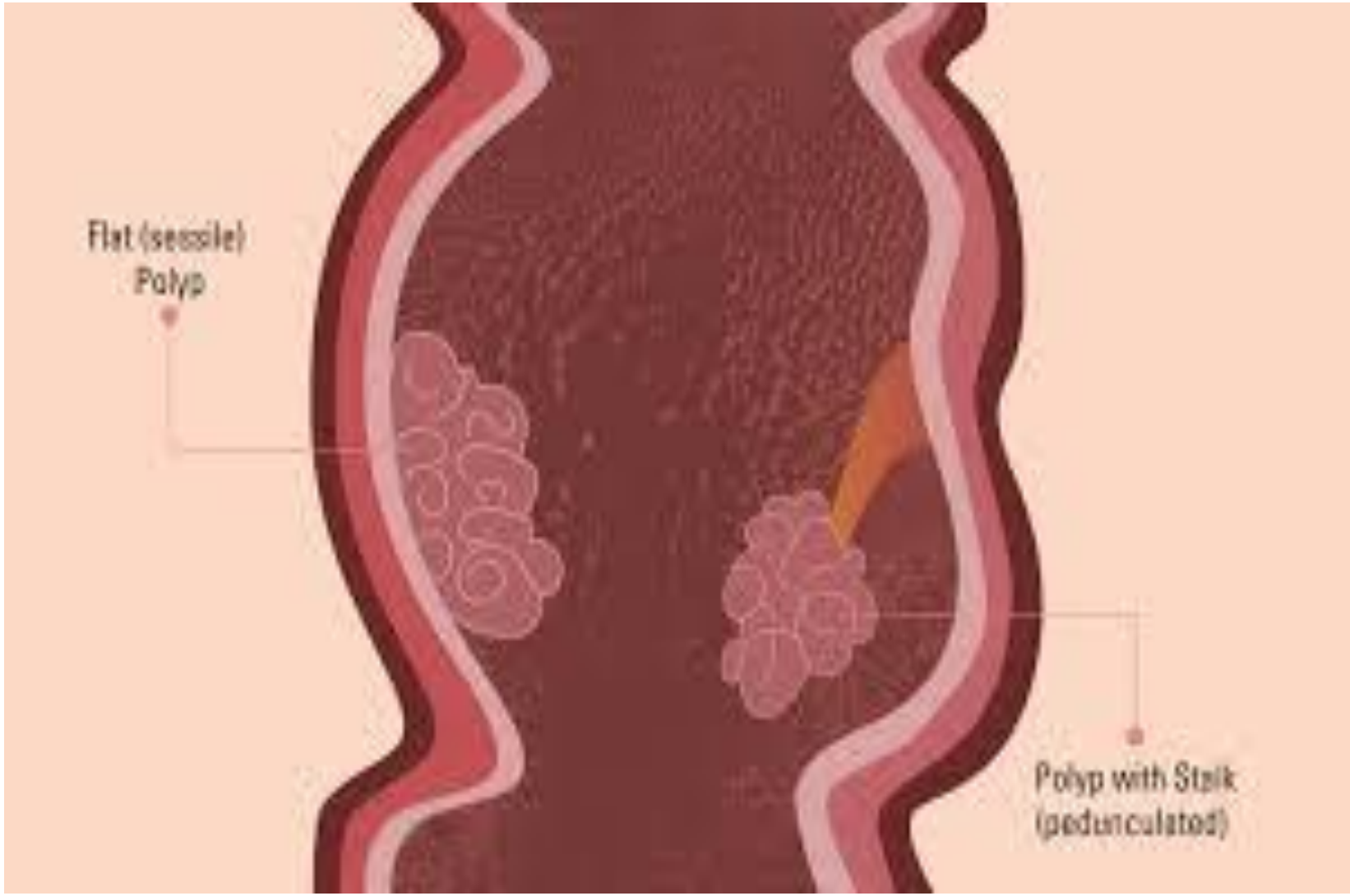
GIT III

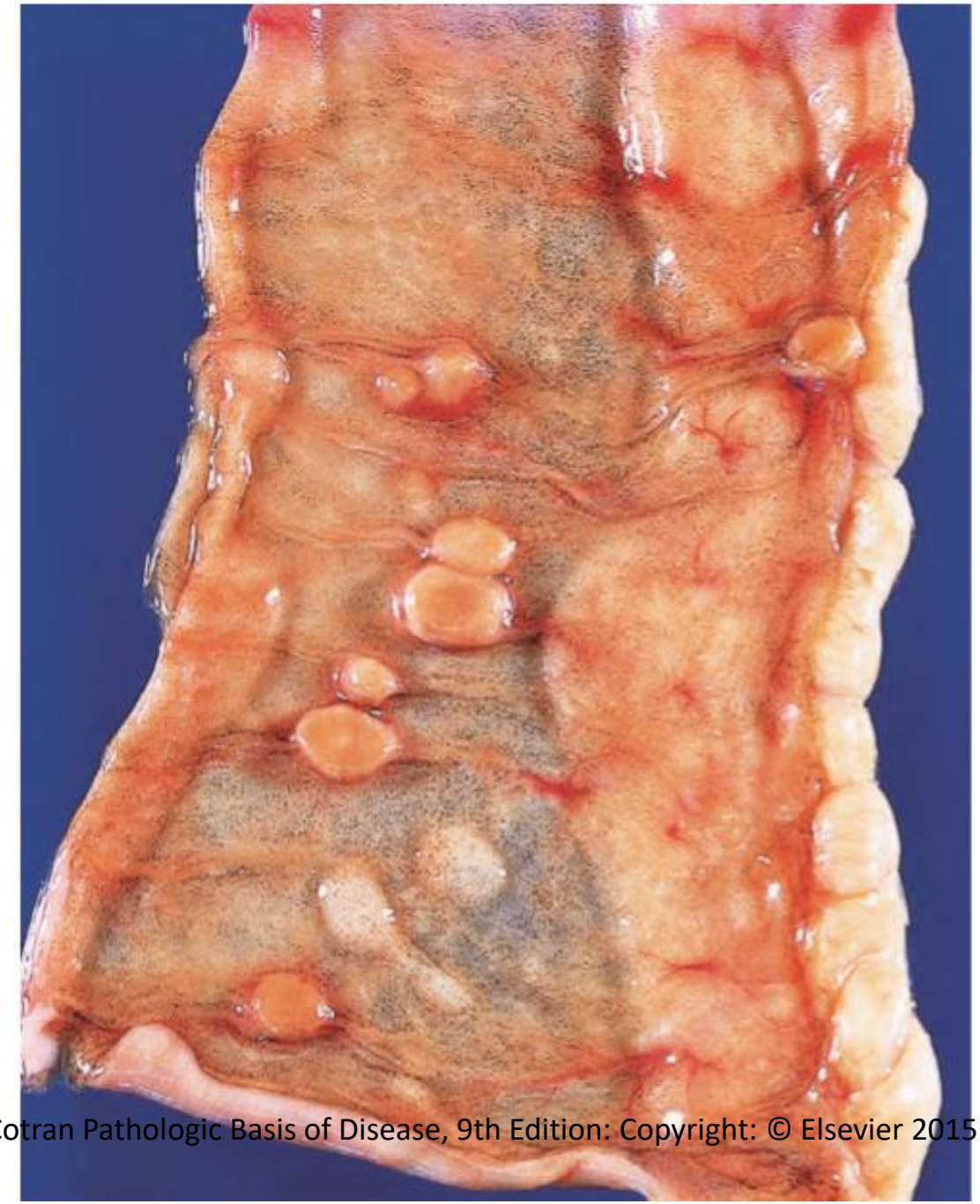
Dr. Preeti Agarwal,
Associate Professor,
Department of Pathology
KGMU

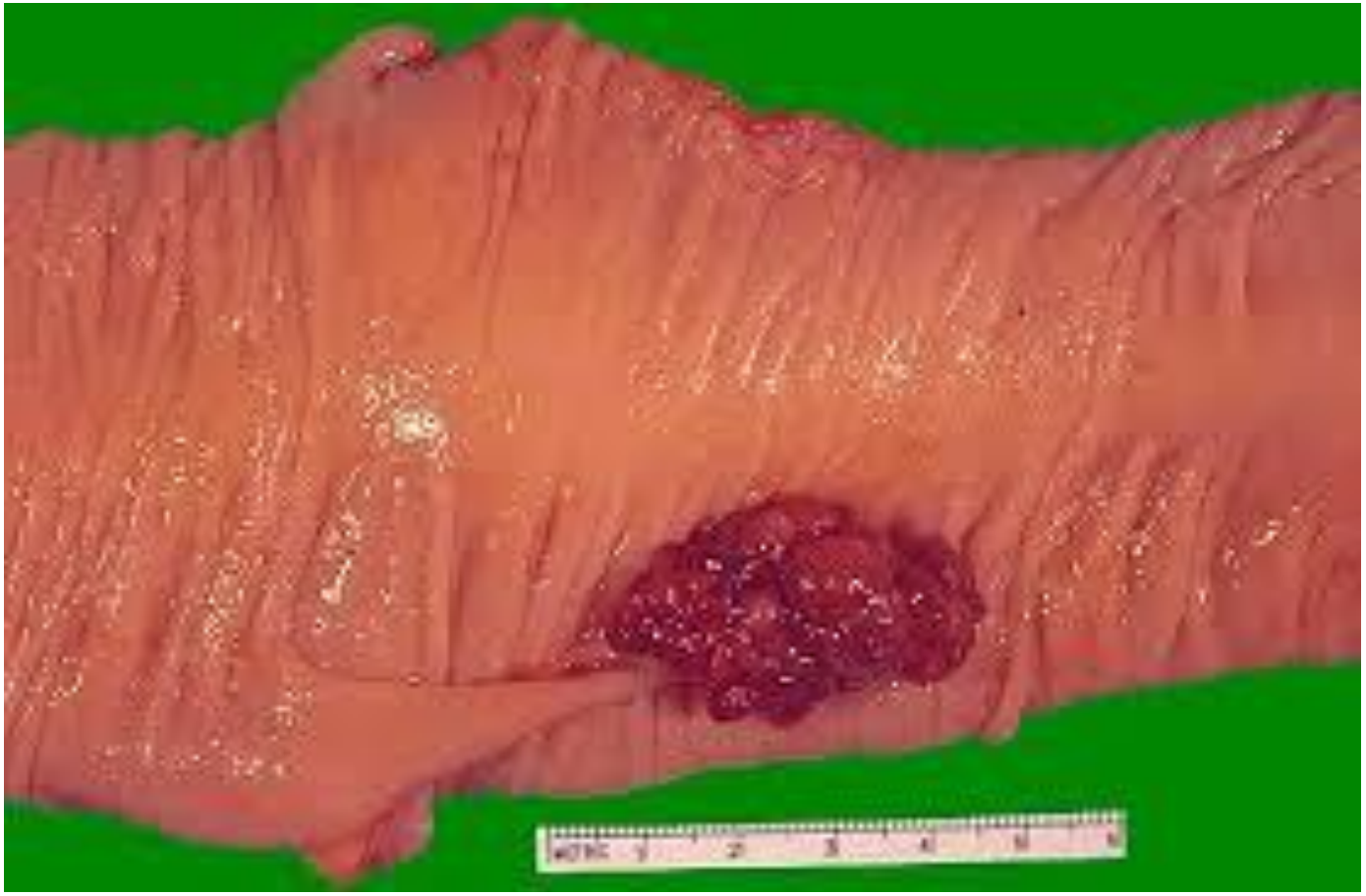
Polyps

- Most common in the colon but may occur in the esophagus, stomach, or small intestine
- Sessile
- Pedunculated

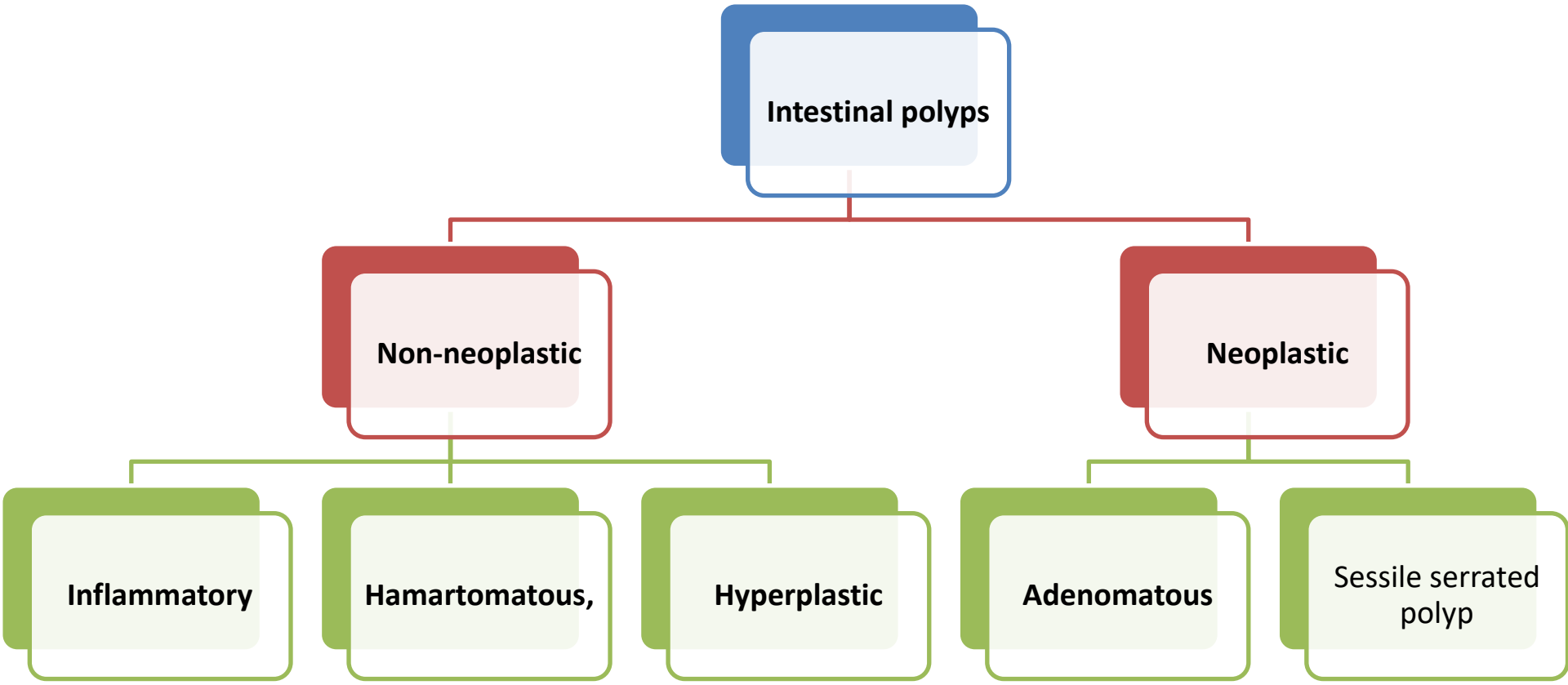


* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015





* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015


Intestinal polyps
Non-neoplastic
Neoplastic
Inflammatory
Hamartomatous,
Hyperplastic
Adenomatous
Sessile serrated polyp

INFLAMMATORY POLYPS

- Purely inflammatory lesion
- Example: solitary rectal ulcer
- Result of chronic cycles of injury and healing.

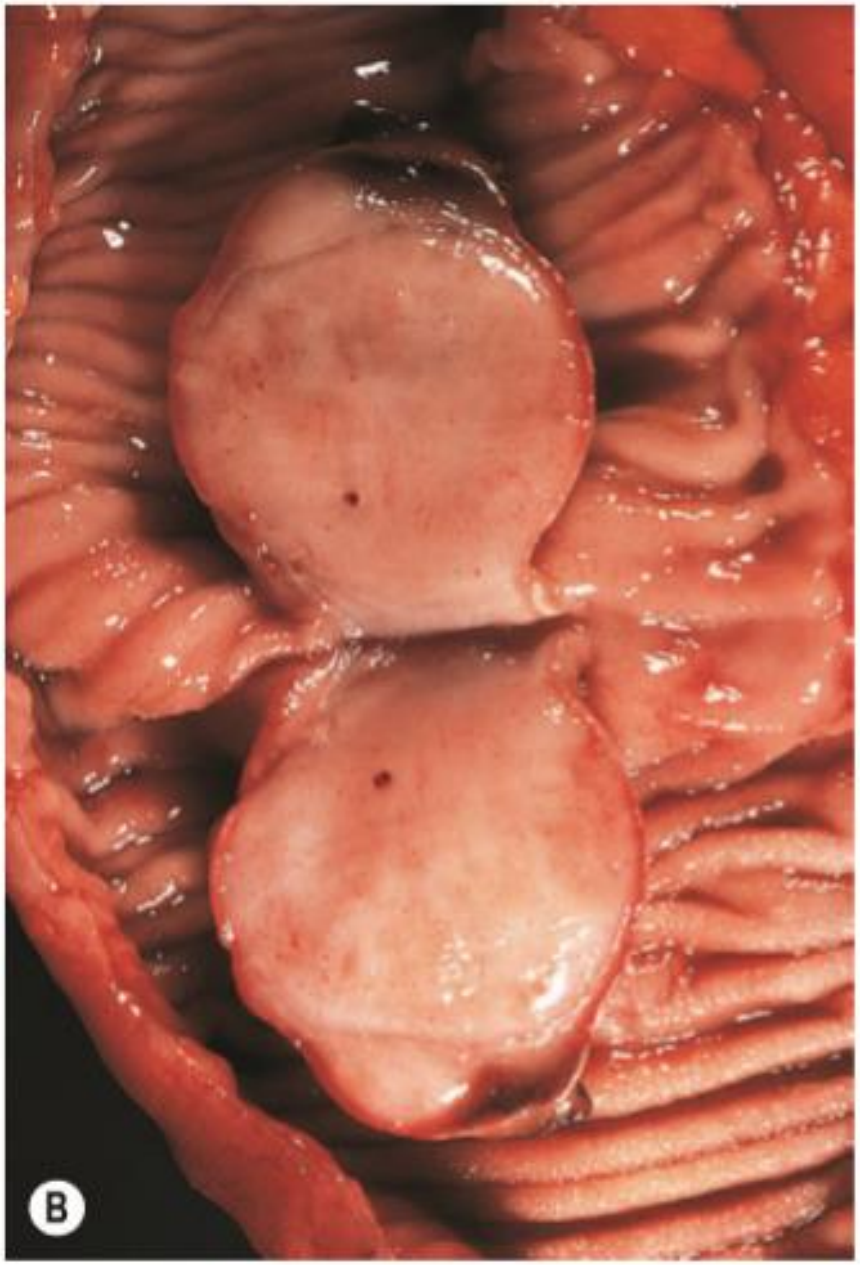
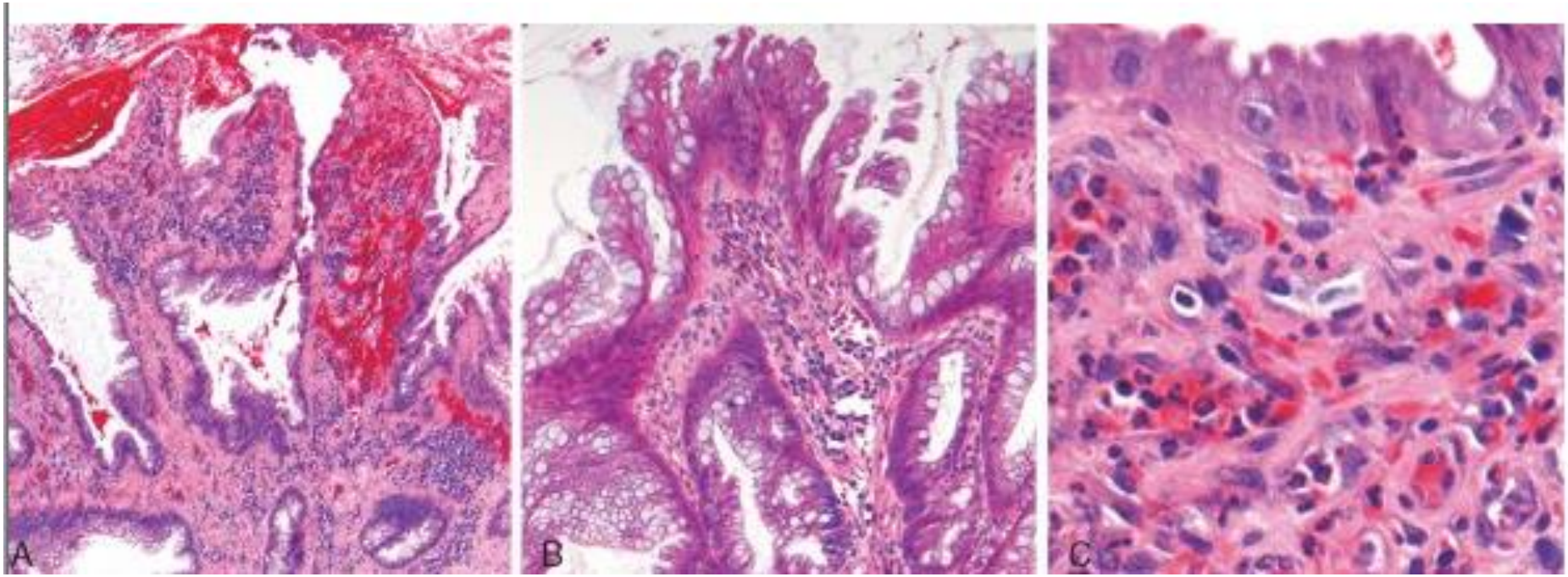


Fig. 11.119 **A** and **B**, Gross appearance of inflammatory fibroid polyp.



* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

HAMARTOMATOUS POLYPS

- Sporadically
- Genetically determined or acquired syndromes
- Recall that hamartomas are tumor-like growths composed of mature tissues that are normally present at the site in which they develop.
- Although hamartomatous polyposis syndromes are rare, they are important to recognize because of associated intestinal and extra-intestinal manifestations and the possibility that other family members are affected.

Familial hamartomatous polyposis

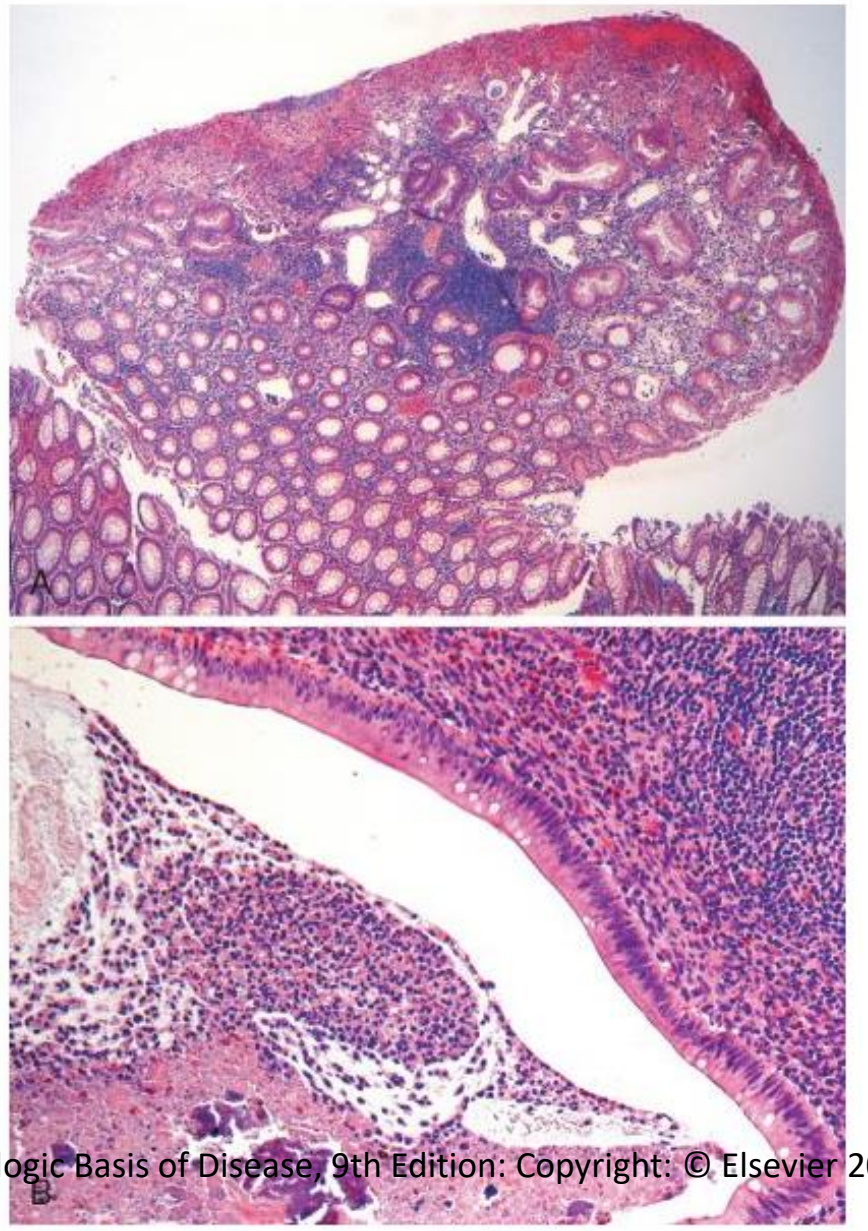
Syndrome	Mean Age	Mutated Gene	Gastrointestinal Lesions	Selected Extra-Gastrointestinal Manifestations
Peutz-Jeghers syndrome	10–15	LKB1/STK11	Arborizing polyps; Small intestine > colon > stomach; colonic adenocarcinoma	Skin macules; increased risk of thyroid, breast, lung, pancreas, gonadal, and bladder cancers
Juvenile polyposis	<5	SMAD4, BMPR1A	Juvenile polyps; risk of gastric, small intestinal, colonic, and pancreatic adenocarcinoma	Pulmonary arteriovenous malformations, digital clubbing
Cowden syndrome, Bannayan-Ruvalcaba-Riley syndrome	<15	PTEN	Hamartomatous polyps, lipomas, ganglioneuromas, inflammatory polyps, risk of colon cancer	Benign skin tumors, benign and malignant thyroid and breast lesions

Familial hamartomatous polyposis

Cronkhite-Canada syndrome	**>50**	**Nonhereditary**	**Hamartomatous colon polyps, crypt dilatation and edema in nonpolypoid mucosa**	**Nail atrophy, hair loss, abnormal skin pigmentation, cachexia, and anemia**
Tuberous sclerosis		TSC1, TSC2	Hamartomatous polyps (rectal)	Facial angiofibroma, cortical tubers, renal angiomyolipoma

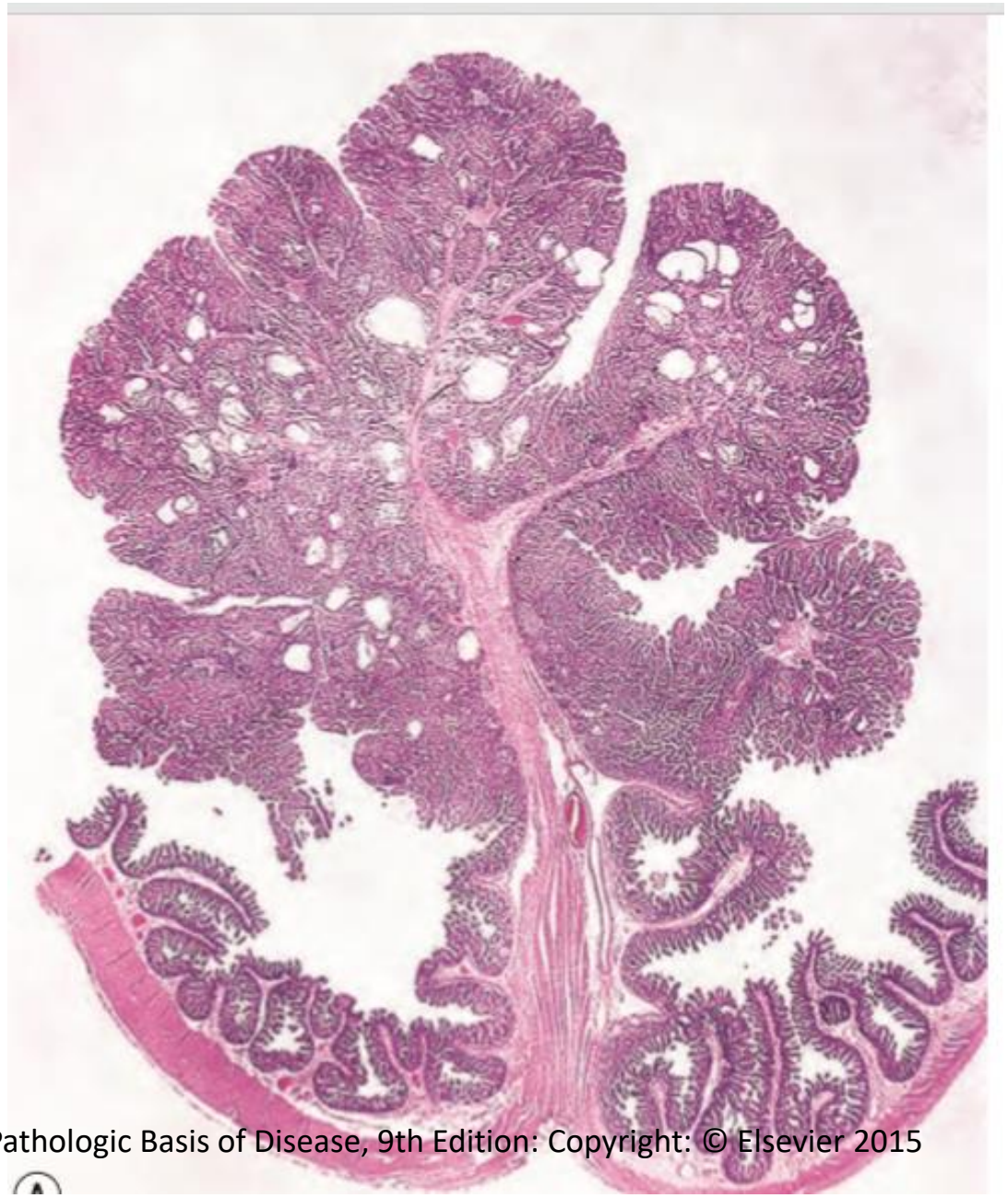
Juvenile Polyps

- Sporadic: retention polyps
- Syndromic
  - Autosomal dominant
  - 3 to as many as 100 polyps
  - Pulmonary arteriovenous malformations are a recognized extra-intestinal manifestation
- Children less than 5 years of age
- Site: rectum
- Pathogenesis: SMAD 4 (Intermediate b/w TGF beta pathway)



Peutz-Jeghers Syndrome

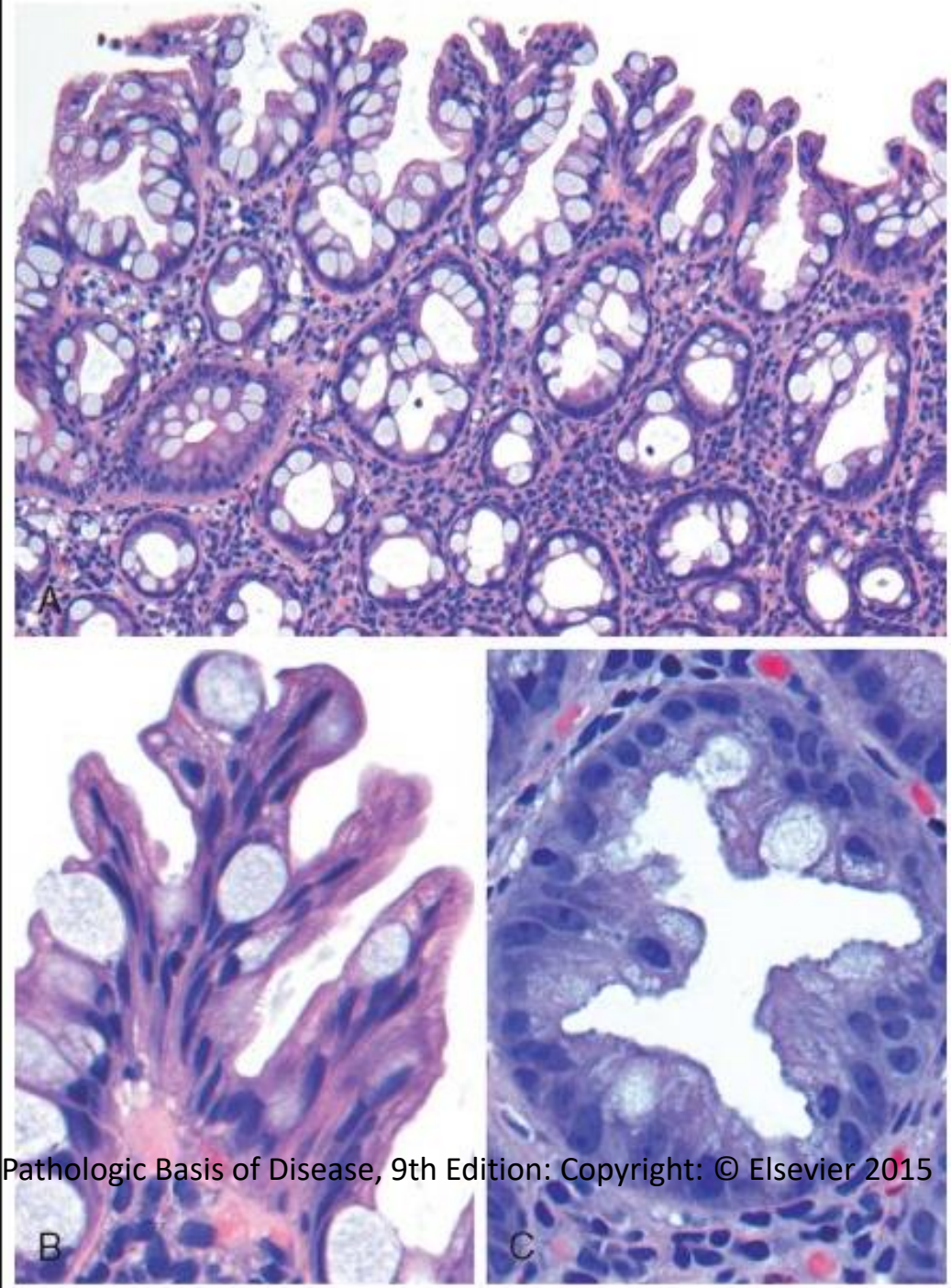
- Autosomal dominant syndrome
- Median age of 11 years
- Multiple GI hamartomatous polyps and mucocutaneous hyperpigmentation
- Increased risk of several malignancies, including cancers of the colon, pancreas, breast, lung, ovaries, uterus, and testicles, as well as other unusual neoplasms, such as sex cord tumors.
- *Pathogenesis*
- Germline heterozygous loss-of-function mutations in the gene lkb1/stk11 (second hit)



* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

HYPERPLASTIC POLYPS

- Common epithelial proliferations
- Sixth and seventh decades
- Lesions are without malignant potential
- Pathogenesis: decreased epithelial cell turnover and delayed shedding of surface epithelial cells
- They must be distinguished from sessile serrated adenomas
- Epithelial hyperplasia can occur as a nonspecific reaction adjacent to or overlying any mass or inflammatory lesion



* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

NEOPLASTIC POLYPS

Colonic adenomas

Benign polyps that are precursors to the majority of colorectal adenocarcinomas.

Intramucosal carcinomas

Carcinoid tumors

Stromal tumors,

Lymphomas,

Metastatic cancers

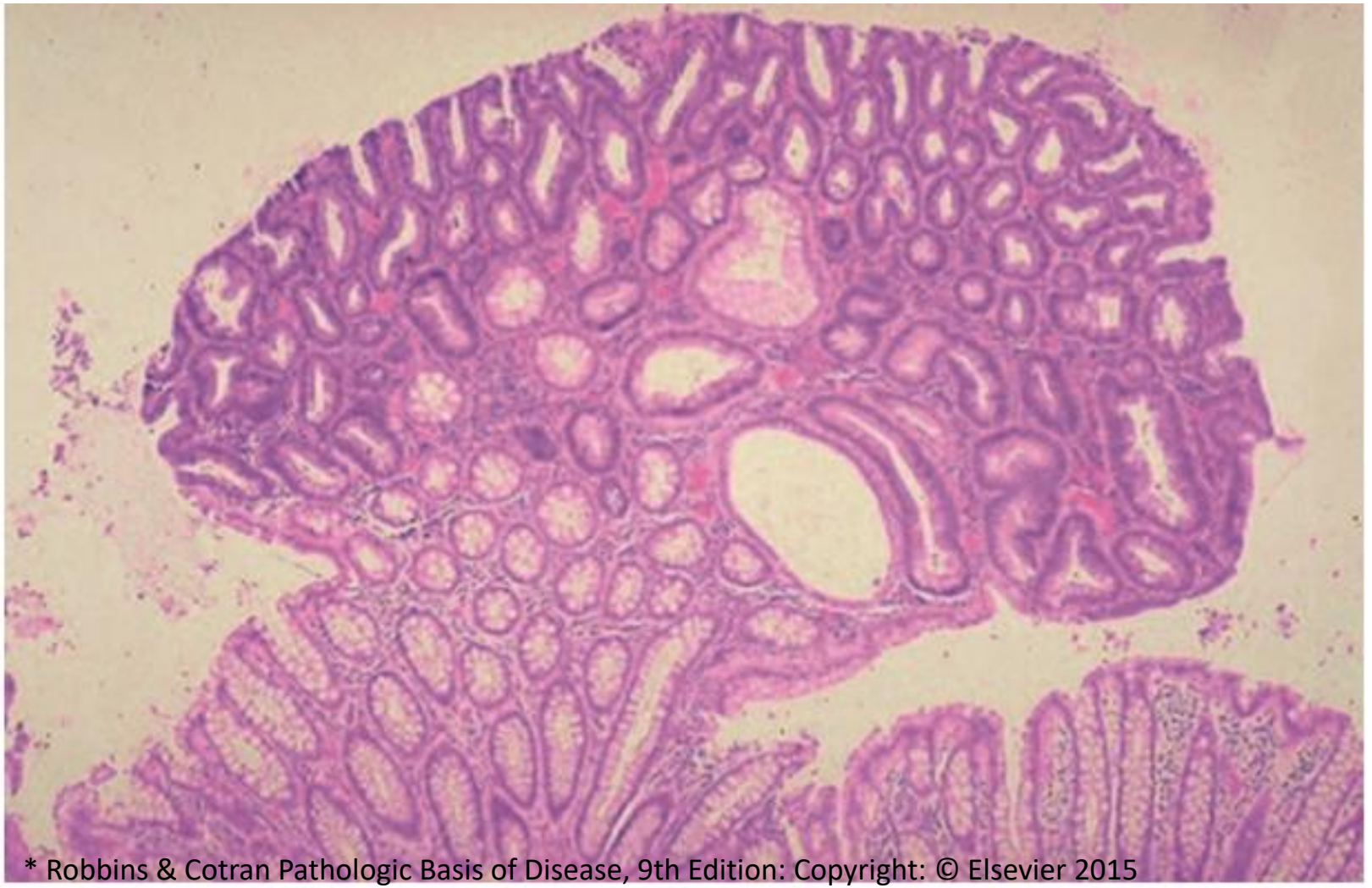
ADENOMAS

- Adenomas are intraepithelial neoplasms that range from small, often pedunculated polyps to large sessile lesions.
- Precursors to colorectal
- West: >50 yrs (universal surveillance; 10yrs before first relative diagnosed)

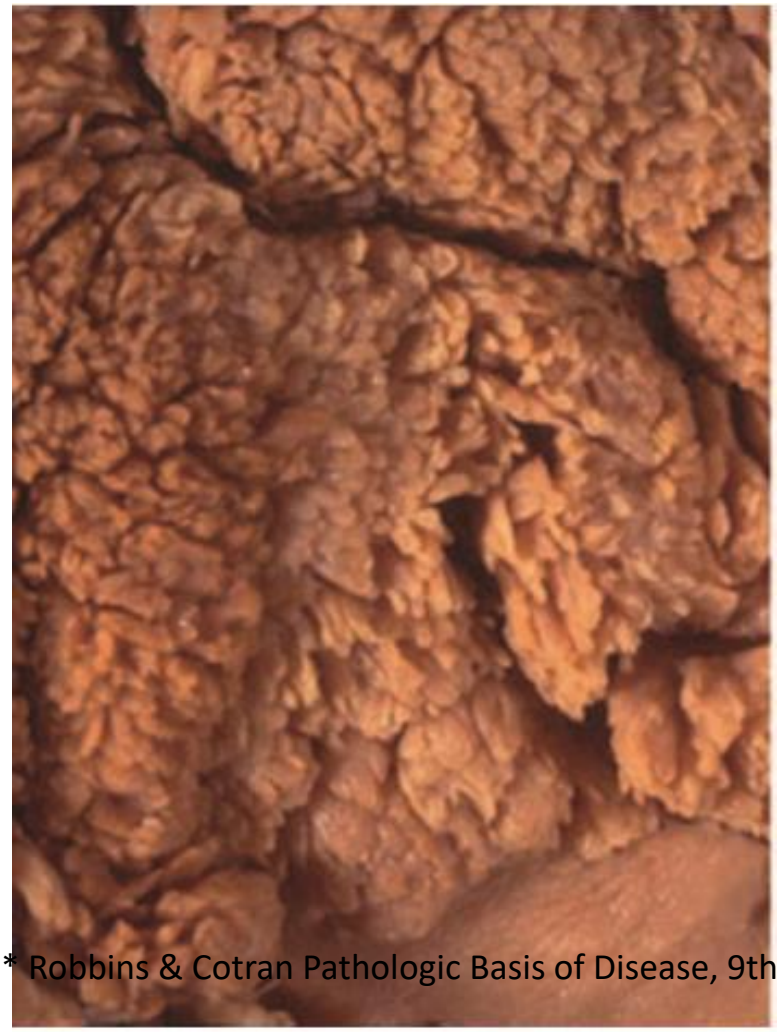
ADENOMAS

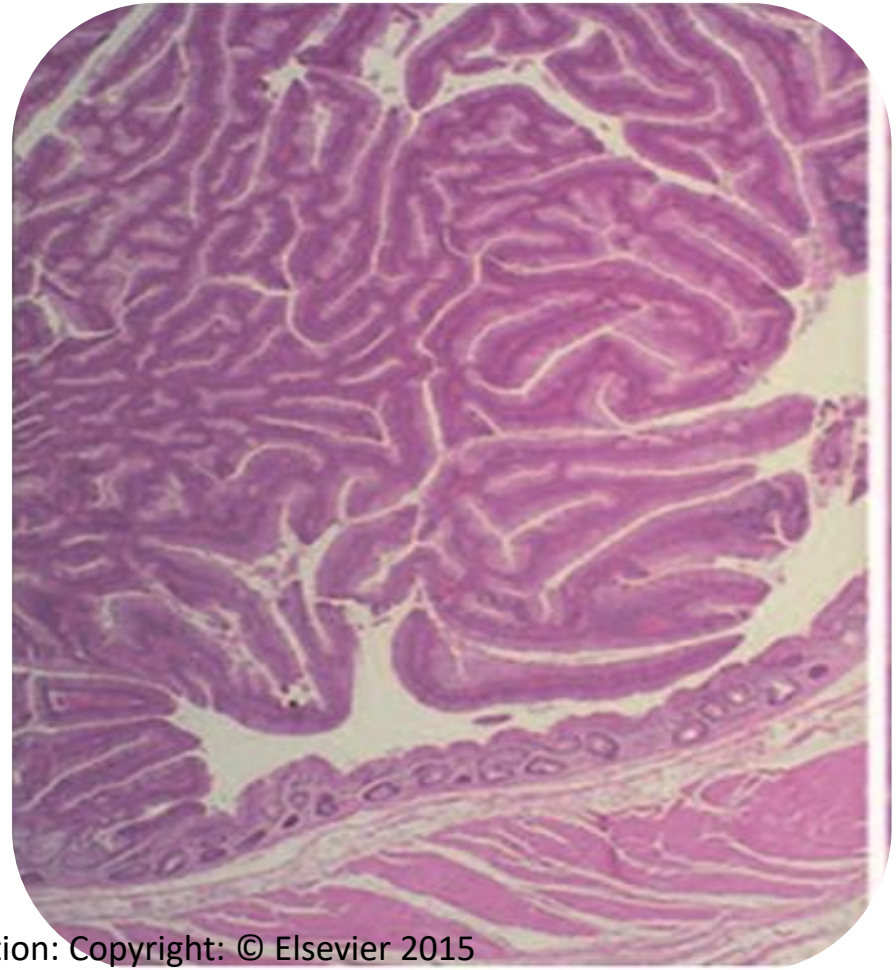
- Tubular
- Villous
- Tubulovillous
- Sessile serrated

TUBULAR



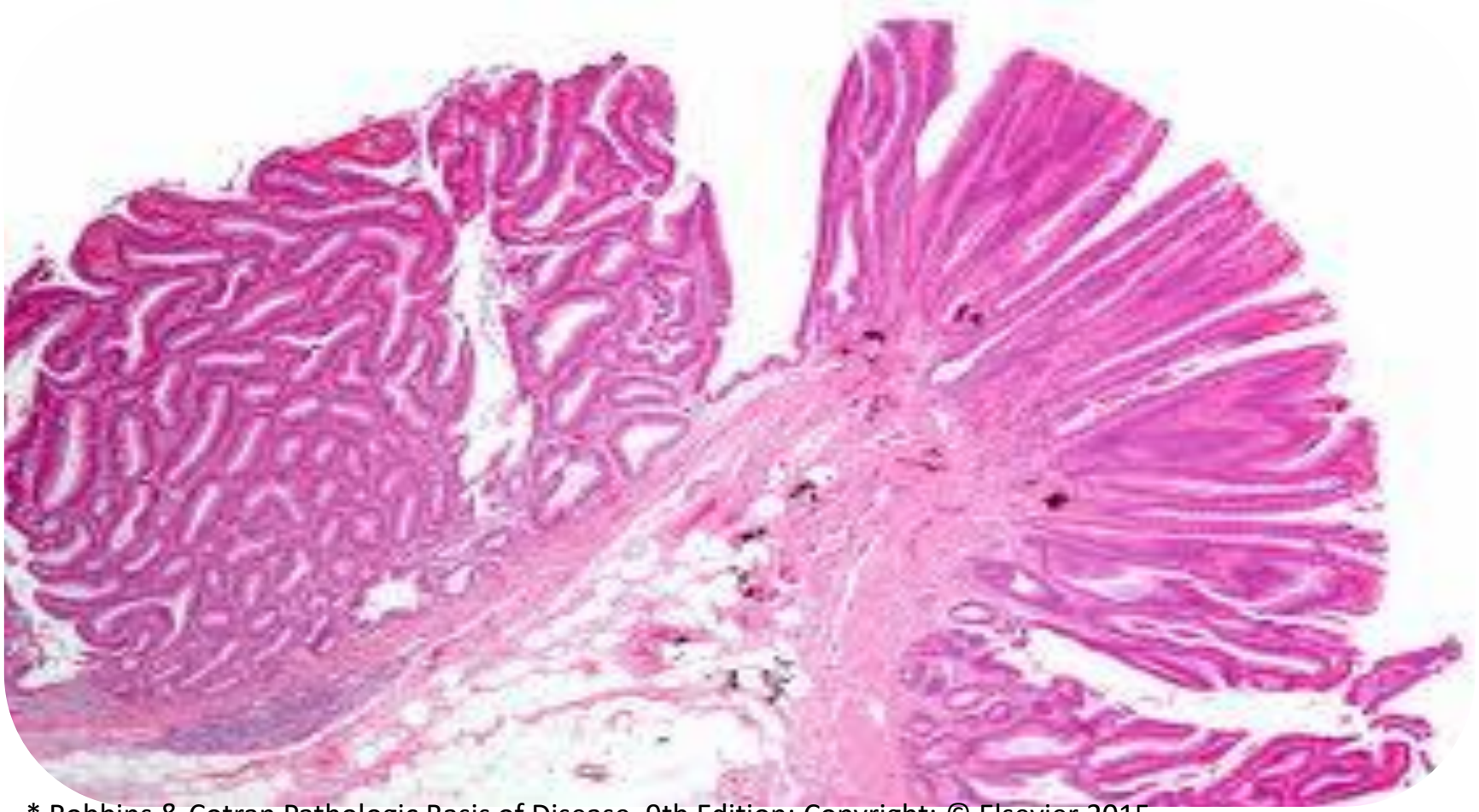
VILLOUS





* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

TUBULOVILLOUS

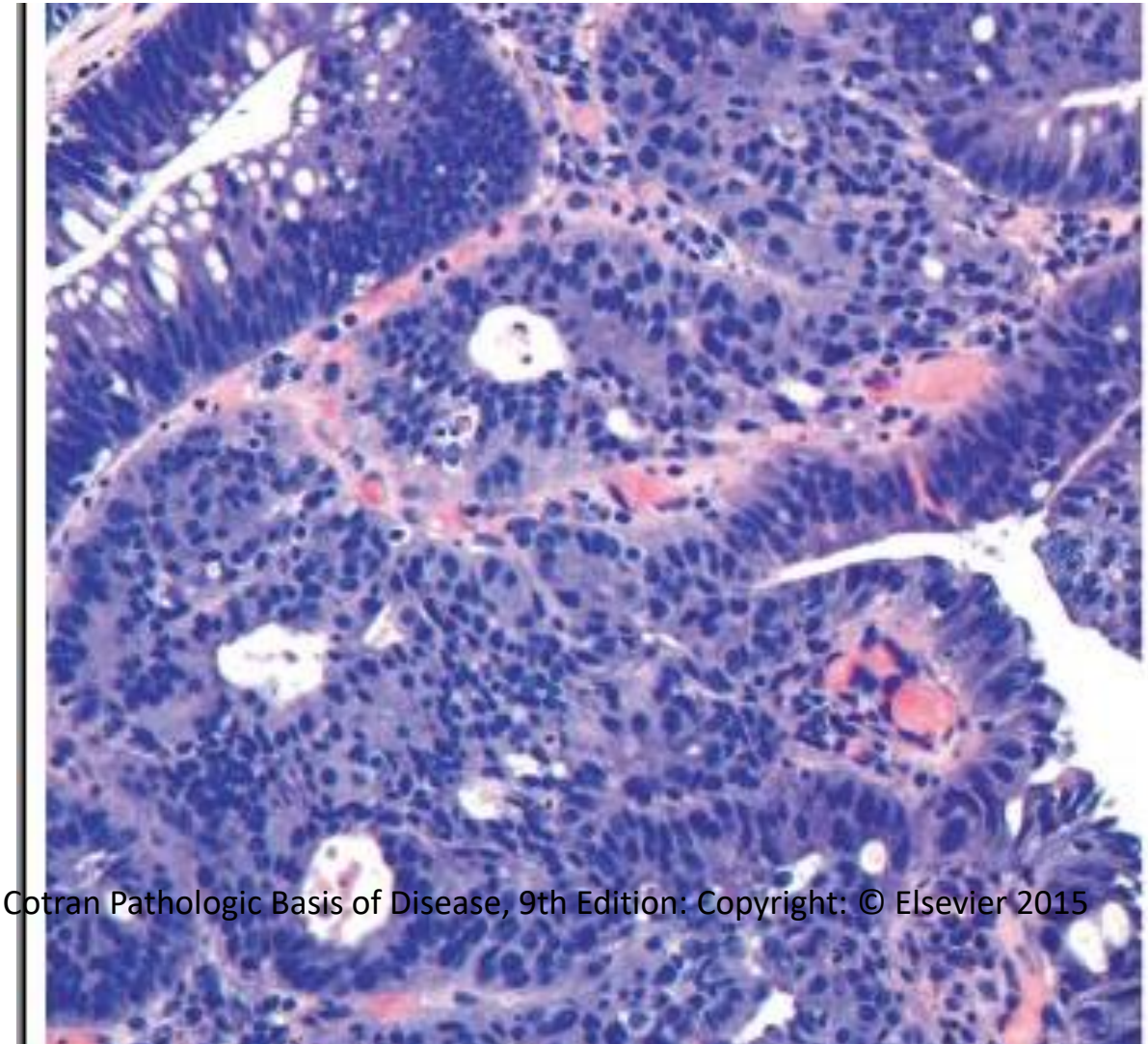


* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

SESSILE SERRATED

* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

INTRAMUCOSAL CARCINOMA



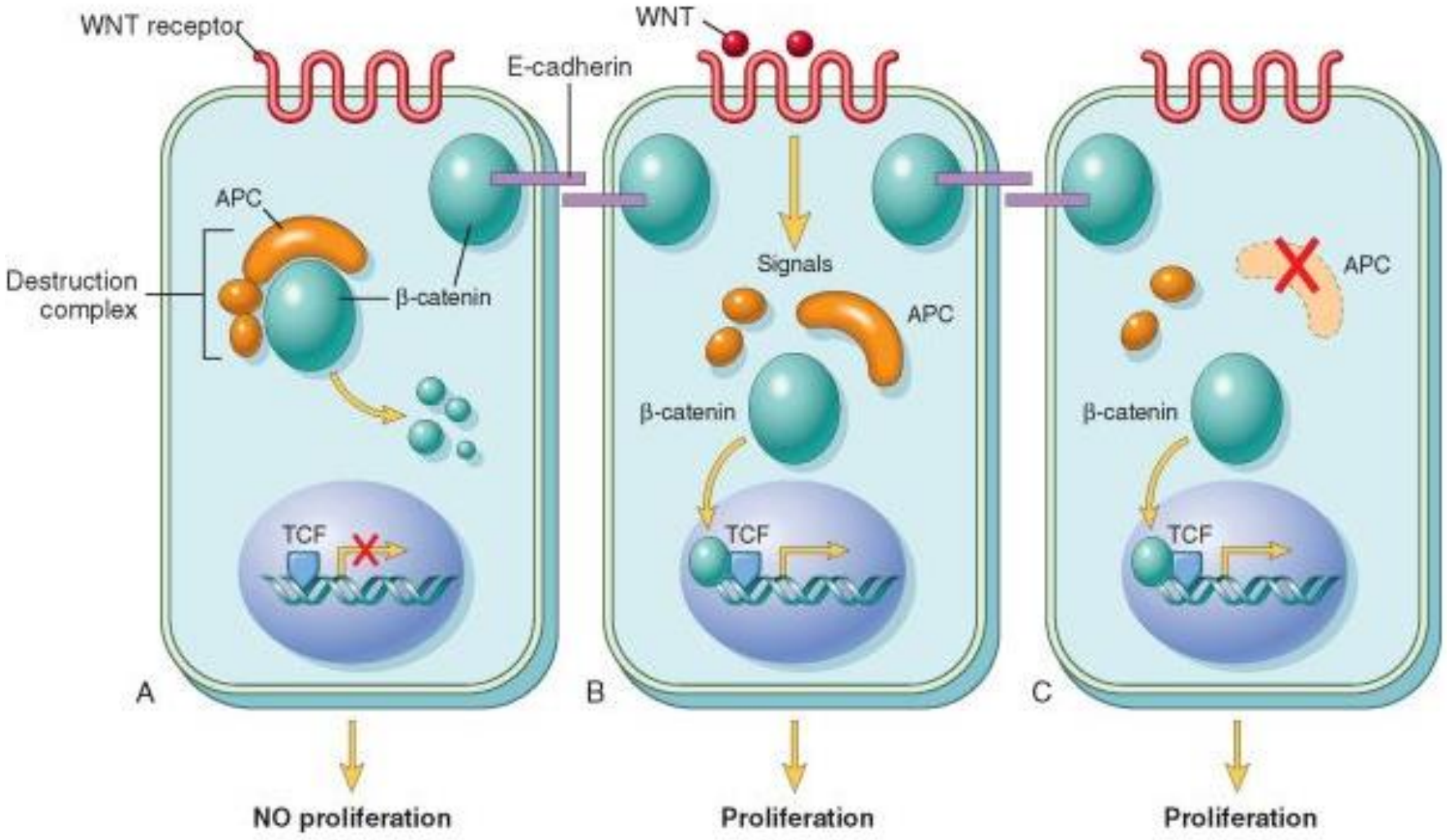
CARCINOMA COLON

- M/C type: Adenocarcinoma
- Others
  - SCC
  - Neuroendocrine
  - NHL
  - Mesenchymal neoplasms

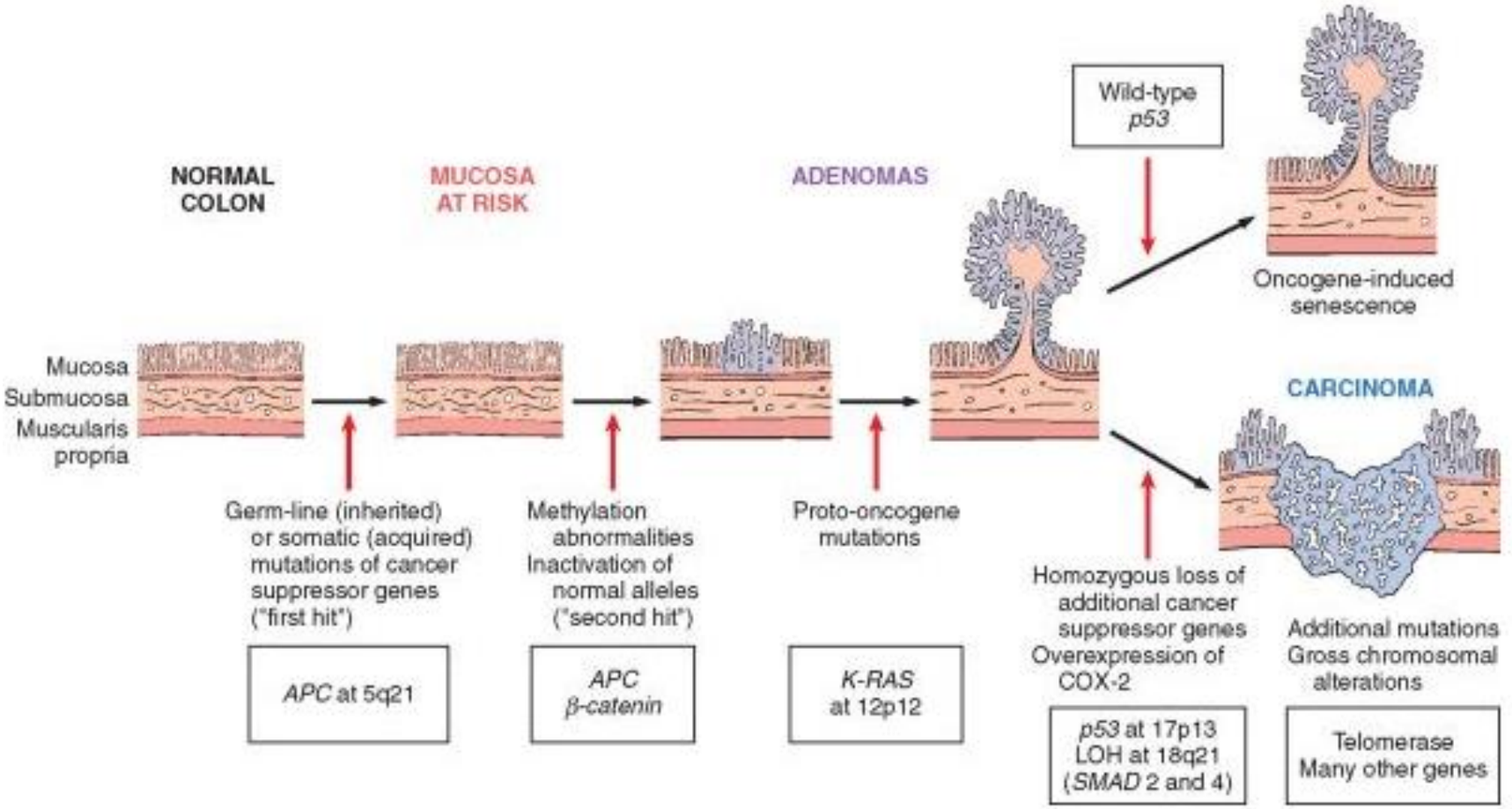
Adenocarcinoma

- Familial syndromes'
- Sporadic

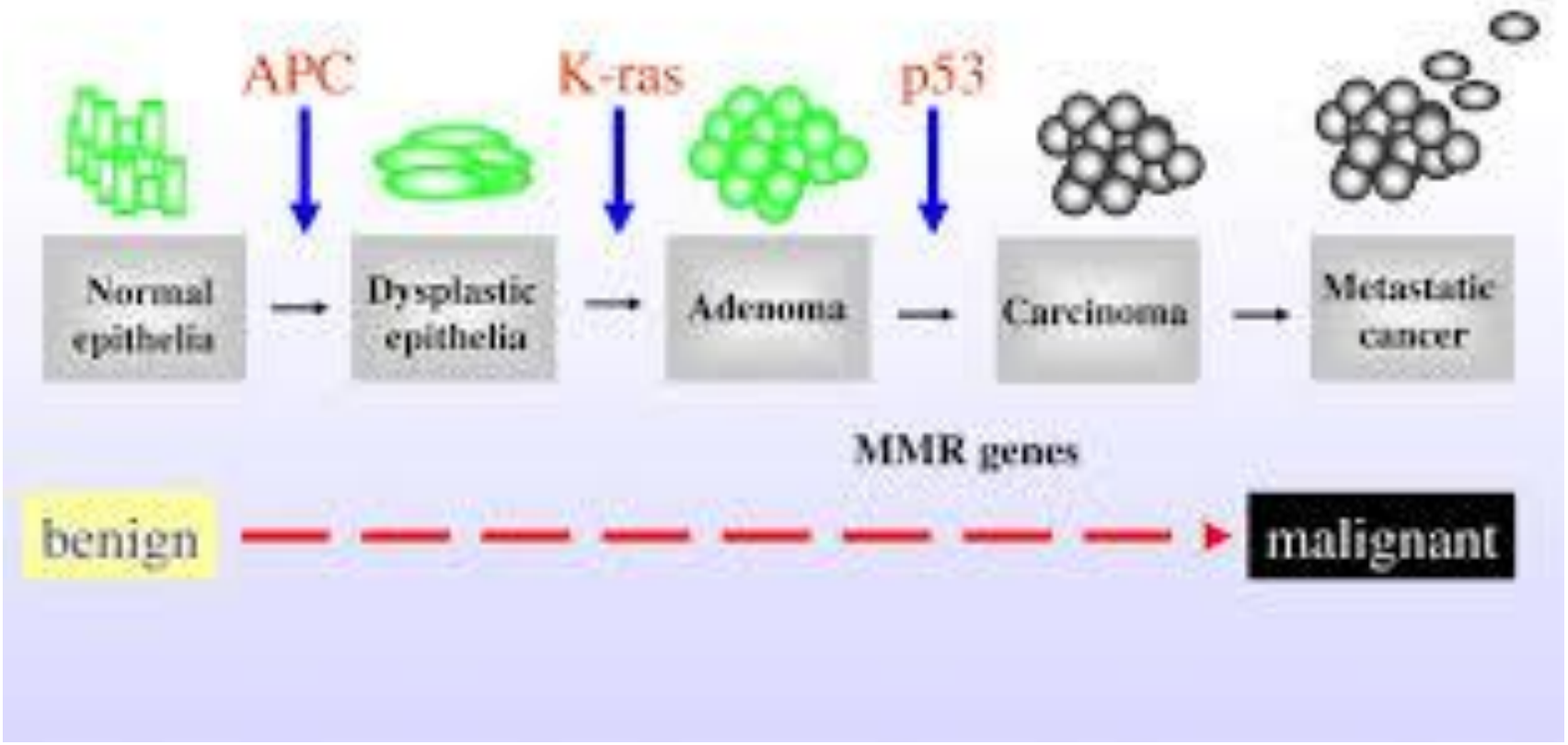
Etiology	Molecular Defect	Target Gene(s)	Transmission	Predominant Site(s)	Histology
Familial adenomatous polyposis (70% of FAP)	APC/WNT pathway	APC	Autosomal dominant	None	Tubular, villous; typical adenocarcinoma
Familial adenomatous polyposis (<10% of FAP)	DNA mismatch repair	MUTYH	None, recessive	None	Sessile serrated adenoma; mucinous adenocarcinoma
Hereditary nonpolyposis colorectal cancer	DNA mismatch repair	MSH2, MLH1	Autosomal	Right side	Sessile serrated adenoma; mucinous adenocarcinoma
Sporadic colon cancer (80%)	APC/WNT pathway	APC	None	Left side	Tubular, villous; typical adenocarcinoma
Sporadic colon cancer (10% to 15%)	DNA mismatch repair	MSH2, MLH1	None	Right side	Sessile serrated adenoma; mucinous adenocarcinoma



* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015

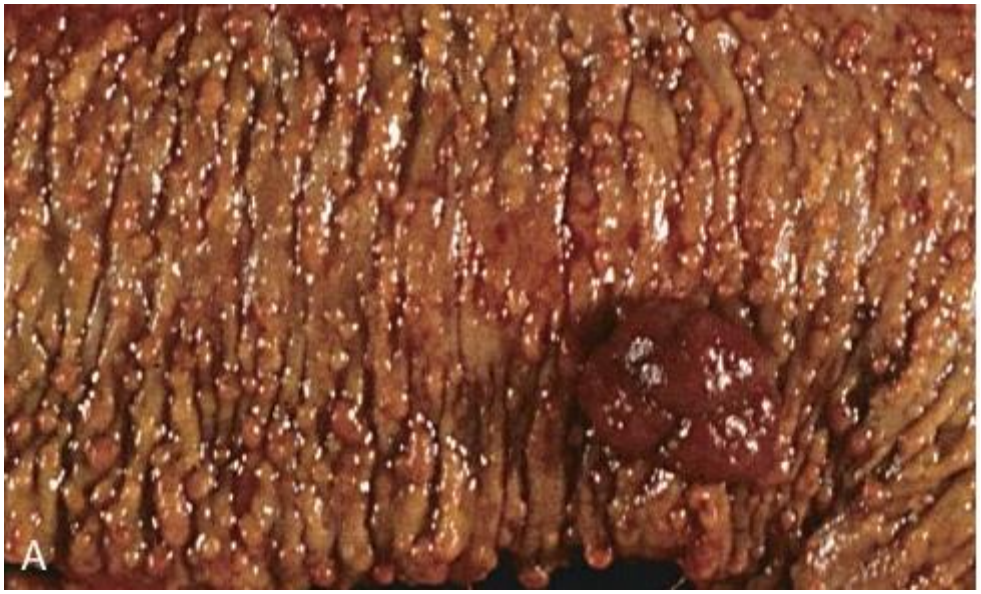


* Robbins & Cotran Pathologic Basis of Disease, 9th Edition: Copyright: © Elsevier 2015


APC
K-ras
p53
Normal epithelia
Dysplastic epithelia
Adenoma
Carcinoma
Metastatic cancer
MMR genes
benign
malignant

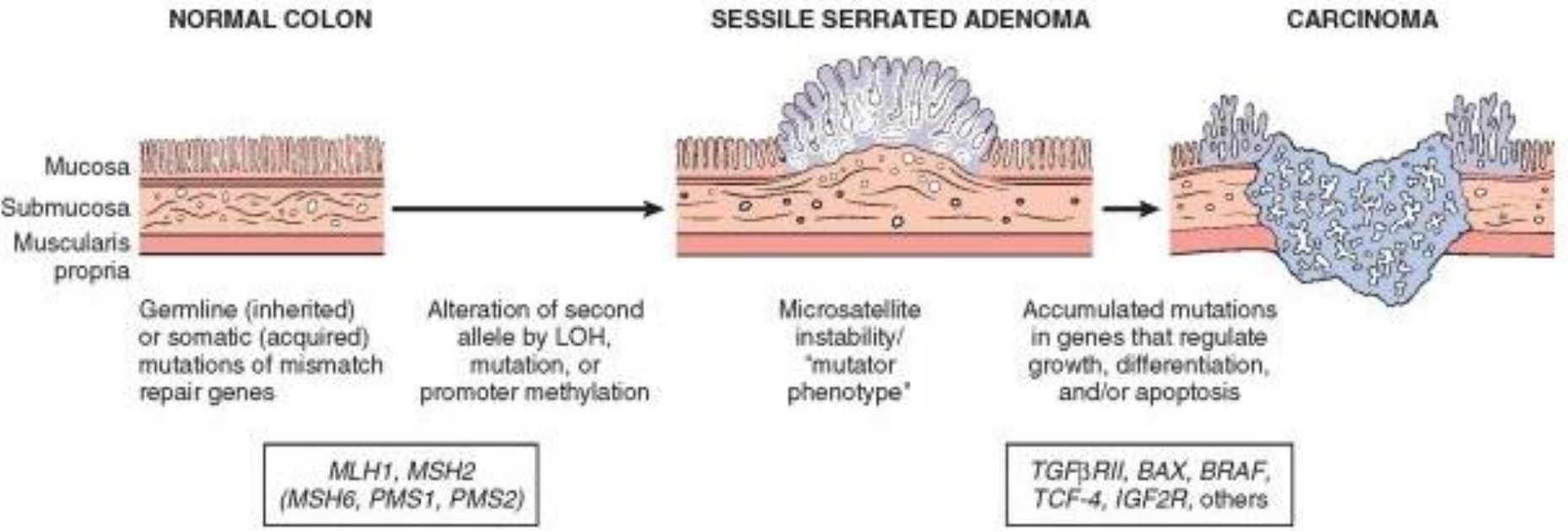
FAP

- At least *100 polyps are necessary for a diagnosis* of classic FAP, and as many as several thousand may be present



HEREDITARY NON-POLYPOSIS COLORECTAL CANCER

- Lynch syndrome
- Familial clustering : colorectum, endometrium, stomach, ovary, ureters, brain, small bowel, hepatobiliary tract, and skin.
- Inherited mutations in genes that encode proteins responsible for the detection, excision, and repair of errors that occur during dna replication
- *Msh2* and *Mlh1*.
- Epigenetic silencing
- Defects in mismatch repair lead to the accumulation of mutations at rates up to 1000 times higher than normal, mostly in regions containing short repeating DNA sequences referred to as microsatellite DNA
- Resulting *microsatellite instability*



Revised Bethesda criteria for HNPCC screening

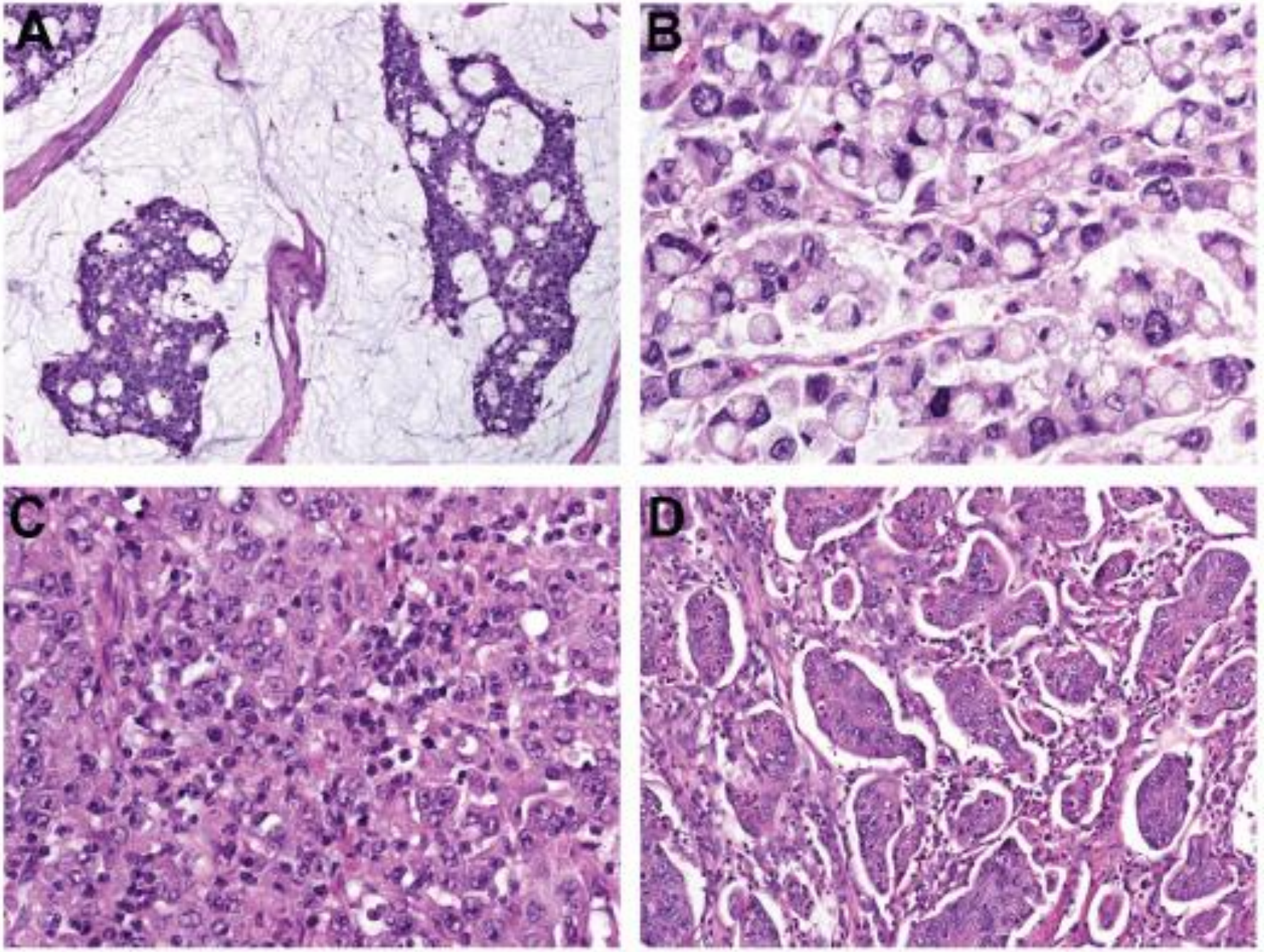
Revised Bethesda: One of the Following Criteria Need to be Met:
Diagnosed with colorectal carcinoma (CRC) before the age of 50 years
Synchronous or metachronous CRC or other Lynch syndrome (HNPCC)-related tumors (stomach, bladder, ureter, renal pelvis, biliary tract, brain (glioblastoma), sebeceous gland adenomas, keratoacanthomas, and small bowel carcinoma, regardless of age.
CRC with a high-microsatellite instability morphology (tumor infiltrating lymphocytes, Crohn-like reaction, mucinous/signet ring differentation, or medullary growth pattern) that was diagnosed before the age of 60 years
CRC with one or more first-degree relative with CRC or other HNPCC-related tumors with one of the cancers being diagnosed under age 50 years (or adenoma under age 40 years)
CRC with two or more relatives with CRC or other HNPCC-related tumors, regardless of age

Adenocarcinoma

- 60 to 70 years of age
- Males
- The dietary factors : low intake of unabsorbable vegetable fiber and high intake of refined carbohydrates and fat.
- It is theorized that reduced fiber content leads to decreased stool bulk and altered composition of the intestinal microbiota.

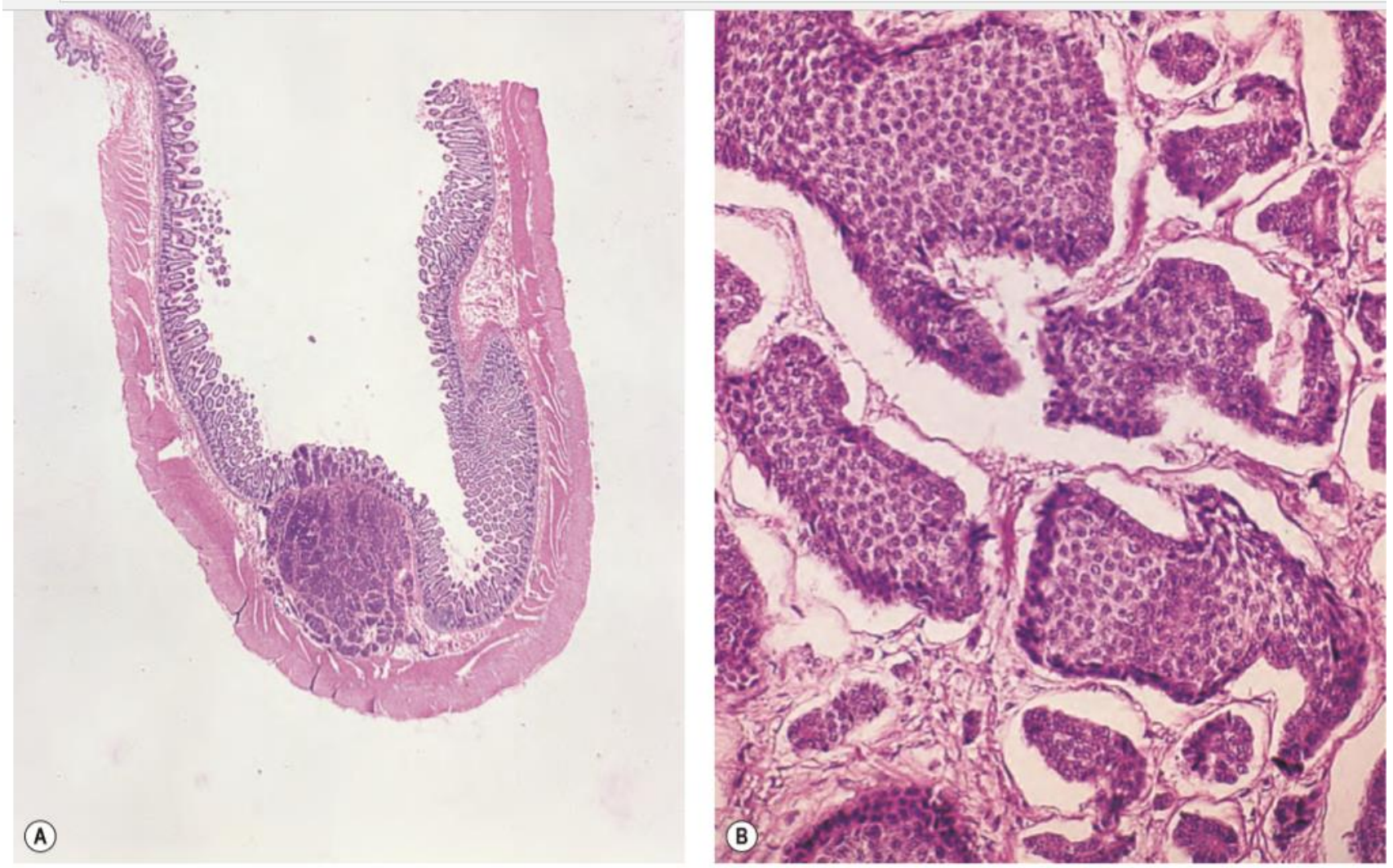
Adenocarcinoma

- Type
  - Intestinal type
  - Mucinous
- Differentiation
  - Well
  - Moderate
  - Poorly
  - Undifferentiated
- Other prognostic variables


A
B
C
D

Stage	Characteristics
Tumor	
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through muscularis propria into subserosa or nonperitonealized pericolic or perirectal tissues
T4	Tumor directly invades other organs or structures and/or perforates visceral peritoneum
Regional nodal metastasis	
NX	Regional lymph nodes cannot be assessed
N0	No nodal metastasis
N1	Metastasis in one to three pericolic or perirectal nodes
N2	Metastasis in four to more pericolic or perirectal nodes
N3	Metastasis in any node along course of a named vascular trunk and/or metastasis to apical node
Distant metastasis	
MX	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Small intestine carcinoid

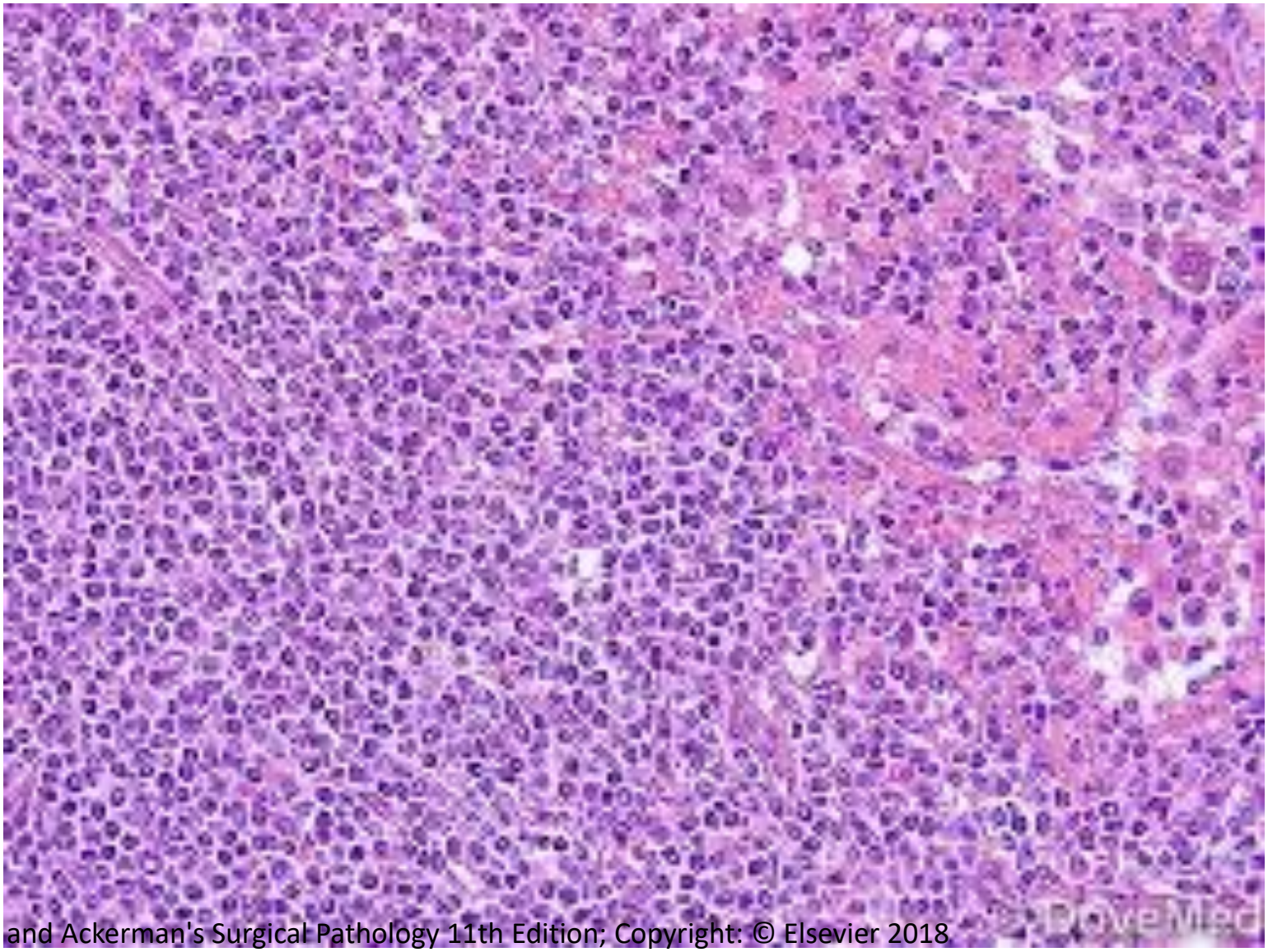


Colorectal Lymphoma

- Less common in colon than small bowel or stomach
- Usually B cell lineage
- T cell patients are younger, associated with perforation and poorer prognosis
- **Risk factors**: transplants, ulcerative colitis and AIDS
- Regional lymph nodes involved in 50% of cases
- Advanced lesions may impair gut motility by destroying muscle wall

Gross description

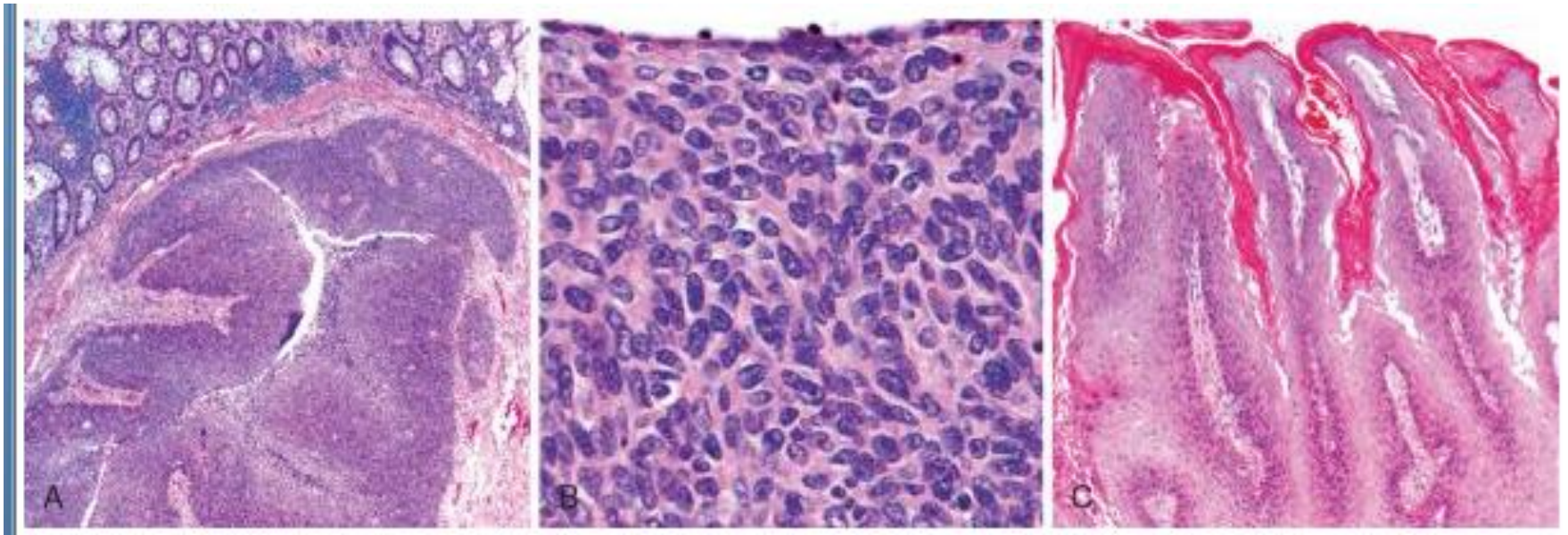
- Plaque-like expansion of mucosa / submucosa, bowel wall thickening, polyps ("multiple lymphomatoid polyposis" if multiple polyps throughout colon) or ulceration



Rosai and Ackerman's Surgical Pathology 11th Edition; Copyright: © Elsevier 2018

Tumors of the Anal Canal

- Upper zone is lined by columnar rectal epithelium
- Middle third by transitional epithelium
- Lower third by stratified squamous epithelium.
- Glandular or squamous (hpv infection, which also causes precursor lesions such as condyloma accuminatum)
- Basaloid (cloacogenic carcinoma)



Appendix

- Normal true diverticulum of the cecum
- Prone to acute and chronic inflammation.
- Lifetime risk for appendicitis is 7%; males are affected slightly more

Pathogenesis

- Progressive increases in intraluminal pressure that compromise venous outflow
  - Luminal obstruction
  - Fecalith
  - Gallstone,
  - Tumor,
  - Mass of worms (oxyuriasis vermicularis)

APPENDICITIS

- Peak incidence 10-12 years
- Begins as dull, steady pain in periumbilical area... Progresses over 4-6 hours & localizes to right lower quadrant

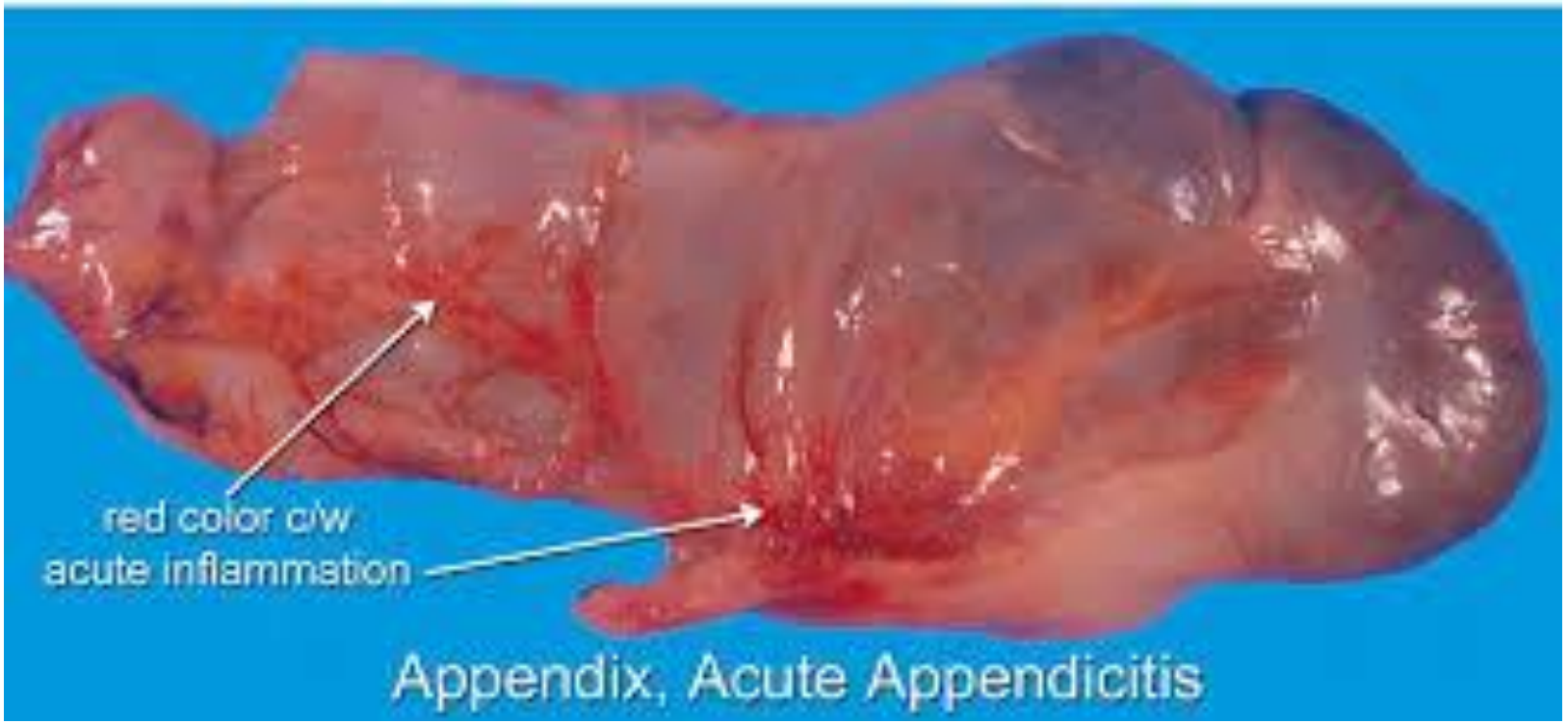
- Low grade fever
- Nausea
- Anorexia

- Sudden pain relief may indicate rupture of appendix (Leads to peritonitis)

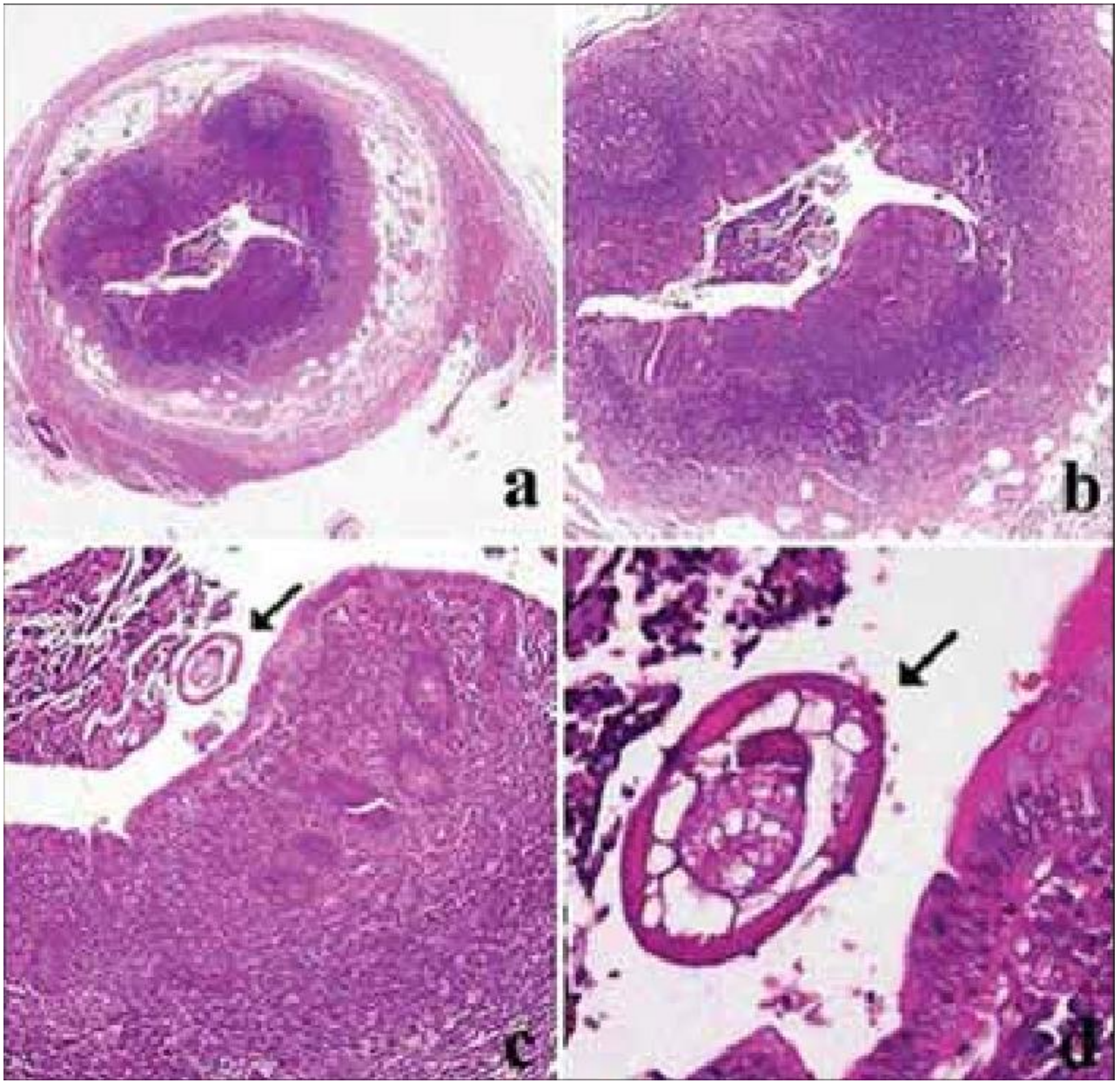
Diagnosis

- Clinical signs and symptoms
- ↑ WBC
- Abdominal Sonogram
- Exploratory Lap

- Rebound Pain or Tenderness (RLQ) at McBurney's Point



Appendix, Acute Appendicitis


a
b
c
d

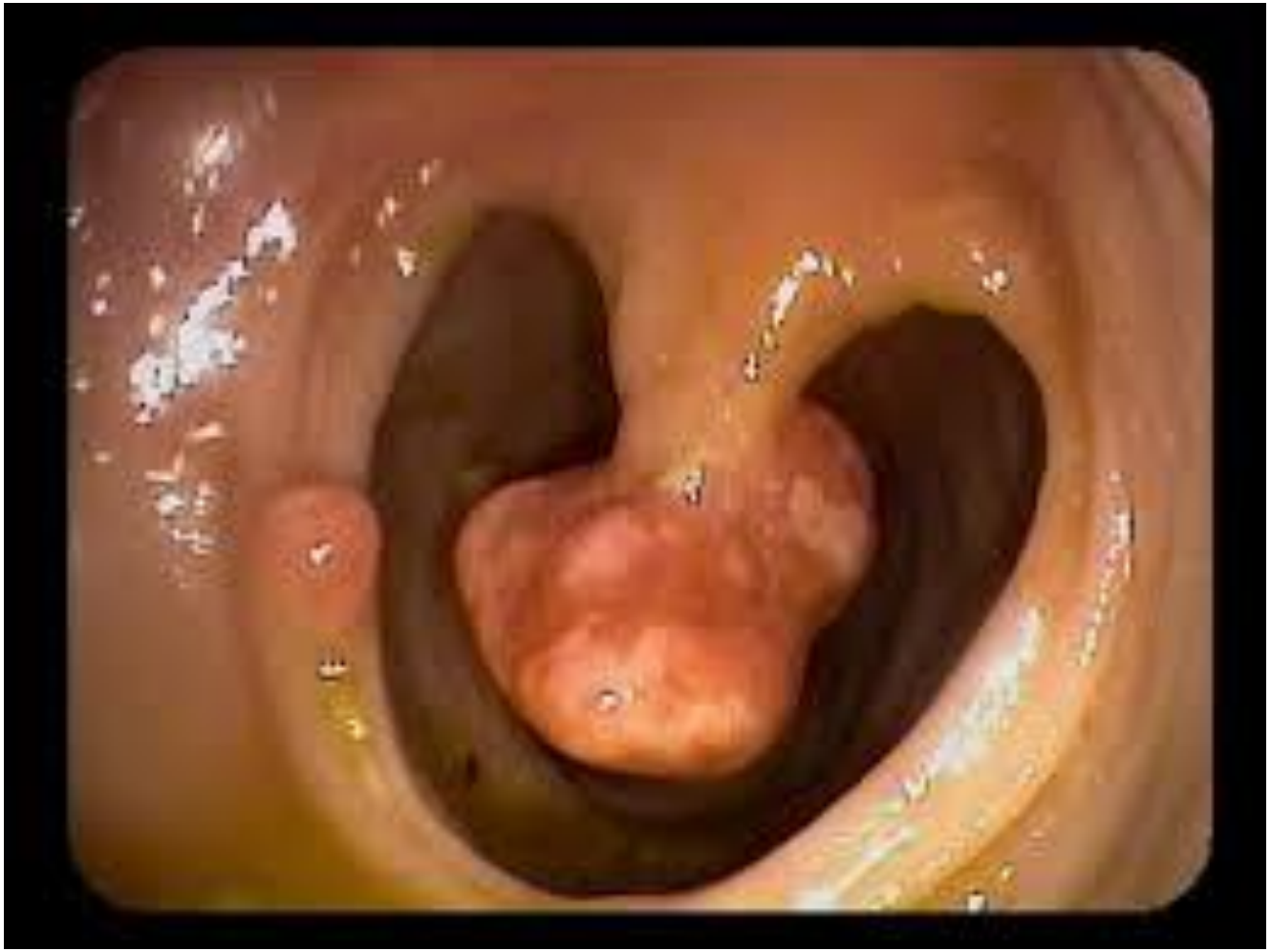
Case based study GIT III

Case 1

- 56 year male presented with vague abdominal aches and pains and mild anaemia to a physician after routine lab investigations.

  – Order further evaluation

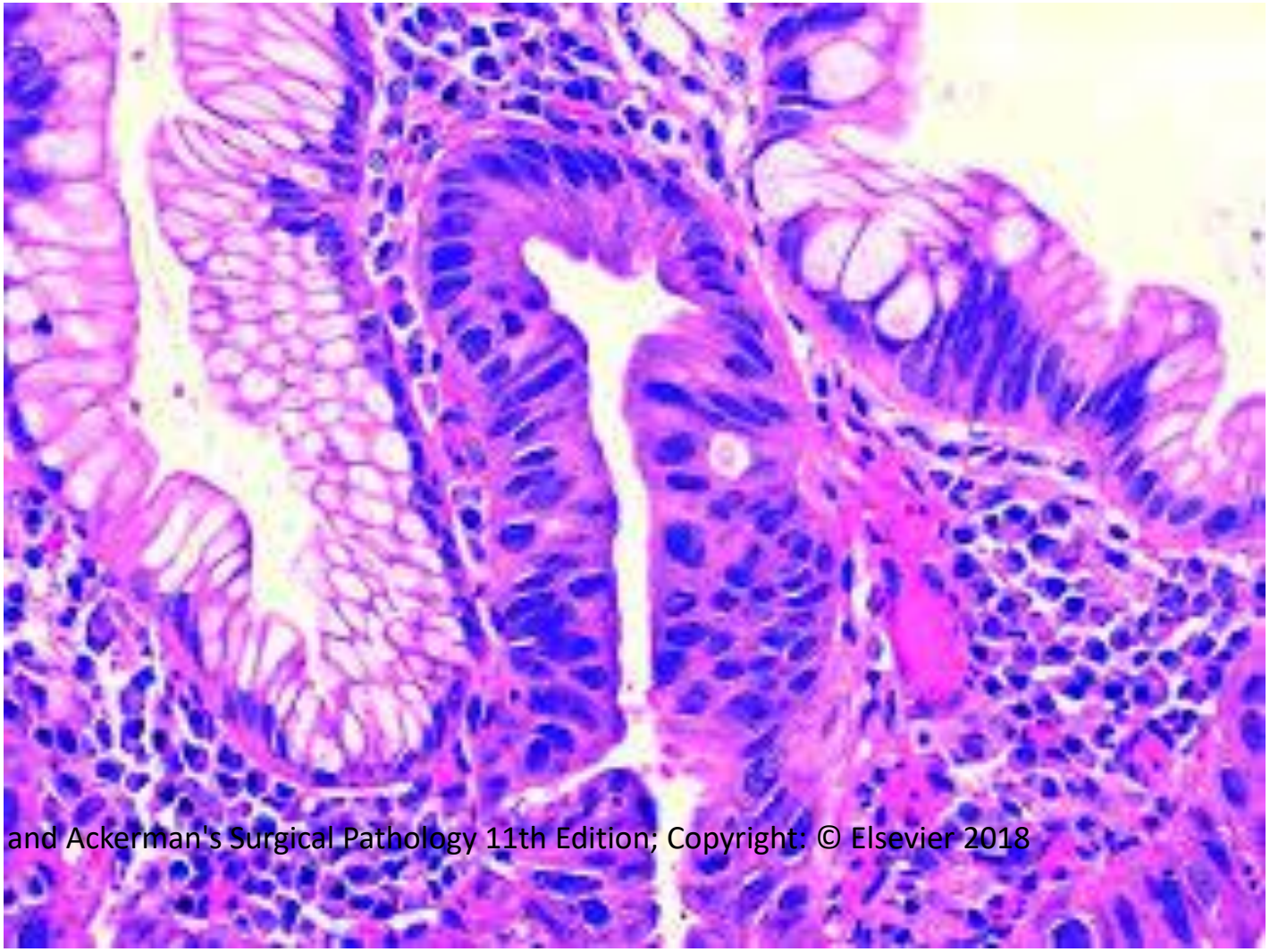
Colonoscopy



Gross

Microscopy

Microscopy



- Diagnosis
- Futher work up
- Management

A definite increased risk of developing colon cancer is associated with which one or more of the following?

A. Diet high in fiber
B. Diet low in animal fat & protein
C. Ulcerative colitis
D. Familial polyposis
E. Strong family history of colon cancer in several preceding generations

Select the most common mode of spread of colon cancer

A. Hematogenous
B. Lymphatic
C. Direct extension
D. Implantation

Which of the following is the most important prognostic determinant of survival after treatment for colorectal cancer?

A. Lymph node involvement
B. Transmural extension
C. Tumor size
D. Histologic differentiation
E. DNA content

With regard to colorectal polyps, which of the following is/are considered precancerous ?

A. Hyperplastic polyp
B. Juvenile polyp
C. Tubulovillous adenoma
D. Retention adenoma

A 68-year-old man presents to his primary care physician with anaemia. The patient's medical history is significant for hypertension. The patient is found to have guaiac-positive stools and is subsequently referred for colonoscopy. Colonoscopy reveals a "golf ball"-size, near-obstructing tumor in the descending colon, not admitting the scope. The biopsy is positive for adenocarcinoma of the colon.

Q. Which of the following is the next step in the management of this patient?

A. Full metastatic workup first, and if negative, then plan for colon resection
B. A course of radiation therapy prior to any resection
C. Plan for pre-operative chemotherapy
D. Do metastatic work up, but plan for colon resection anyway
E. Schedule a barium enema to evaluate the proximal colon

Q. A 60-year-old man presents for an annual physical examination. The examination is normal except for a palpable mass in the rectum on digital rectal examination. The patient denies any change in bowel habits and feels well. Rectal cancer is suspected. What is the next best step in the evaluation of this patient?

A. Computed tomography scan of the abdomen and pelvis
B. Double-contrast barium enema
C. Flexible sigmoidoscopy with biopsy of the lesion
D. Full colonoscopy with biopsy of the lesion
E. Magnetic resonance imaging scan of the abdomen and pelvis

Q. A 70-year-old man with severe atherosclerosis who takes 1 aspirin (75 mg) daily undergoes cardiac catheterization because of chest pain. Later in the day, he develops severe abdominal pain and passes a large amount of bloody diarrhea. Physical examination reveals no peritoneal signs. Which of the following is the most likely cause of the patient's bleeding?

A. Colon cancer
B. Diverticulitis
C. Hemorrhoids
D. Mesenteric ischemia
E. Nonsteroidal anti-inflammatory drug enteropathy

CASE 2

- 15 year old boy presented with acute pain in abdomen.
- On exmination
- Pale, feeble pulse
- low heart rate, low BP, fever.
- Abdomen is tender with no bowel sounds

- Order investigations

- CBC:
  - TLC: 25200
  - DLC: P85, L15
  - PC: 2.5
- Management