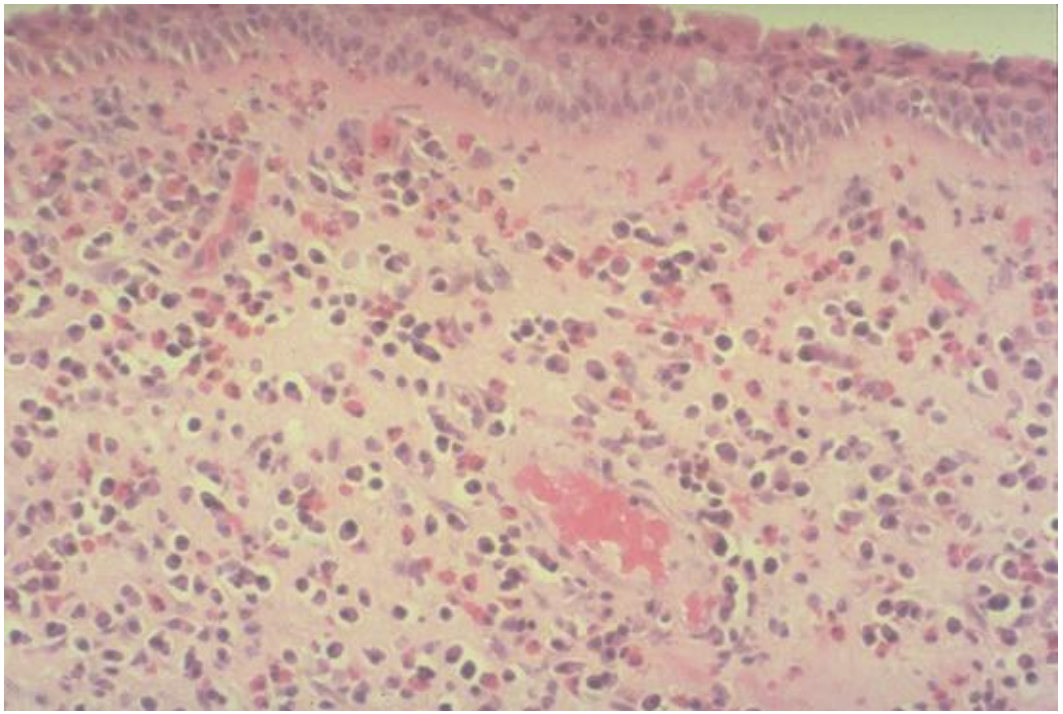
Peutz-Jehgers Syndrome

Syndrome	Mean Age at Presentation (Years)	Mutated Gene(s)	GI Lesions	Selected Extragastrointestinal Manifestations
Peutz-Jeghers syndrome	10–15	*LKB1/STK11*	Arborizing polyps—small intestine > colon > stomach; colonic adenocarcinoma	Mucocutaneous pigmentation; increased risk for thyroid, breast, lung, pancreas, gonadal, and bladder cancers

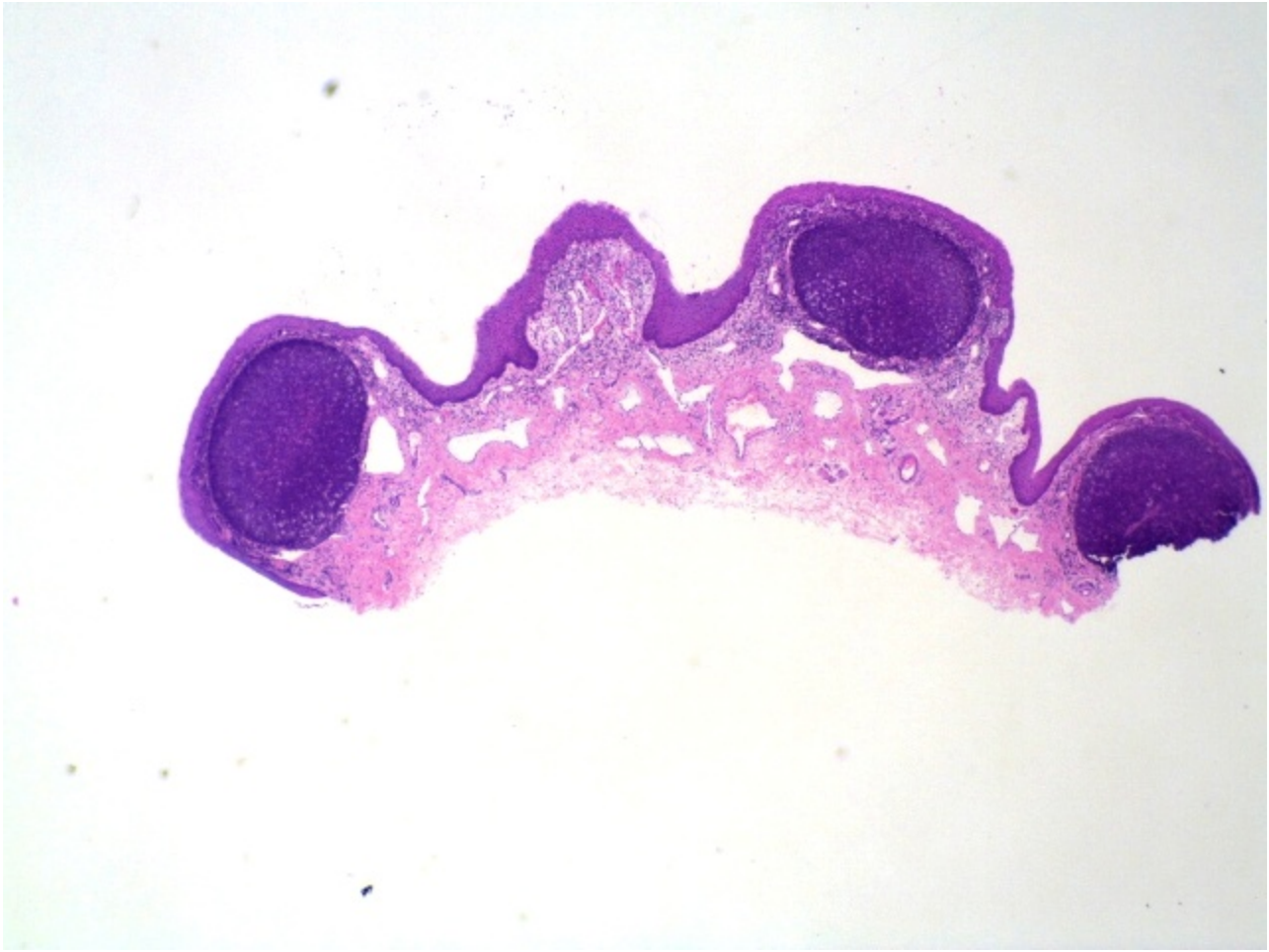
LKB1/STK11 encodes a tumor suppressive protein kinase that regulates cellular metabolism

Inflammatory Polyps

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



LYMPHOID POLYPS



Neoplastic Polyps (Adenomas)

Adenomatous Polyp (adenoma)

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

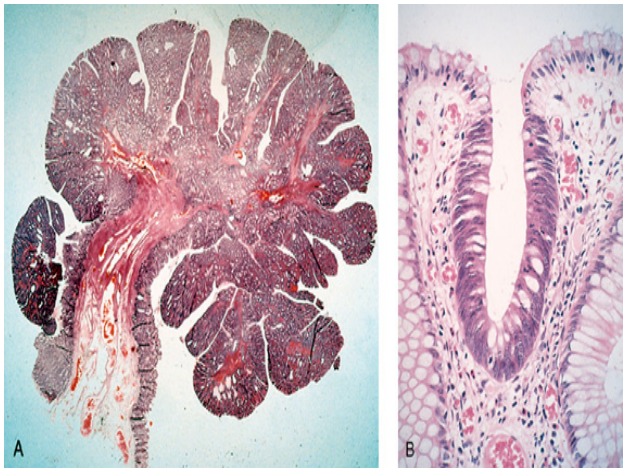
Neoplastic Polyps (Adenomas)

Adenomatous Polyp (adenoma)

- Divided into:
  1. Tubular adenoma: less than 25% villous architecture
  2. Villous adenoma: villous architecture over 50%
  3. Tubulovillous adenoma: villous architecture between 25 and 50%.

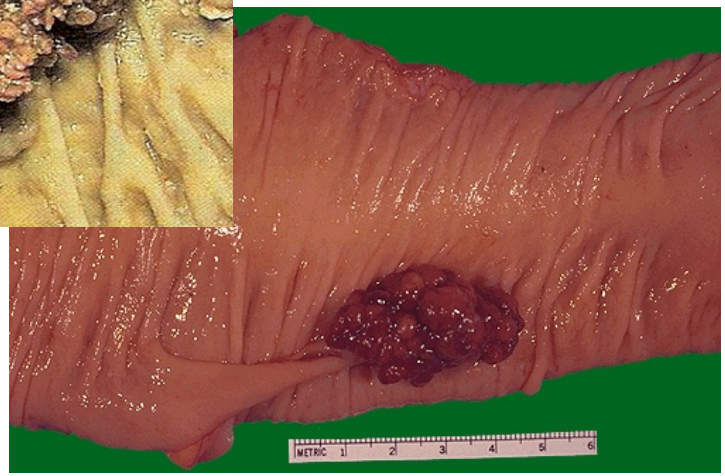
Tubular adenoma

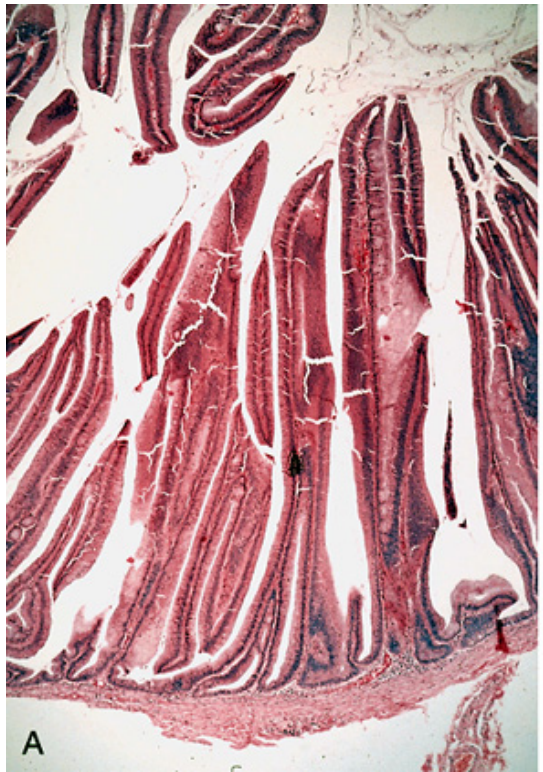
- Represents 75% of all neoplastic polyps.
- 75 % occur in the distal colon and rectum
- Sigmoid colon most common site.



VILLOUS ADENOMA

- The least common, largest and most ominous of epithelial polyps (most likely to undergo malignant transformation).
- Age: 60 to 65 years, 75% located in rectosigmoid area
- Present with rectal bleeding or anemia, large ones may secrete copious amounts of mucoid material rich in protein and potassium
- Large tumors can produce hypoalbuminemia and hypokalemia.



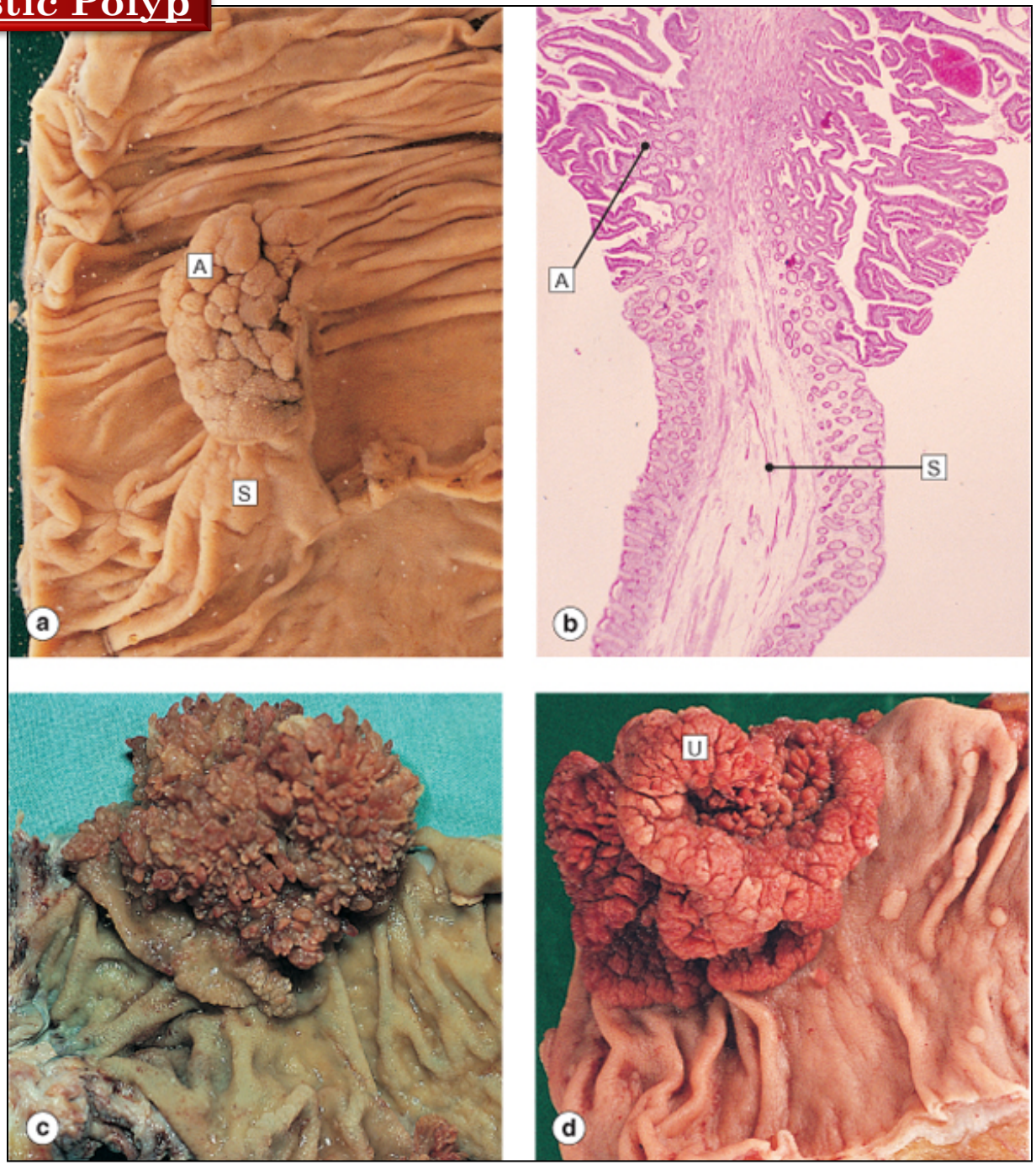


Neoplastic Polyps

3] *Tubulovillous adenoma*

- 20%–30% of polyps
- Intermmediate in size, degree of dysplasia and malignant potential between tubular and villous adenomas.

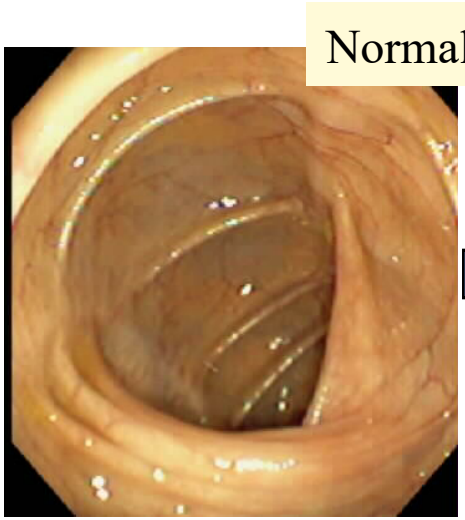
Neoplastic Polyp

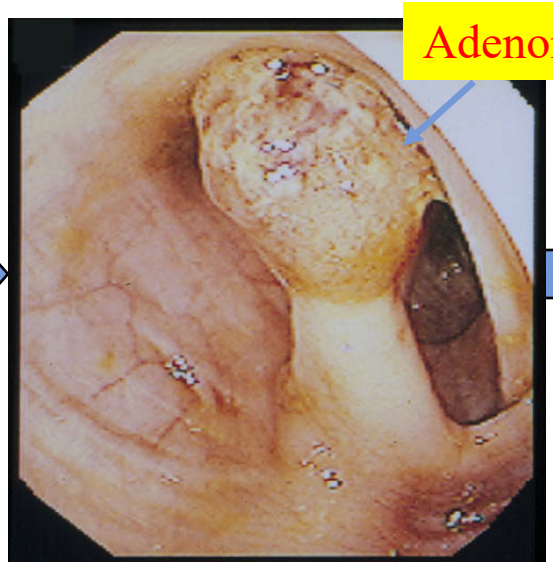


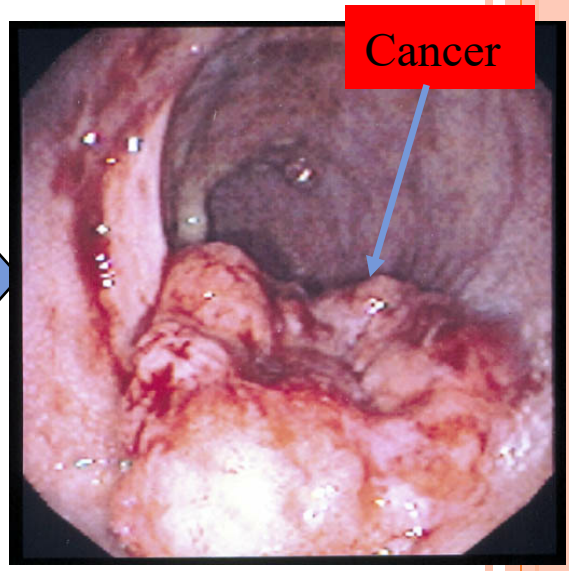
Relationship of Neoplastic Polyps to Carcinoma

- Adenoma to carcinoma sequence is documented by several genetic alterations.

Adenoma to Carcinoma Pathway







APC loss

K-ras mutation

Chrom 18 loss

p53 loss

Normal Epithelium → Hyper-proliferation → Early Adenoma → Intermediate Adenoma → Late Adenoma → Cancer

Relationship of Neoplastic Polyps to Carcinoma

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

  1. The size of the polyp.
  2. The relative proportion of its villous features.
  3. The presence of significant cytologic atypia (dysplasia) in the neoplastic cells.
  4. Multiple polyps

Familial Polyposis Syndrome

- Patients have genetic tendencies to develop neoplastic polyps.
  - ***Familial polyposis coli (FPC)***
  - ***Gardener's syndrome***
  - ***Turcot syndrome***

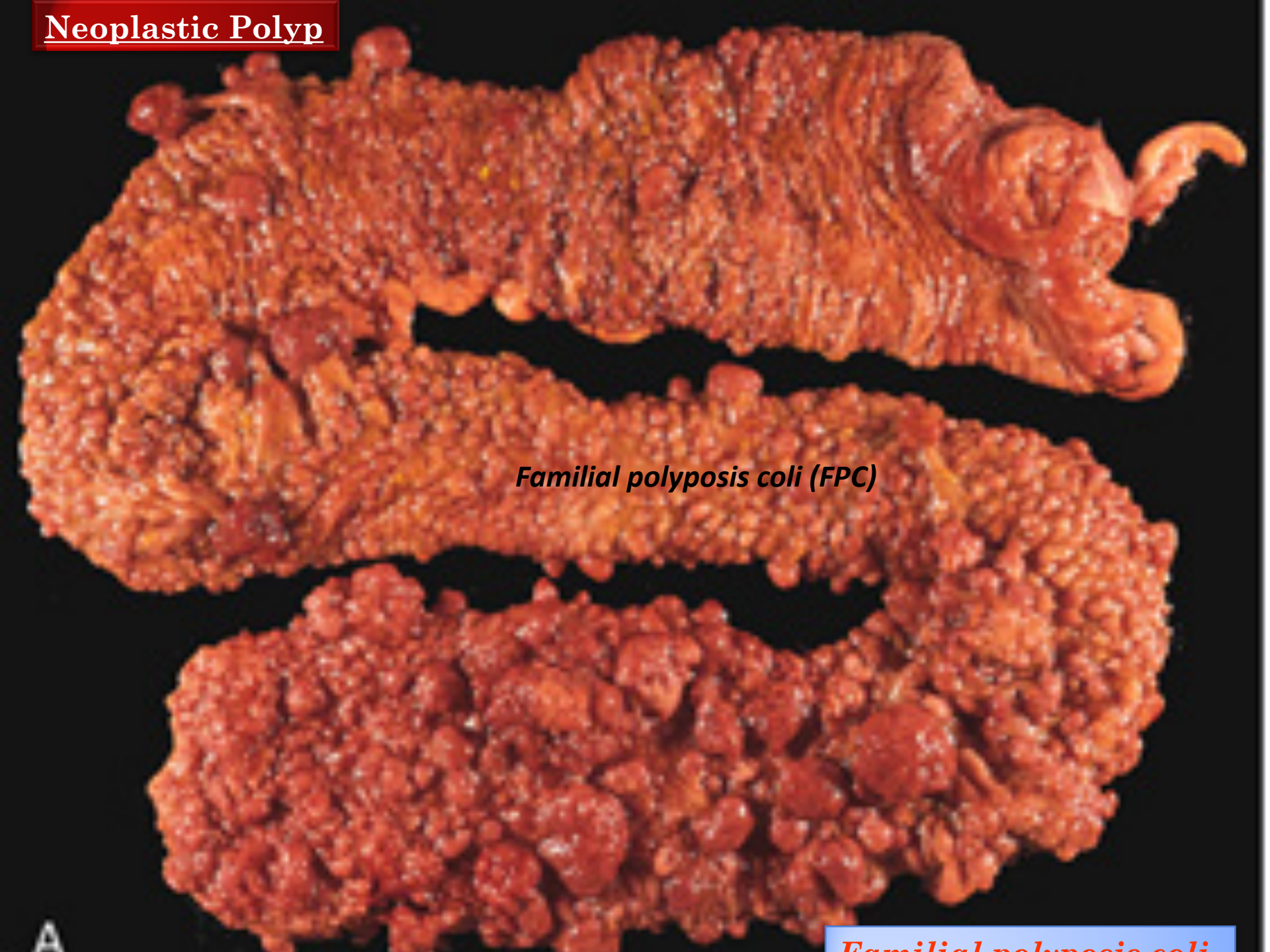
Familial Polyposis Syndrome

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.

Gardener's syndrome
Turcot syndrome

Neoplastic Polyp



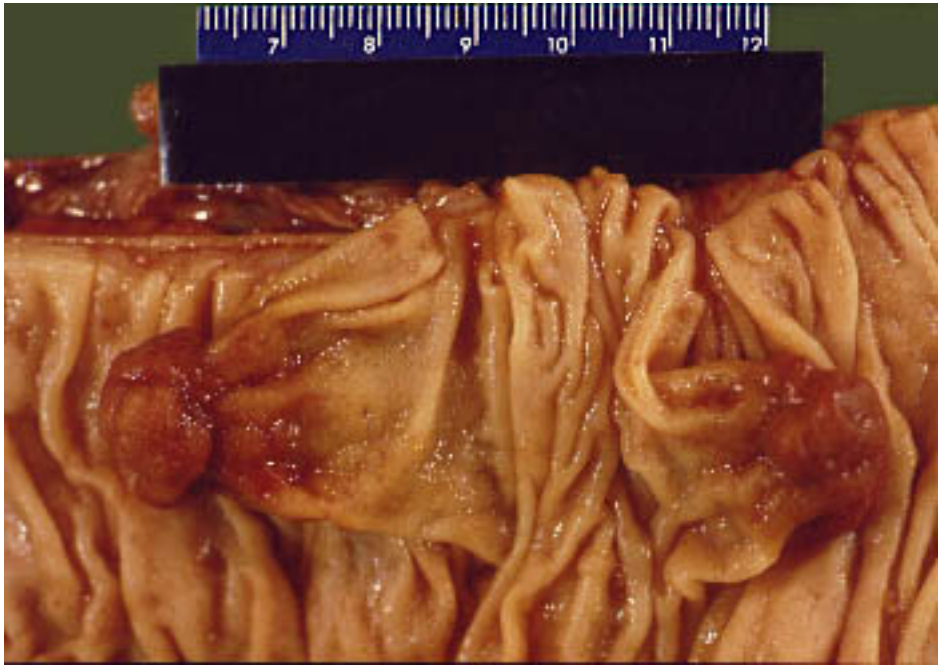
Familial polyposis coli

Familial adenomatous polyposis (FAP)

Syndrome	Mean Age at Presentation (Years)	Mutated Gene(s)	GI Lesions	Selected Extragastrointestinal Manifestations
Classic FAP	10–15	*APC*	Multiple adenomas	Congenital RPE hypertrophy
Attenuated FAP	40–50	*APC*	Multiple adenomas	
Gardner syndrome	10–15	*APC*	Multiple adenomas	Osteomas, desmoids, skin cysts
Turcot syndrome	10–15	*APC*	Multiple adenomas	CNS tumors, medulloblastoma

A	B
1. Crypt abscess 2. Smooth muscle in lamina propria 3. Star-shaped crypts 4. Peutz-Jeghers disease 5. Turcot syndrome 6. Dysplasia 7. Juvenile polyp 8. Mucocutaneous pigmentation 9. Neoplastic polyp 10. APC mutation 11. K RAS mutation 12. Developmental malformation 13. retention cysts	A. Hyperplastic polyps B. Hamartomatous polyps C. Inflammatory polyps D. Adenomatous polyp

Colon, pedunculated adenomatous polyp



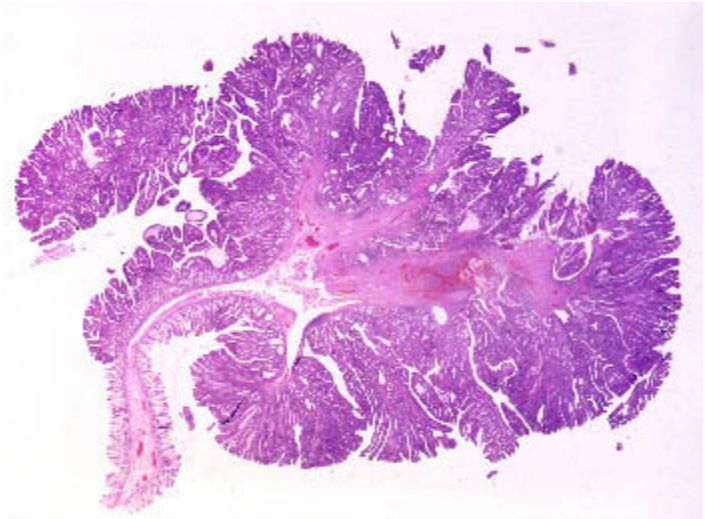
Did this patient have familial polyposis syndrome?

No. there are two isolated polyps. Patients with familial adenomatous polyposis syndrome have at least 100 polyps, and usually many more polyps, carpeting their colonic mucosa.

Can isolated polyps like the ones illustrated develop into colonic ca?

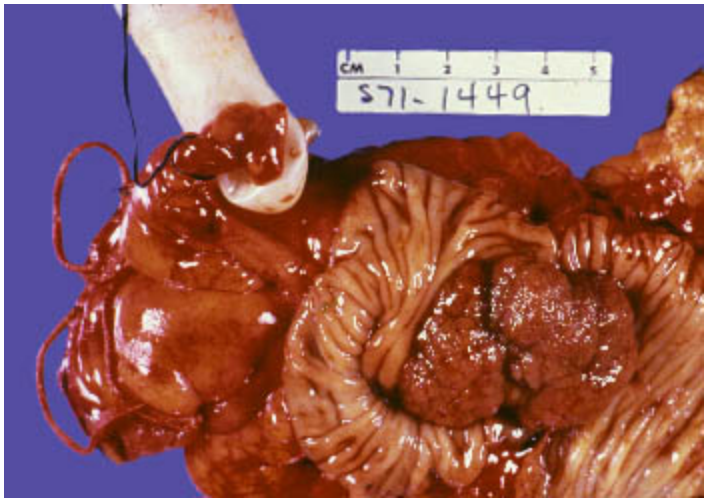
Yes. Although all polyps do not progress to carcinoma, it is thought that most colonic carcinomas start as polyps.

Colon, pedunculated adenomatous polyp



Are all polyps neoplastic?
No. Polyps can result from focal hyperplasia of the mucosa. Hyperplastic polyps do not have malignant potential

What variables determine the likelihood of malignant change in a polyp?
Three interrelated features determine the risk of cancerous transformation: polyp size, histologic architecture, and severity of dysplasia.
(1) Cancer is rare in tubular adenomas less than 1 cm in diameter.
(2) The likelihood of cancer is high (about 50%) in sessile villous adenomas that are greater than 4 cm in diameter.
(3) Severe dysplasia is likely to progress to cancer. Such dysplasias are found in villous areas. Of all these, size is the most important factor.



What types of mutations are likely to be present in such a lesion?
There is progressive accumulation of mutations during the conversion of adenomas to carcinomas. In this scheme, mutations of the *APC* gene (resulting in homozygous loss of this tumor suppressor gene) are believed to occur first. (Patients with familial adenomatous polyposis syndrome are born with loss of one copy of the *APC* gene in all somatic cells.) As the adenomas enlarge, mutations in the RAS proto-oncogene and *LOH 18q (Smad4)* tumor suppressor genes occur. Eventually, mutations of TP53 and several other genes are superimposed.

In this large sessile villous adenoma, it is likely that the *APC, LOH 18q*, and *RAS* genes have been affected.