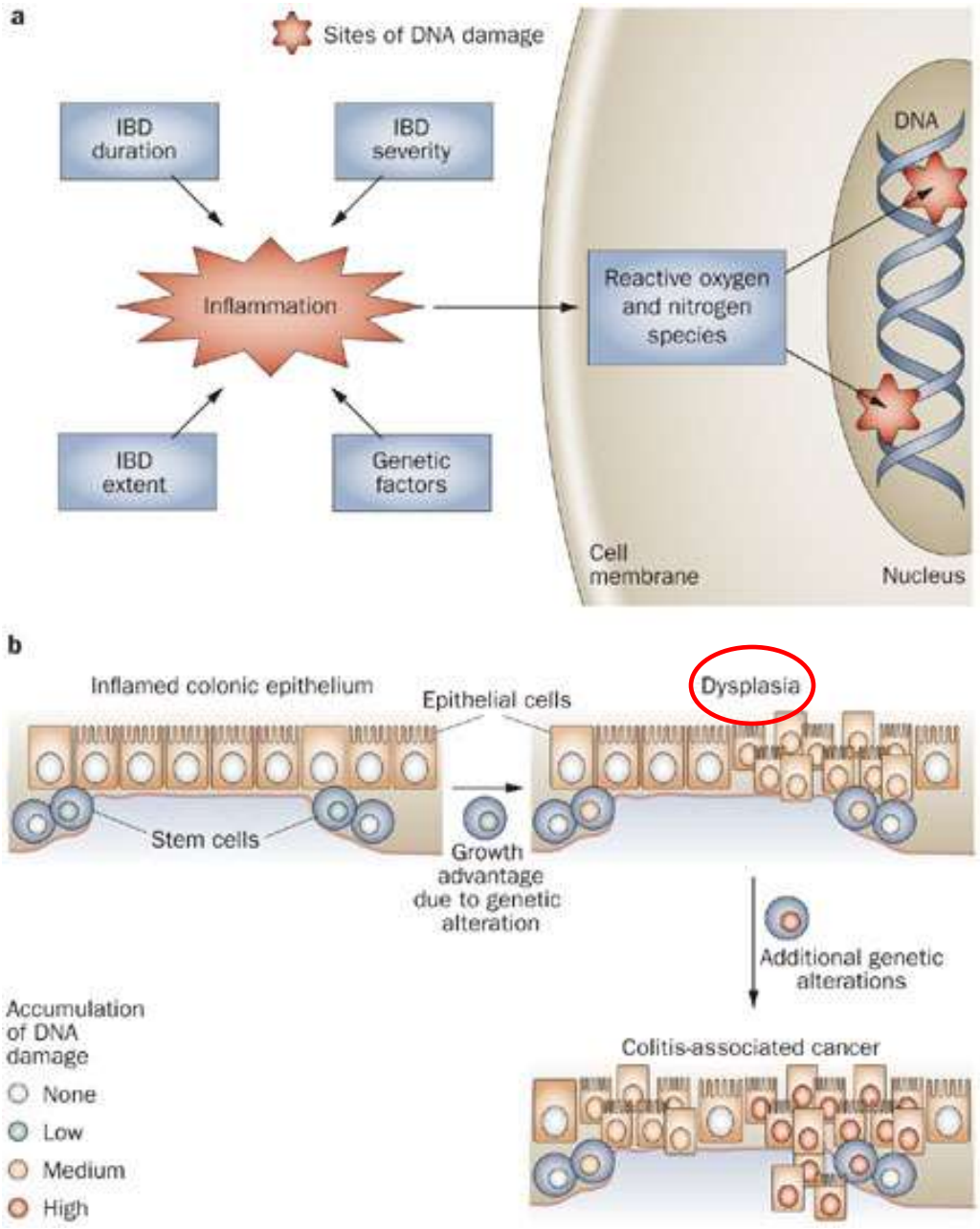


Colitis associated neoplasia

Inflammation

↓

Free radicals

↓

DNA damage

and/or

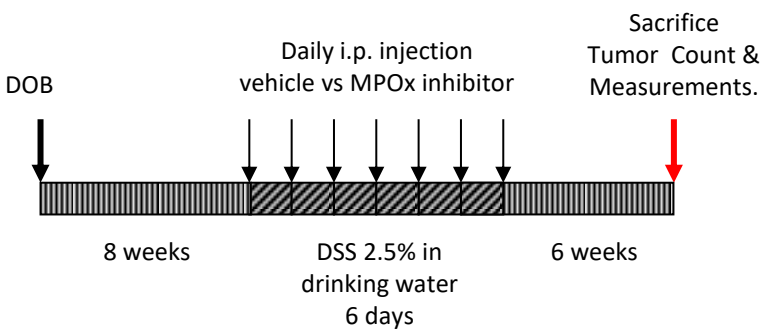
Protein modification

- Oncogene activation
- Tumor suppressor inactivation

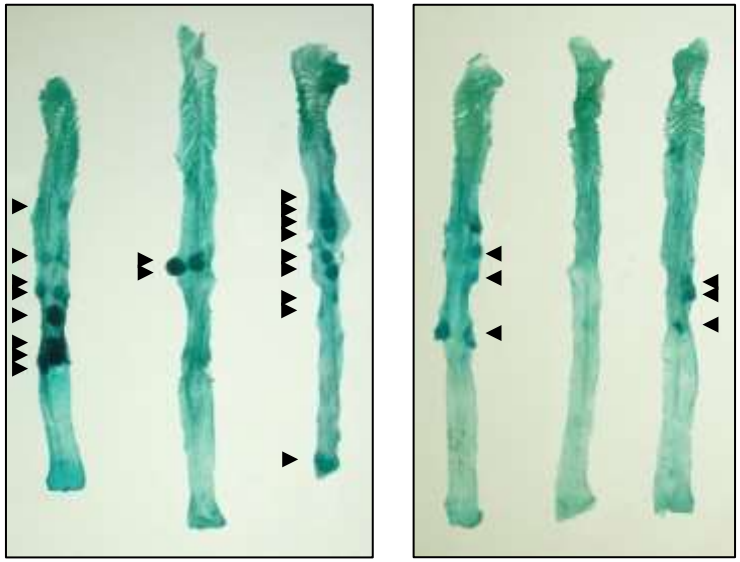
Time/severity of inflammation increase risk (especially those with PSC)

The molecular biology of it

A



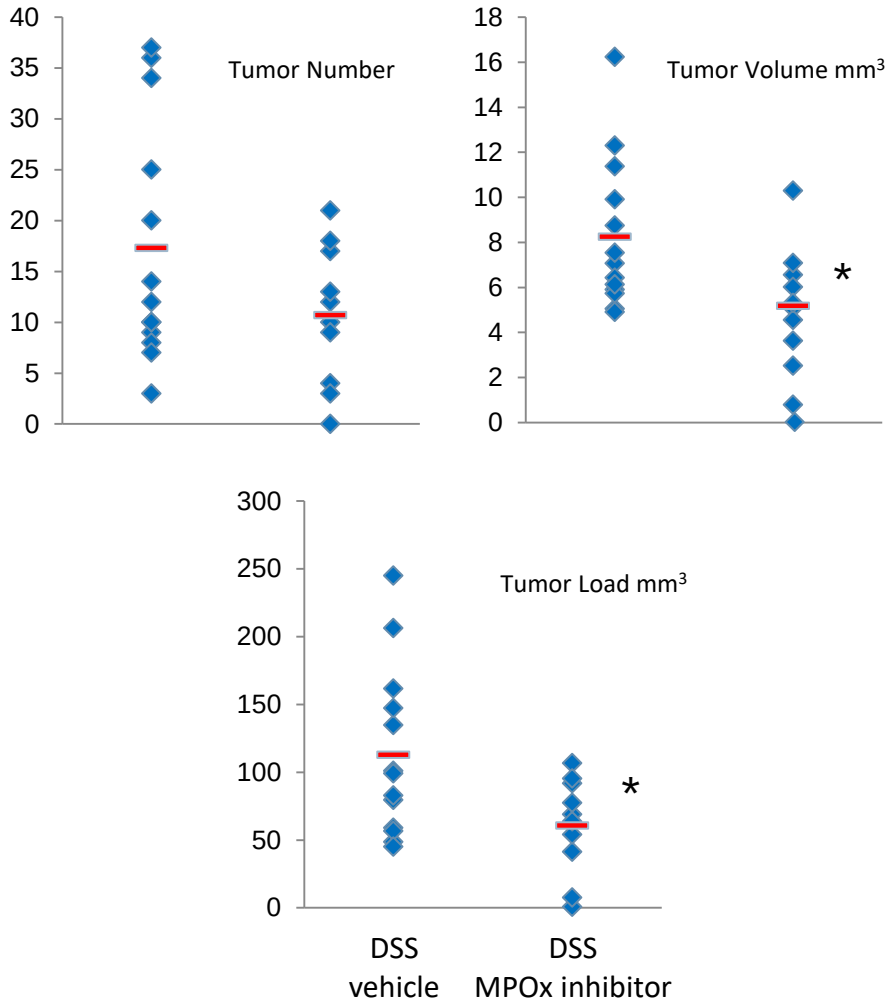
B

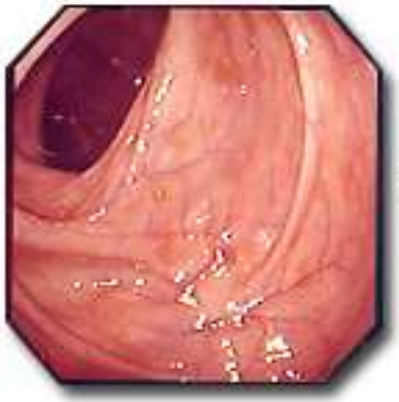


DSS-*Apc* $^{Min/+}$ mice
+ vehicle

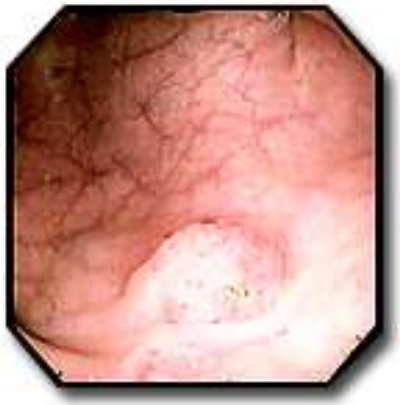
DSS-*Apc* $^{Min/+}$ mice
+ MPOx inhibitor

C

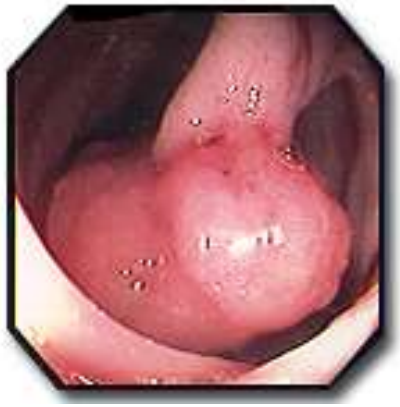




Normal colon



Sessile polyp



Pedunculated polyp

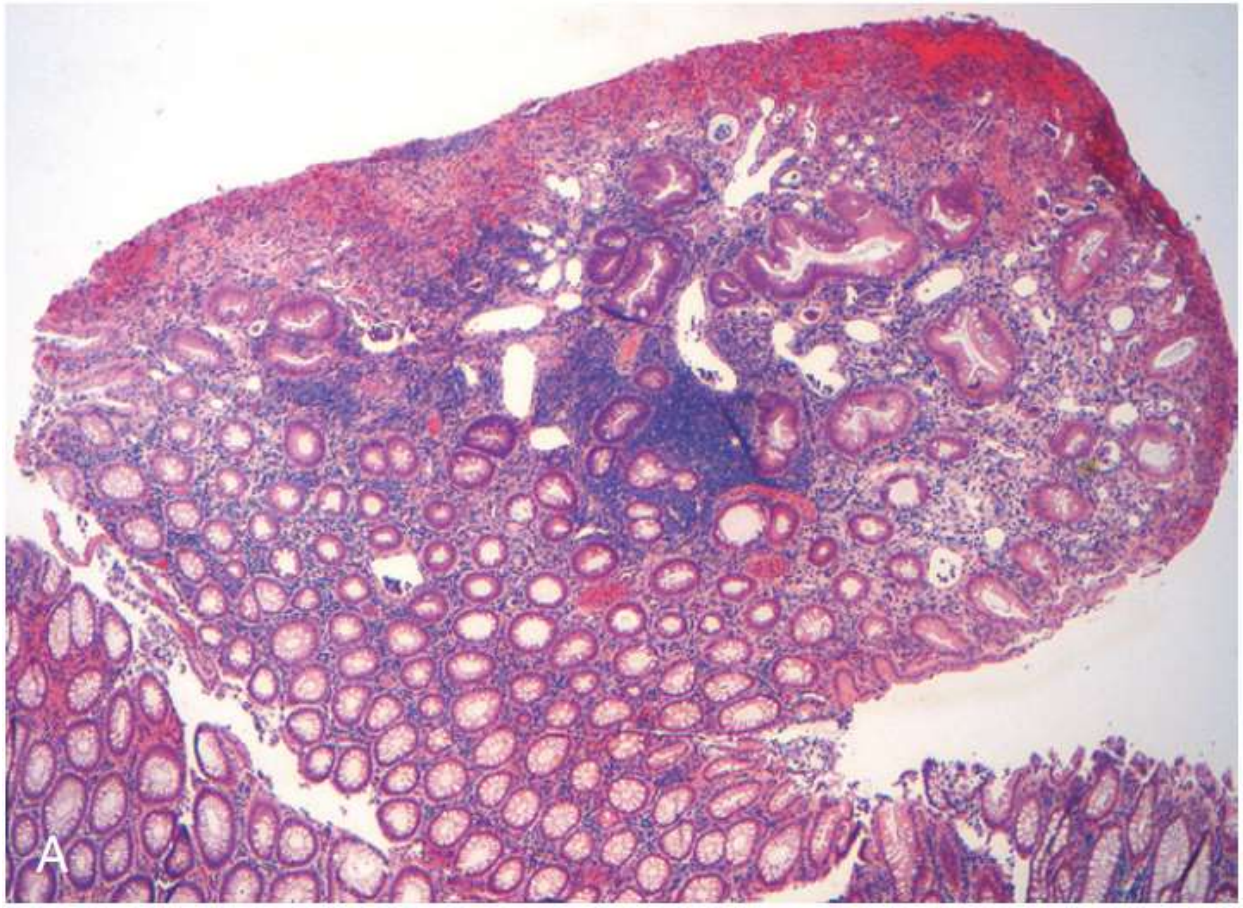
Intestinal Polyps

Most common in the colon

- Sessile
- Pedunculated

- Inflammatory
- Hamartomatous
- Hyperplastic
- Neoplastic

pedunculated, smooth surfaced, reddish lesions <3cm



surface erosion
cystically dilated crypts
filled with mucus, neutrophils, and debris

Hamartomatous Polyps

Juvenile Polyps

Most common hamartomatous

Sporadic (typically single) or syndromic (multiple)

Juvenile polyposis (AD)

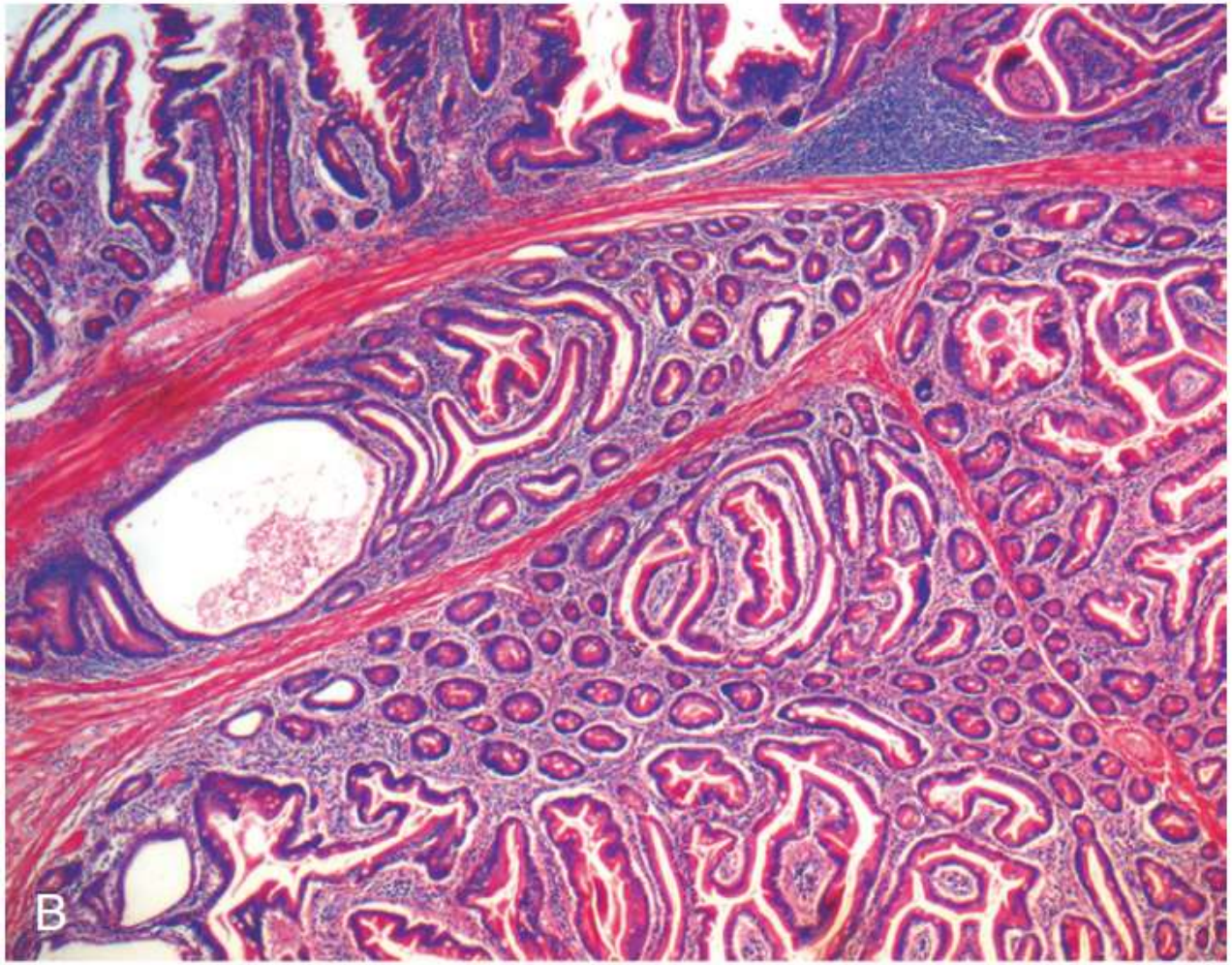
Age <5yrs

Location: Rectum

Presentation
- Bleeding
- Prolapse

↑ adenocarcinoma risk

Large, pedunculated with a lobulated contour



Complex glandular architecture and bundles of smooth muscle

Hamartomatous Polyps

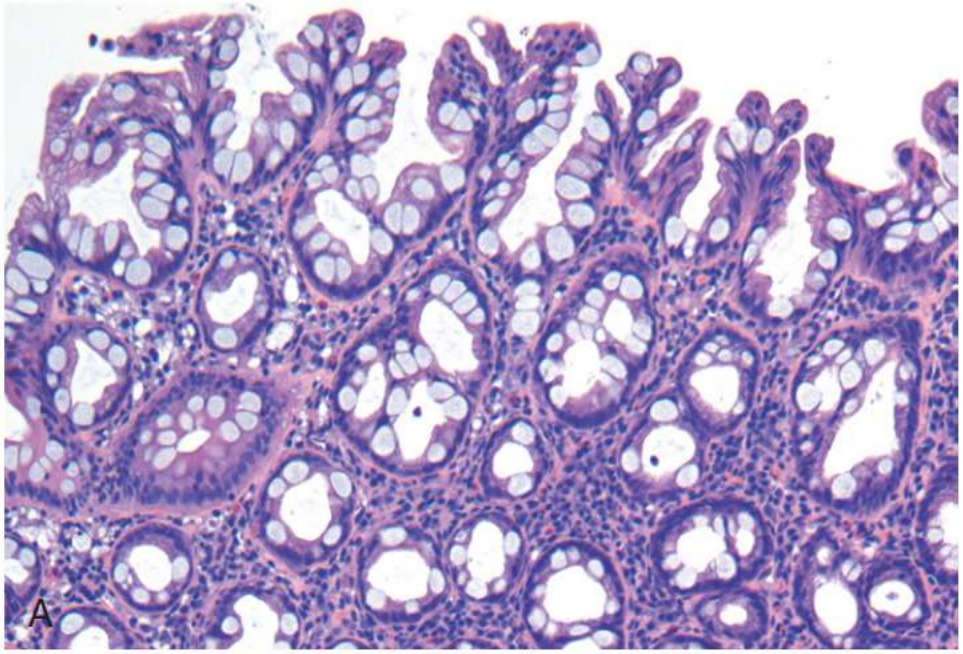
Peutz-Jeghers Syndrome (AD)

STK11/LKB1 mutation

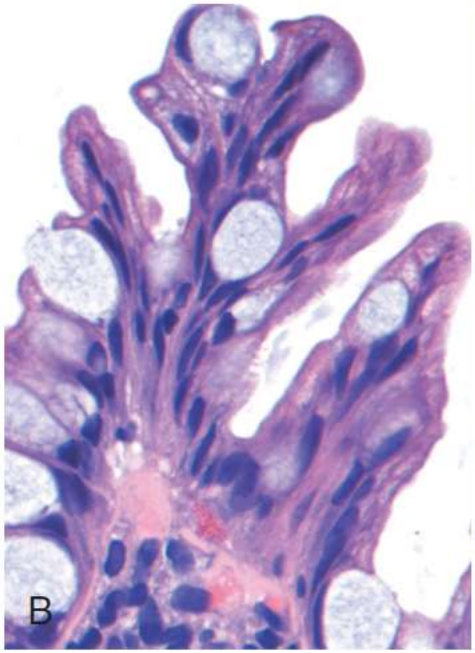
- Multiple GI hamartomatous polyps
- Mucocutaneous hyperpigmentation
- ↑ malignancy risk

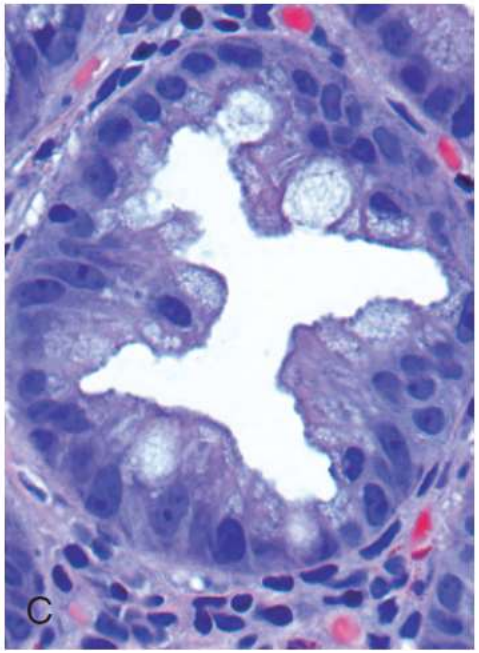
Common in SI, can also occur in stomach, colon, bladder, lungs

Smooth, nodular protrusions of the mucosa, often on the crests of mucosal folds



Delayed shedding of mature goblet and absorptive cells creates a serrated surface





Hyperplastic Polyps

6-7th decade of life

No malignant potential

Frequently multiple

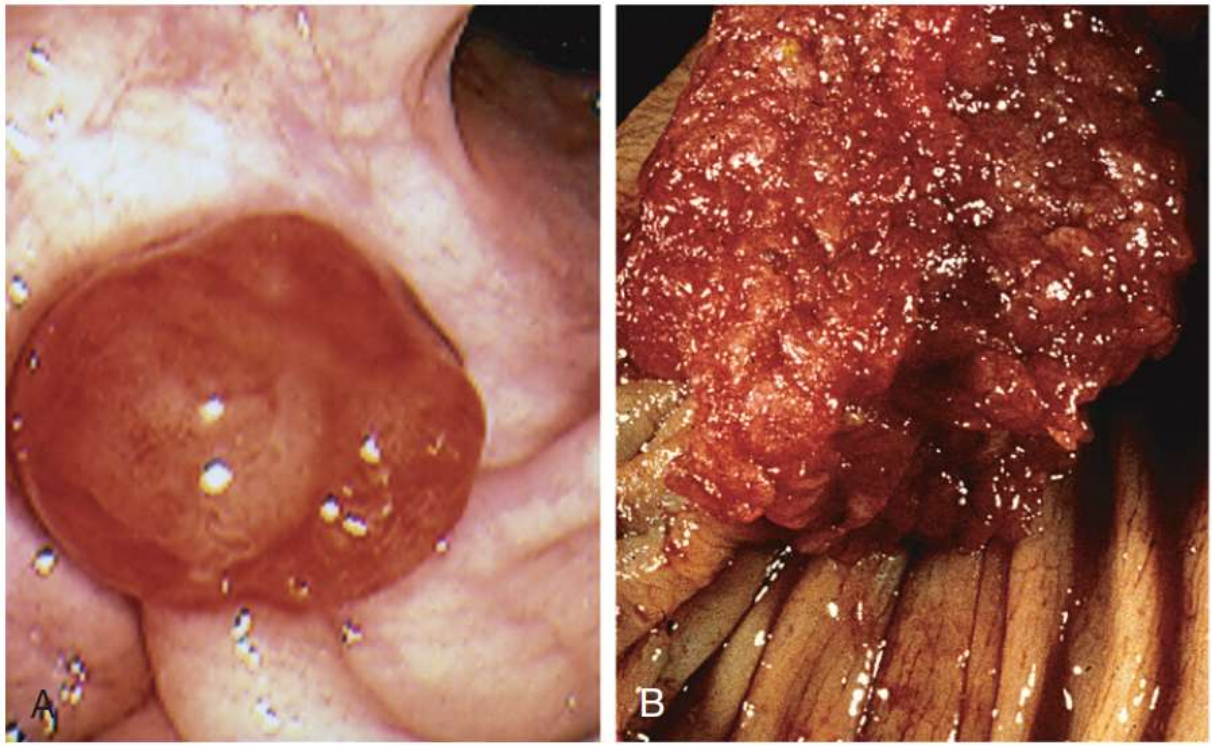
Typically left colon
<0.5cm

decreased epithelial cell turnover and delayed shedding (over-crowding)

DDx of sessile serrated adenomas that do have malignant potential

Pedunculated

Sessile



surface texture of both types resemble velvet or a raspberry

Adenomas

Most common neoplastic

Epithelial dysplasia is characteristic

Give rise to a majority of colorectal adenocarcinomas

Most adenomas do not progress to adenocarcinoma

Adenomas

Most common neoplastic

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Give rise to a majority of colorectal adenocarcinomas

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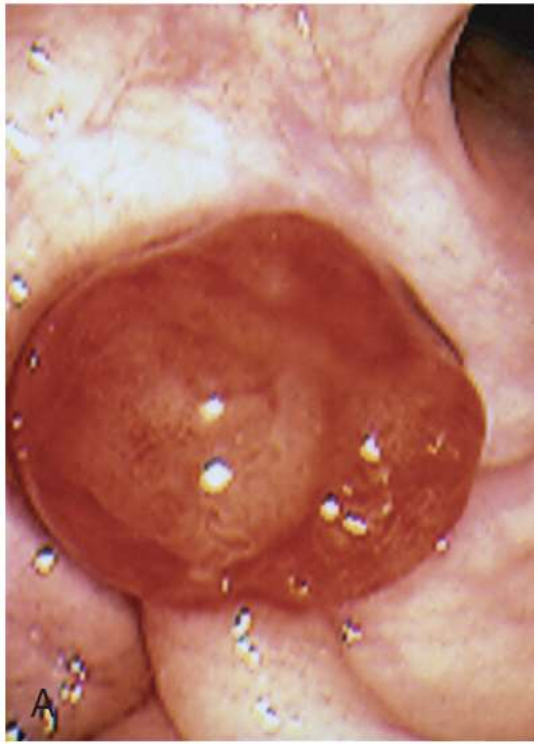

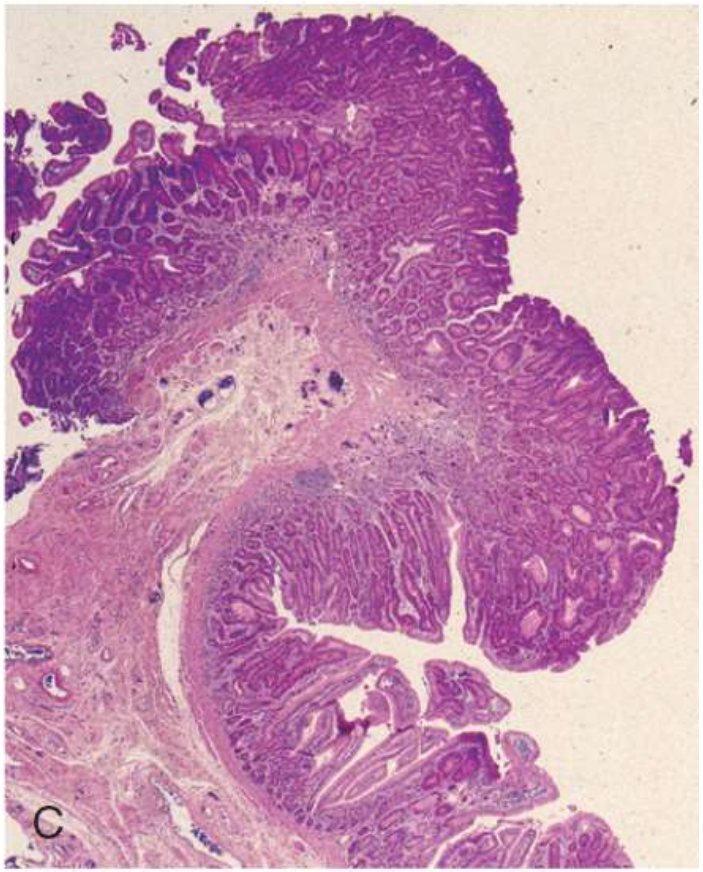

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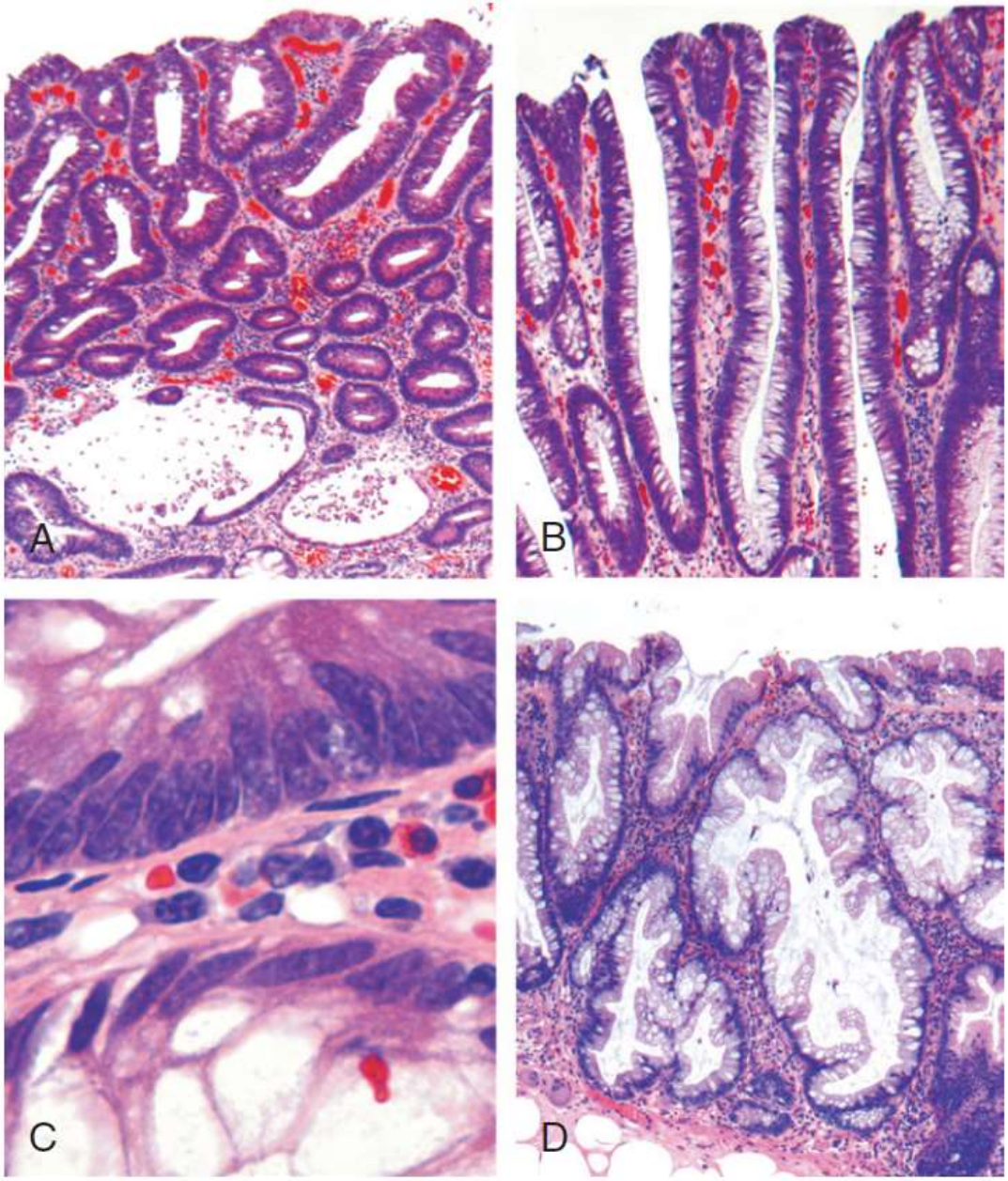


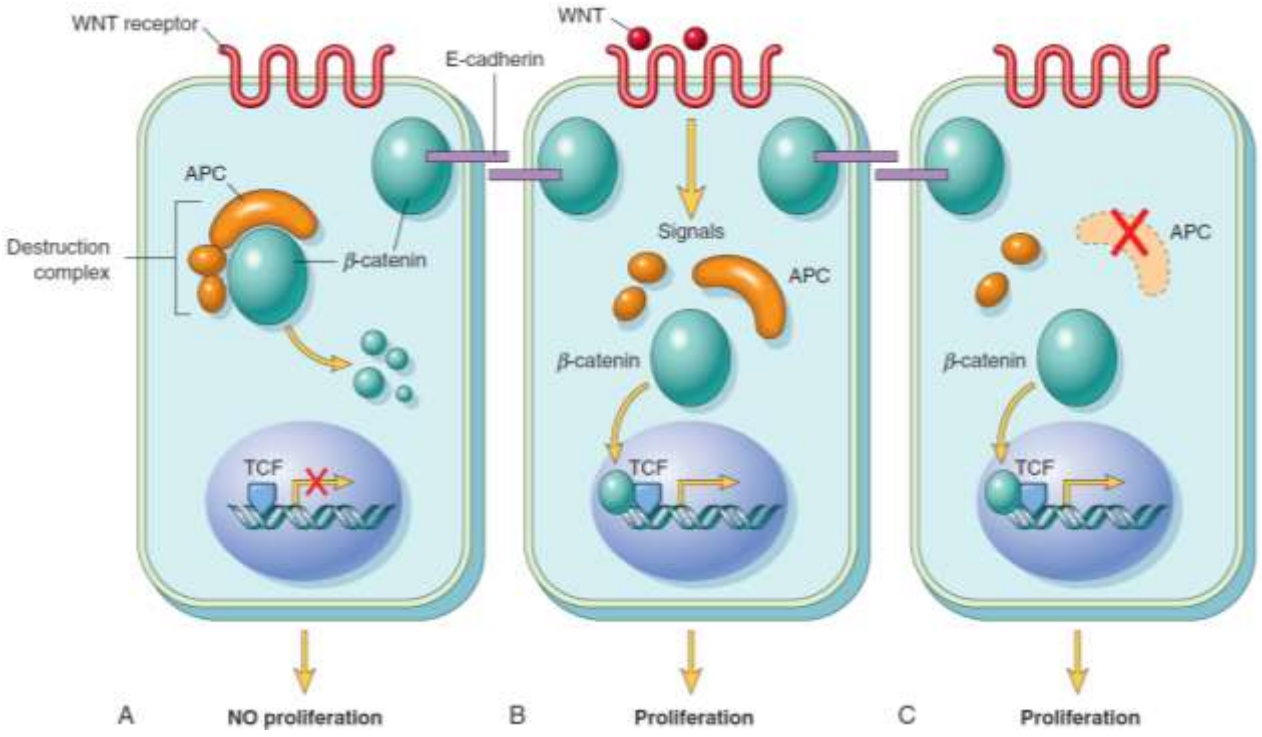
Adenomas

Architecture
- Tubular (A) small
- Tubulovillous
- Villous (B) Large

Epithelial dysplasia (C) (nuclear hyperchromasia, elongation, & stratification TOP)

Sessile serrated adenoma (D) similar to hyperplastic polyps but in right colon, no dysplasia, serration is present all the way down to the crypt

SIZE



Familial Syndromes (FAP)

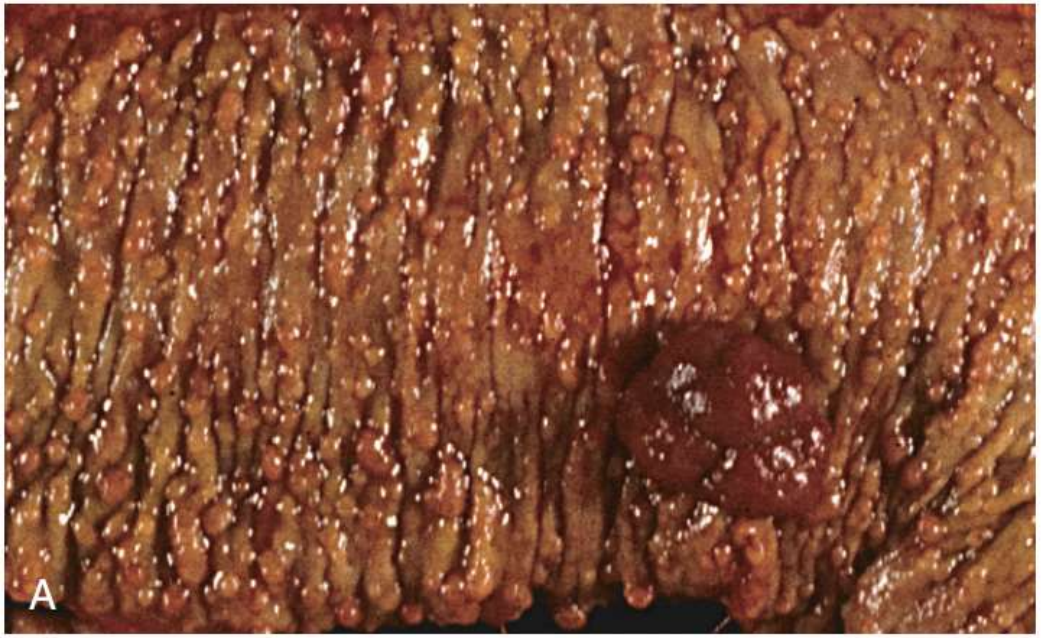
AD

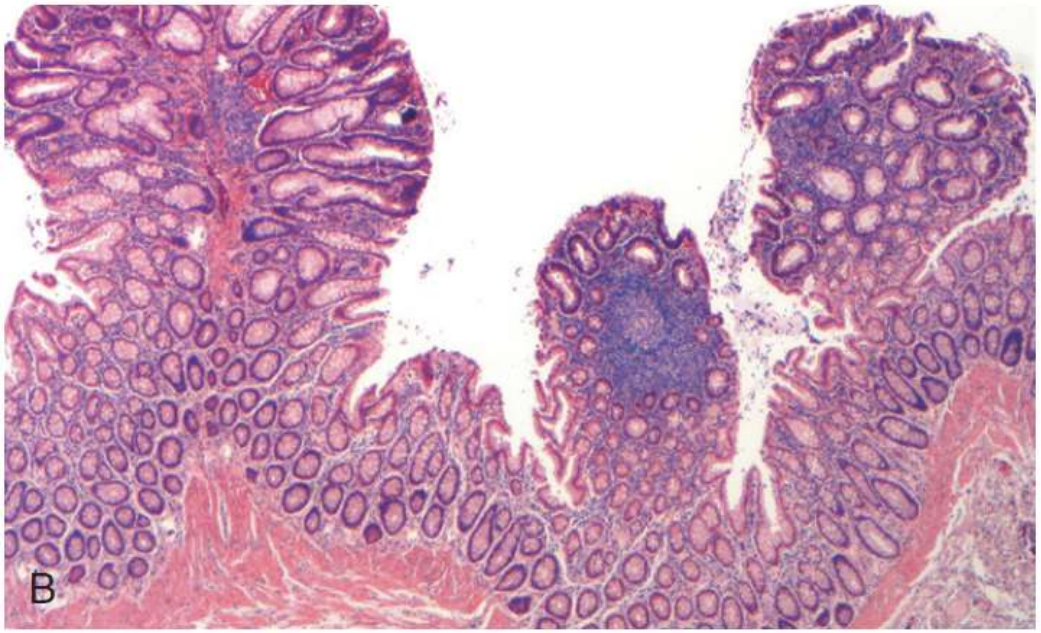
APC or less common *MUTYH* (base excision repair)

Variants

- Gardner syndrome
  Osteomas, desmoids, skin cysts, thyroid neoplasia…

- Turcot syndrome
  CNS tumors, medulloblastoma vs glioblastoma



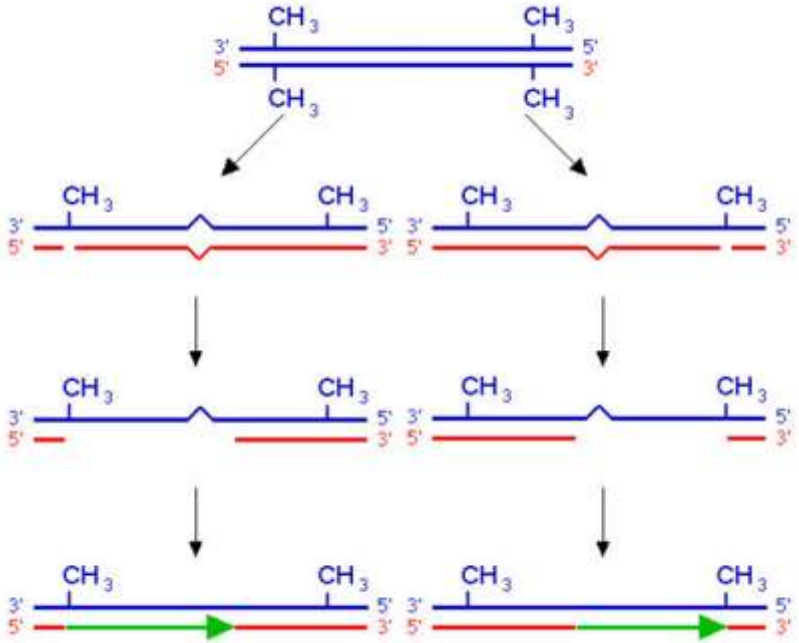


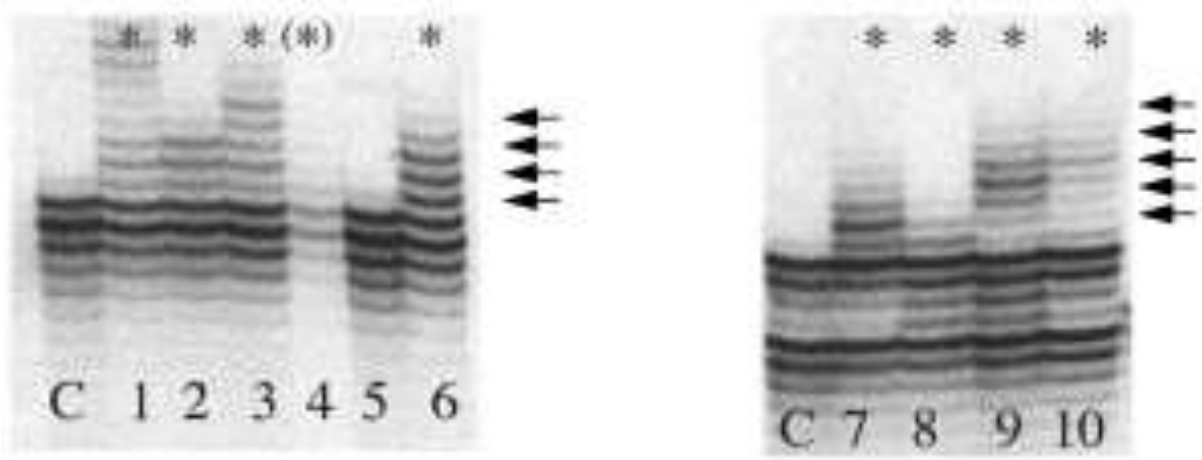
Familial Syndromes (FAP)

Hundreds to thousands but morphologically indistinguishable from sporadic adenomas

Colorectal adenocarcinoma develops in 100% of patients with untreated FAP, often before age 30

Tx: prophylactic colectomy





Hereditary Nonpolyposis Colorectal Cancer

HNPCC/Lynch syndrome

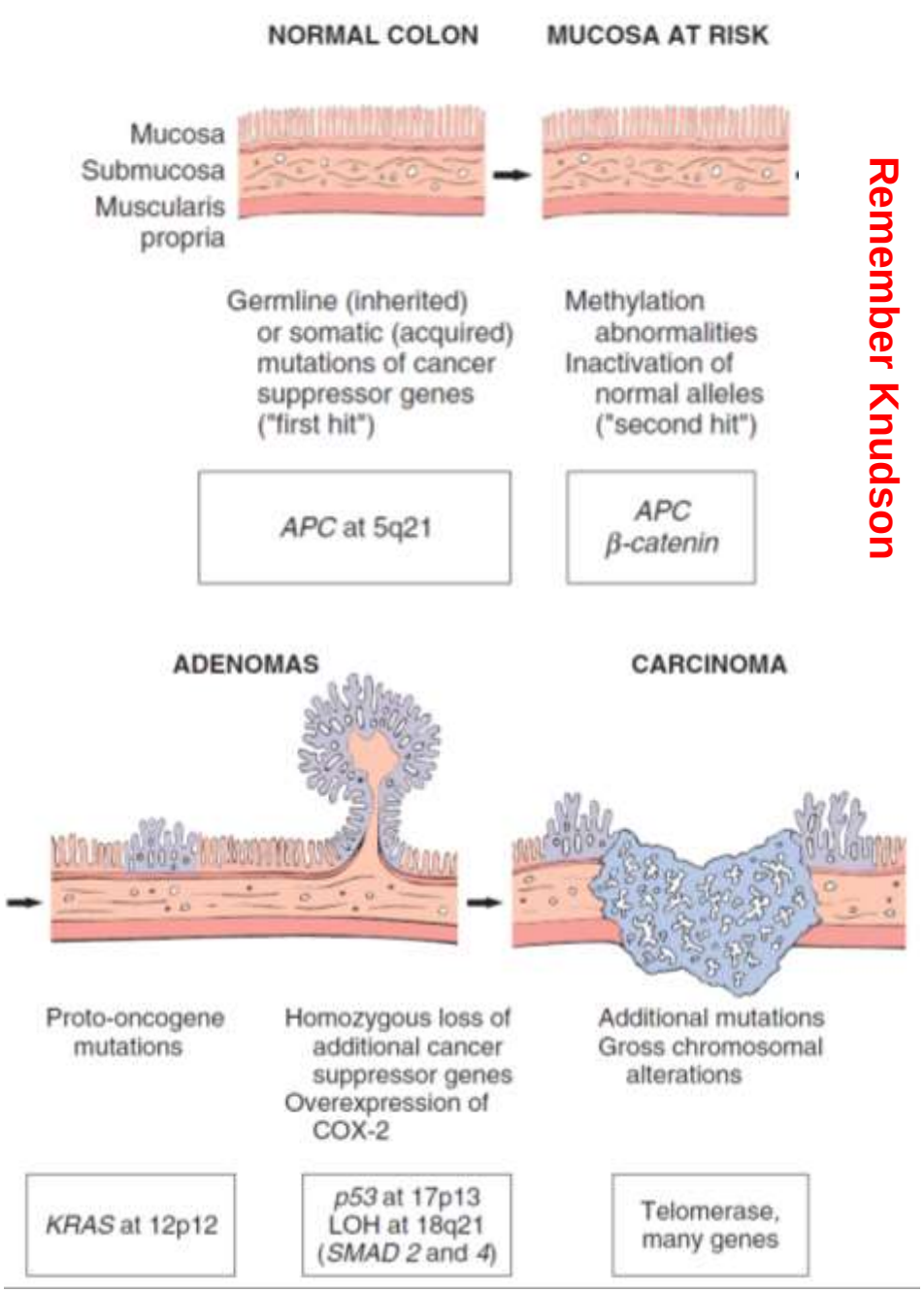
AD

DNA mismatch repair gene defects mostly *MSH2* or *MLH1*

Right colon predilection and at younger ages

Mutator phenotype (e.g. TGFβ type II receptors, BAX)

Microsatellite instability



Remember Knudson

Adenocarcinoma

Most common GIT malignancy is Colon adenocarcinoma

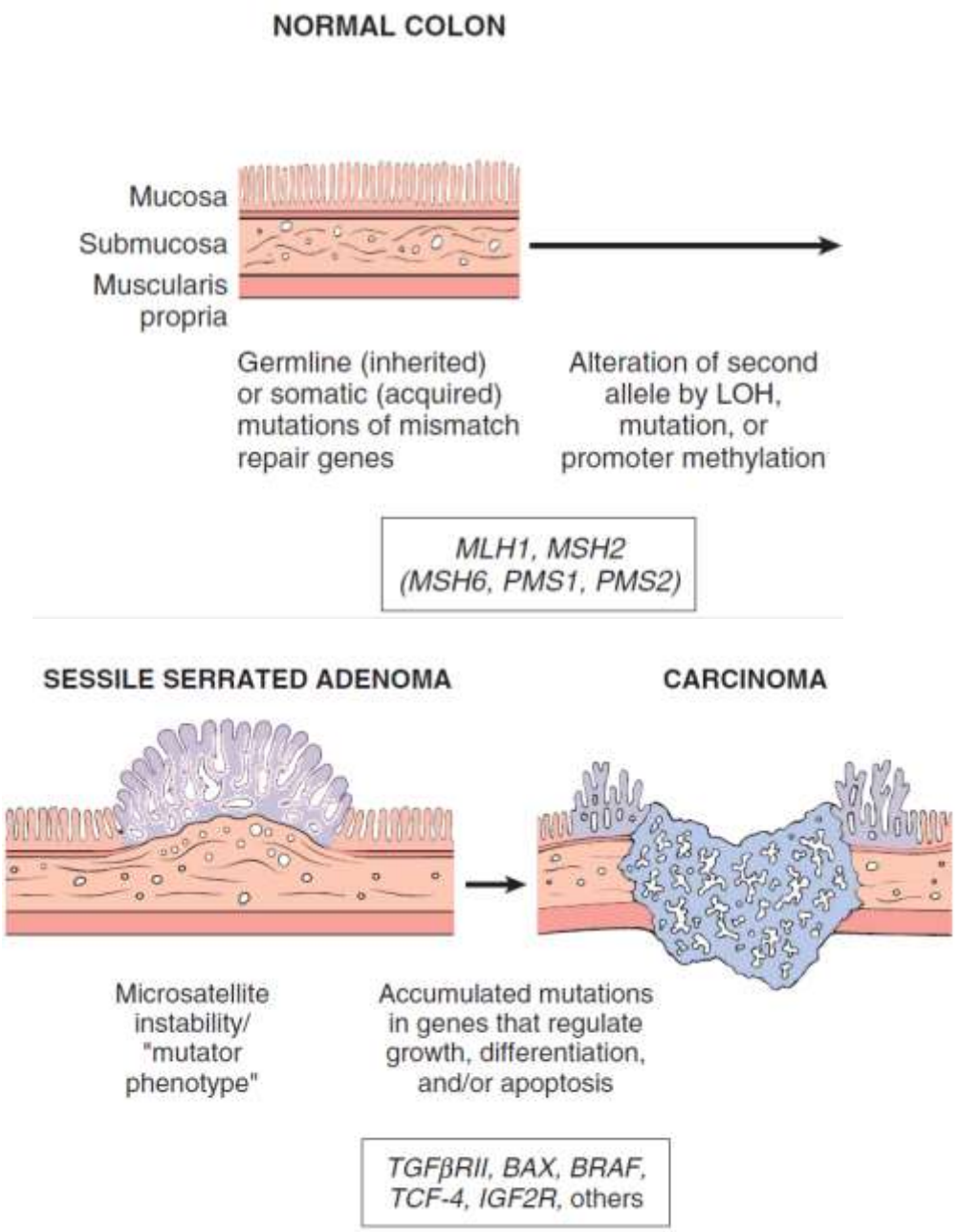
Peak incidence 60-70yrs

Diet effect (high fat/low fiber)

NSAID protective
COX-2 over-expression
90%

Adenoma-Carcinoma sequence (APC/Wnt)

80% of sporadic colon tumors



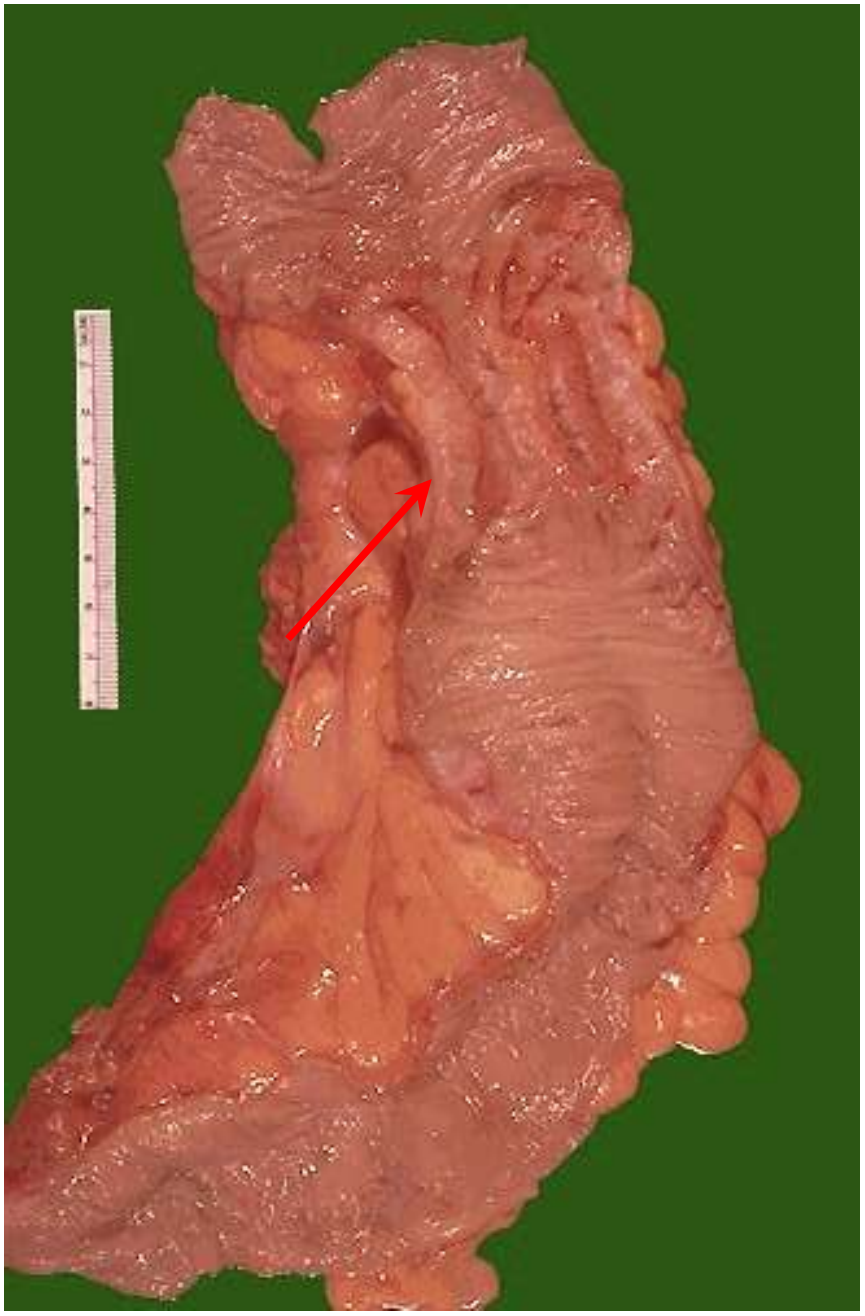
Adenocarcinoma

The microsatellite instability pathway

DNA mismatch repair deficiency

Microsatellite instability

Mutator phenotype



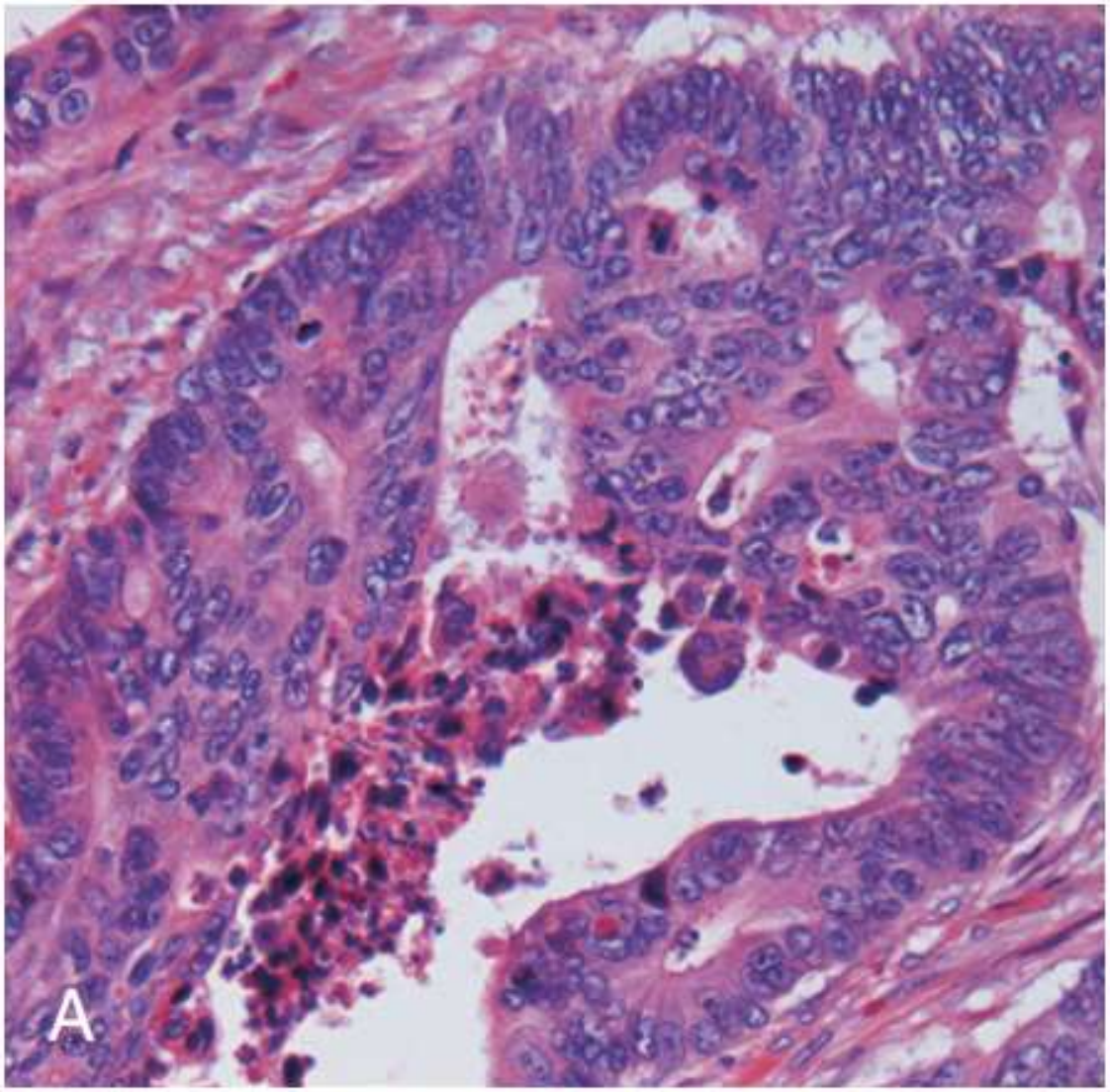
Adenocarcinoma

Morphology

Proximal colon: polypoid, exophytic, extend along one wall (rarely cause obstruction)

Distal colon: annular lesions “napkin ring” constrictions (more likely to cause obstruction)

Both forms grow into the bowel wall, become palpable as firm masses (desmoplastic response)

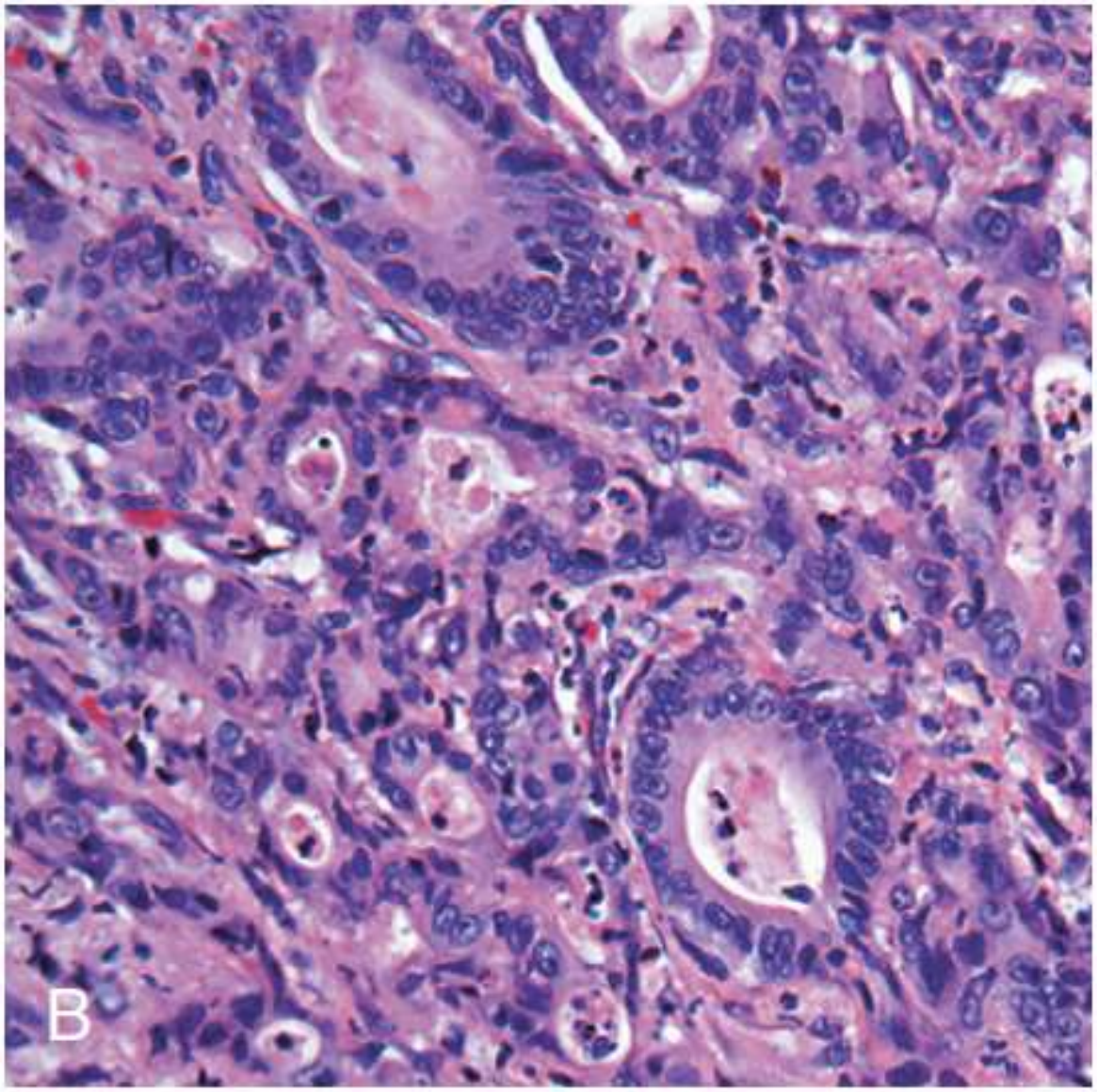


Well-differentiated adenocarcinoma

Adenocarcinoma

Morphology

Tall columnar cells that resemble dysplastic epithelium found in adenomas

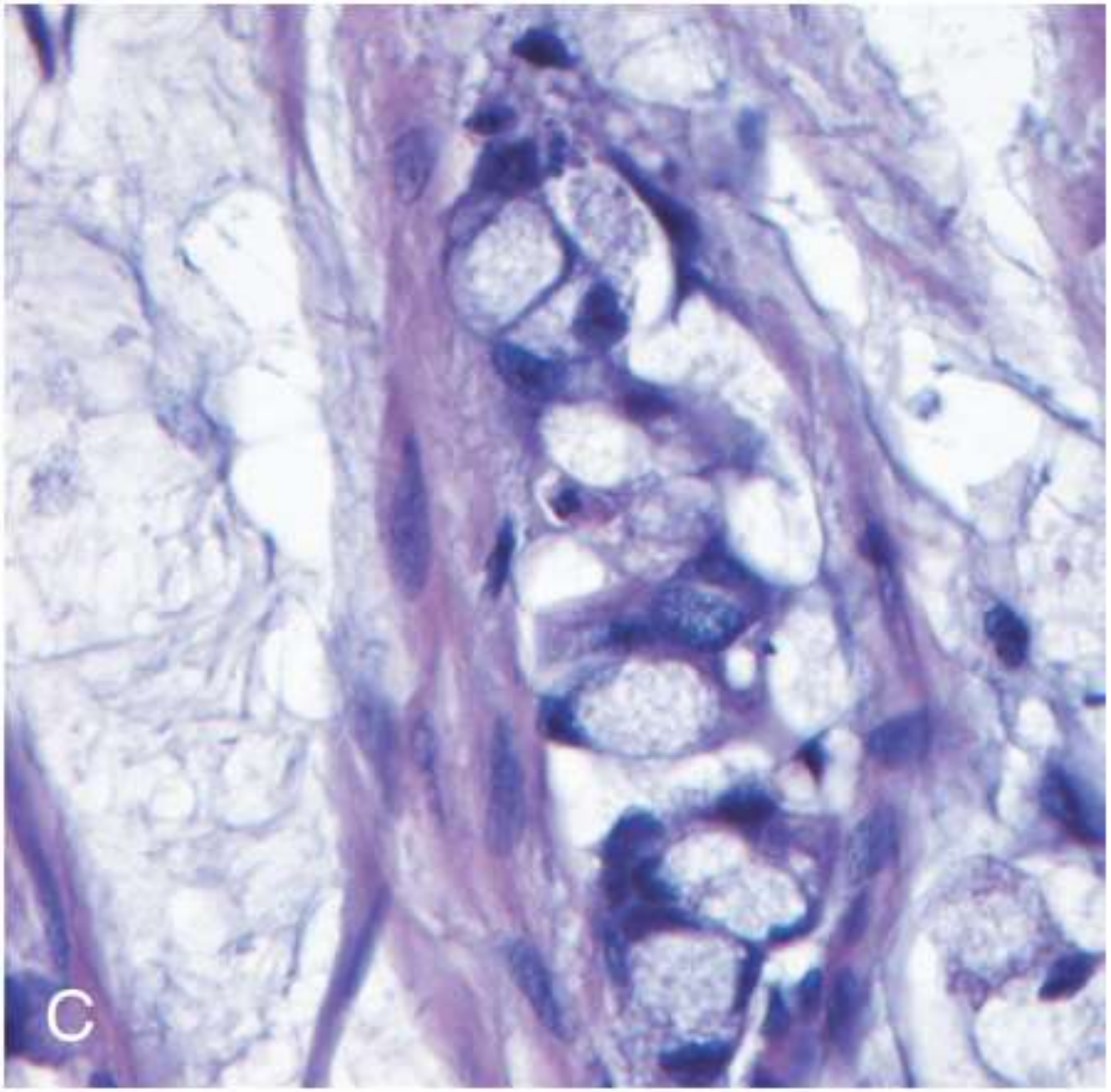


Poorly differentiated adenocarcinoma

Adenocarcinoma

Morphology

Poorly differentiated tumors form few glands



Mucinous adenocarcinoma

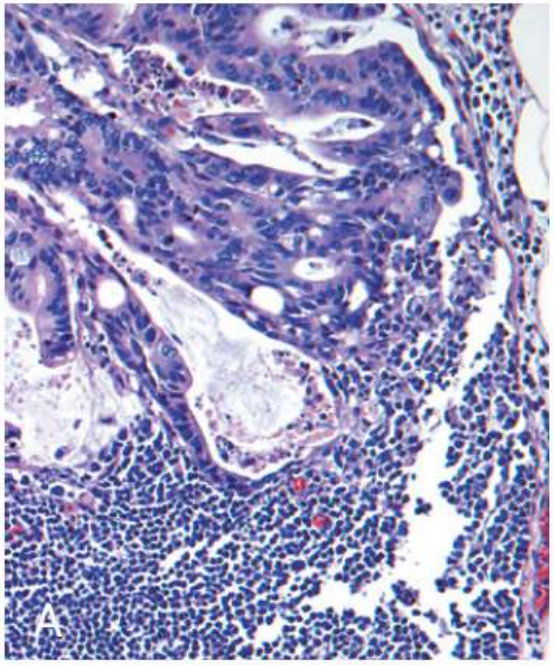
Adenocarcinoma

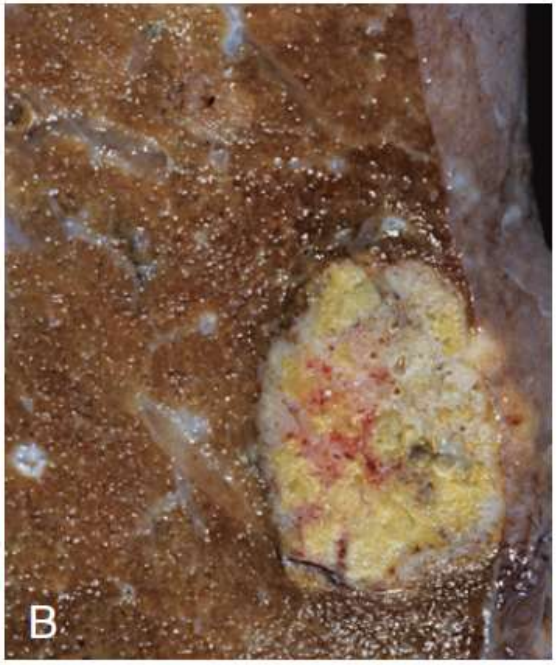
Morphology

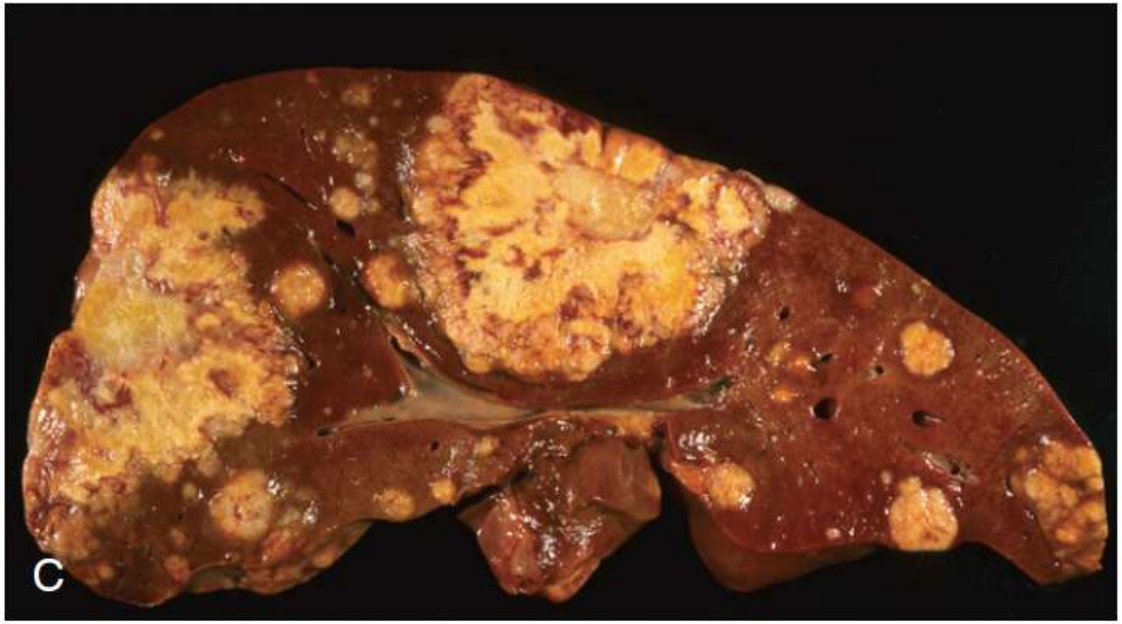
Signet ring cells that are similar to those in gastric cancer

Produce abundant mucin that accumulates within the intestinal wall

Poor prognosis





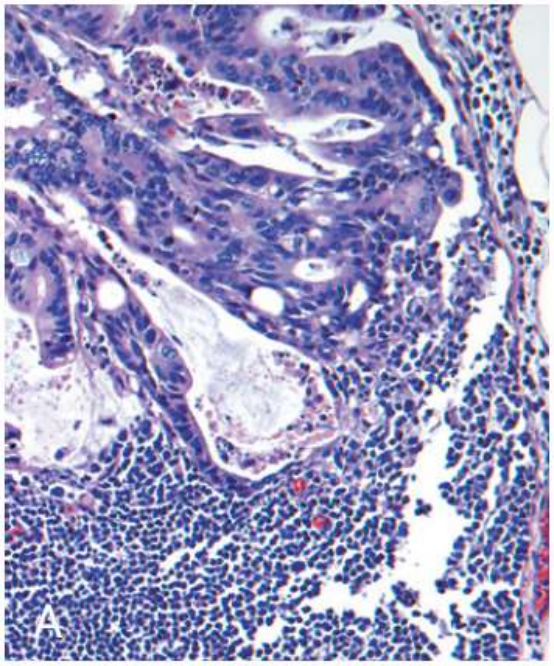


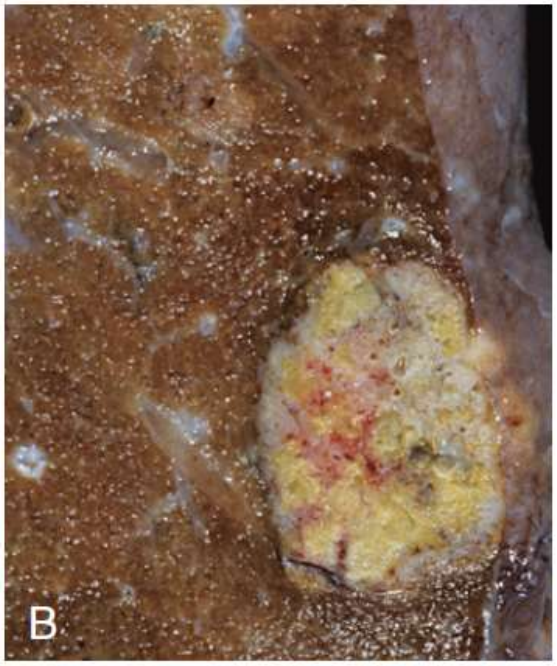
Adenocarcinoma

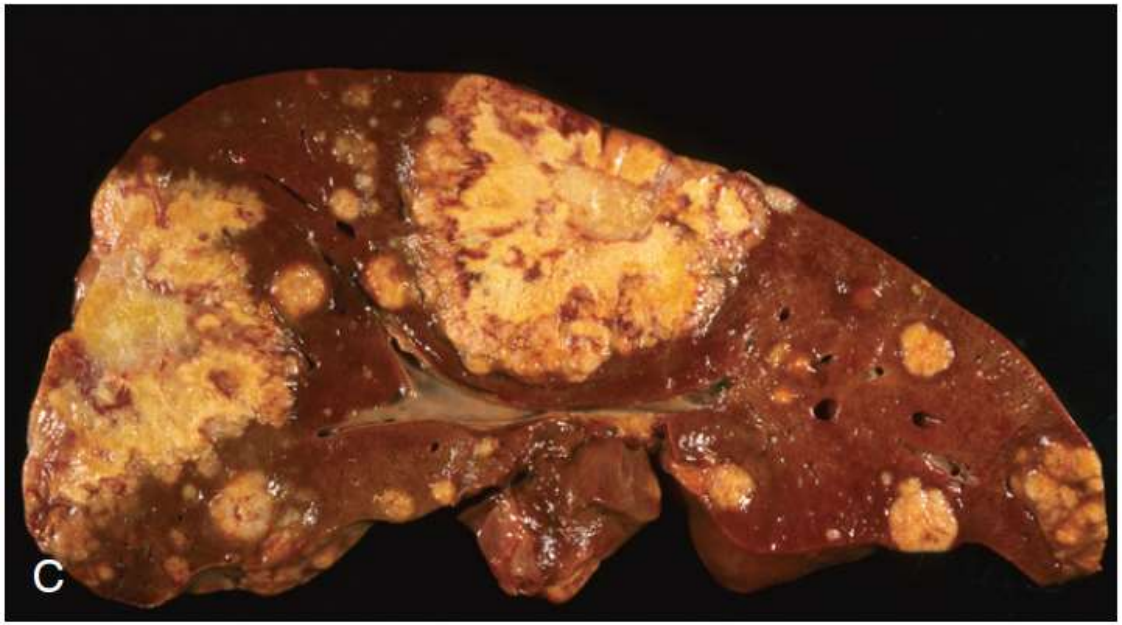
Clinical Features

Right-sided colon cancers most often present with fatigue and weakness due to iron deficiency anemia

Left-sided colorectal adenocarcinomas can present with occult bleeding, changes in bowel habits, or cramping







Adenocarcinoma

Prognosis

- Depth of invasion
- LN metastasis (A)

Lung (B)

Liver (C) the most common metastatic site except for rectum

Grading & Staging (colorectal cancer)

Designation	Description
Tumor	
Tis	In situ dysplasia or intramucosal carcinoma
T1	Tumor invades submucosa
T2	Tumor invades into, but not through, muscularis propria
T3	Tumor invades through muscularis propria
T4	Tumor invades adjacent organs or visceral peritoneum
Regional Lymph Nodes	
NX	Lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in one to three regional lymph nodes
N2	Metastasis in four or more regional lymph nodes
Distant Metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis or seeding of abdominal organs

Stage*	Tumor-Node-Metastasis (TNM) Criteria			5-Year Survival (%)
	T	N	M	
I	T1, T2	N0	M0	74
II				
IIA	T3	N0	M0	67
IIB	T4	N0	M0	59
III				
IIIA	T1, T2	N1	M0	73
IIIB	T3, T4	N1	M0	46
IIIC	Any T	N2	M0	28
IV	Any T	Any N	M1	6