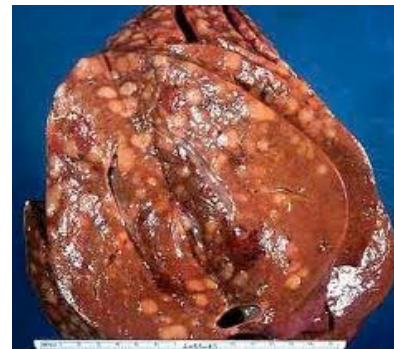
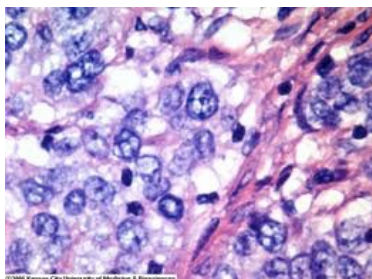
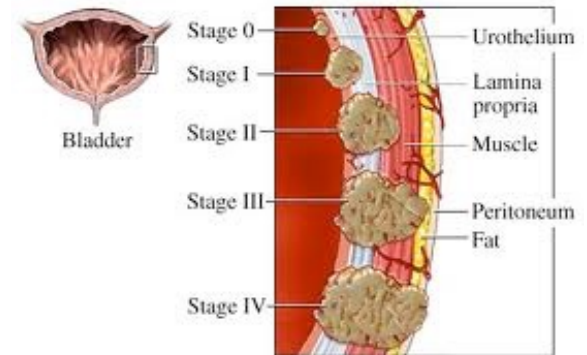
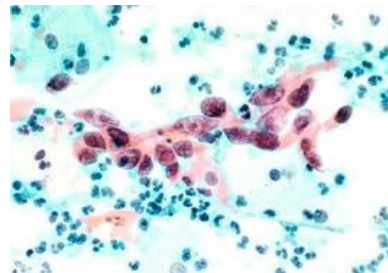


Principles of Neoplasia



Henry Sánchez, M.D.



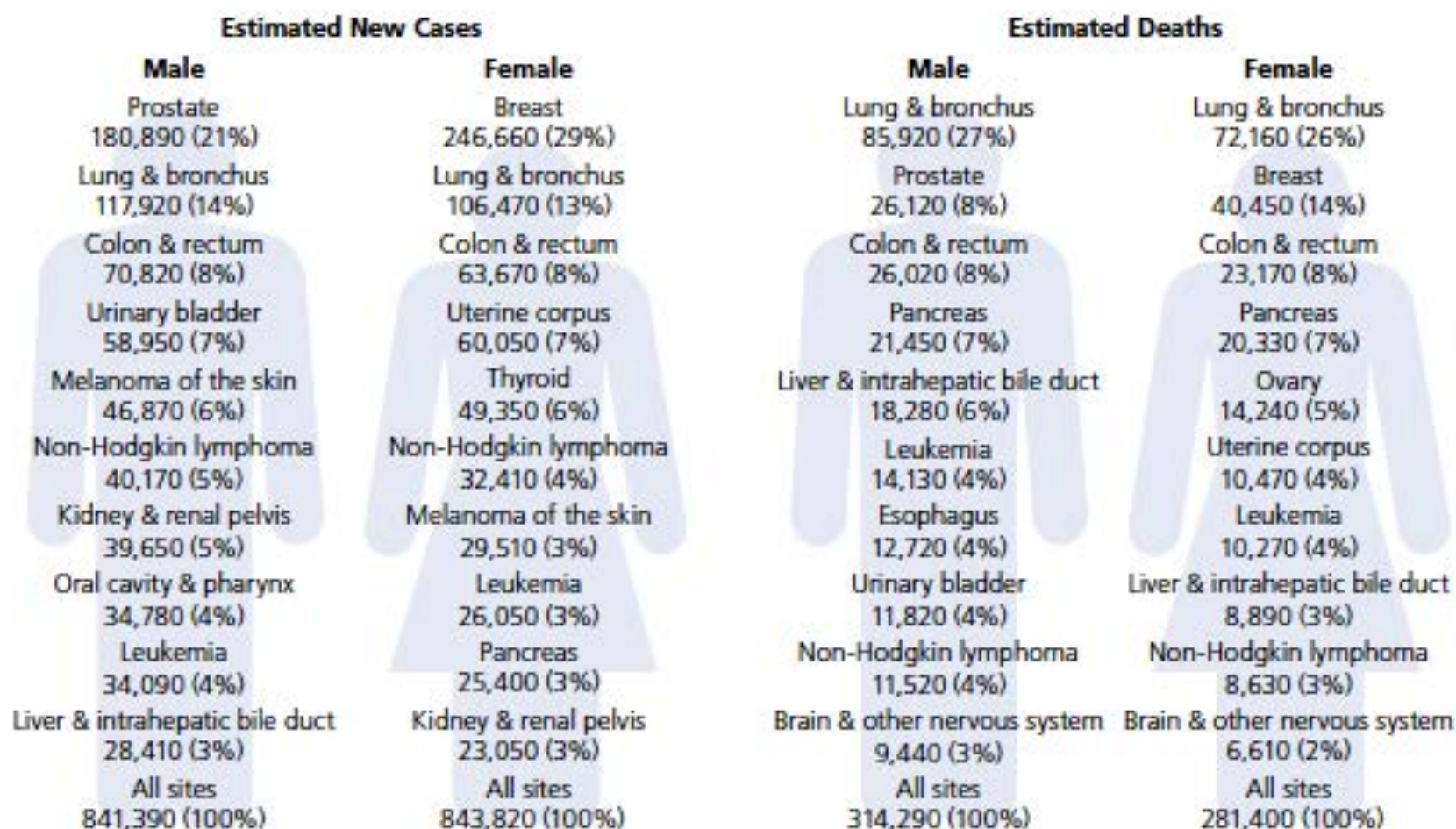
Neoplasia

- Definition - an abnormal tissue whose growth exceeds and is uncoordinated with that of adjacent normal tissue and whose growth persists after cessation of the stimuli that provoked it.

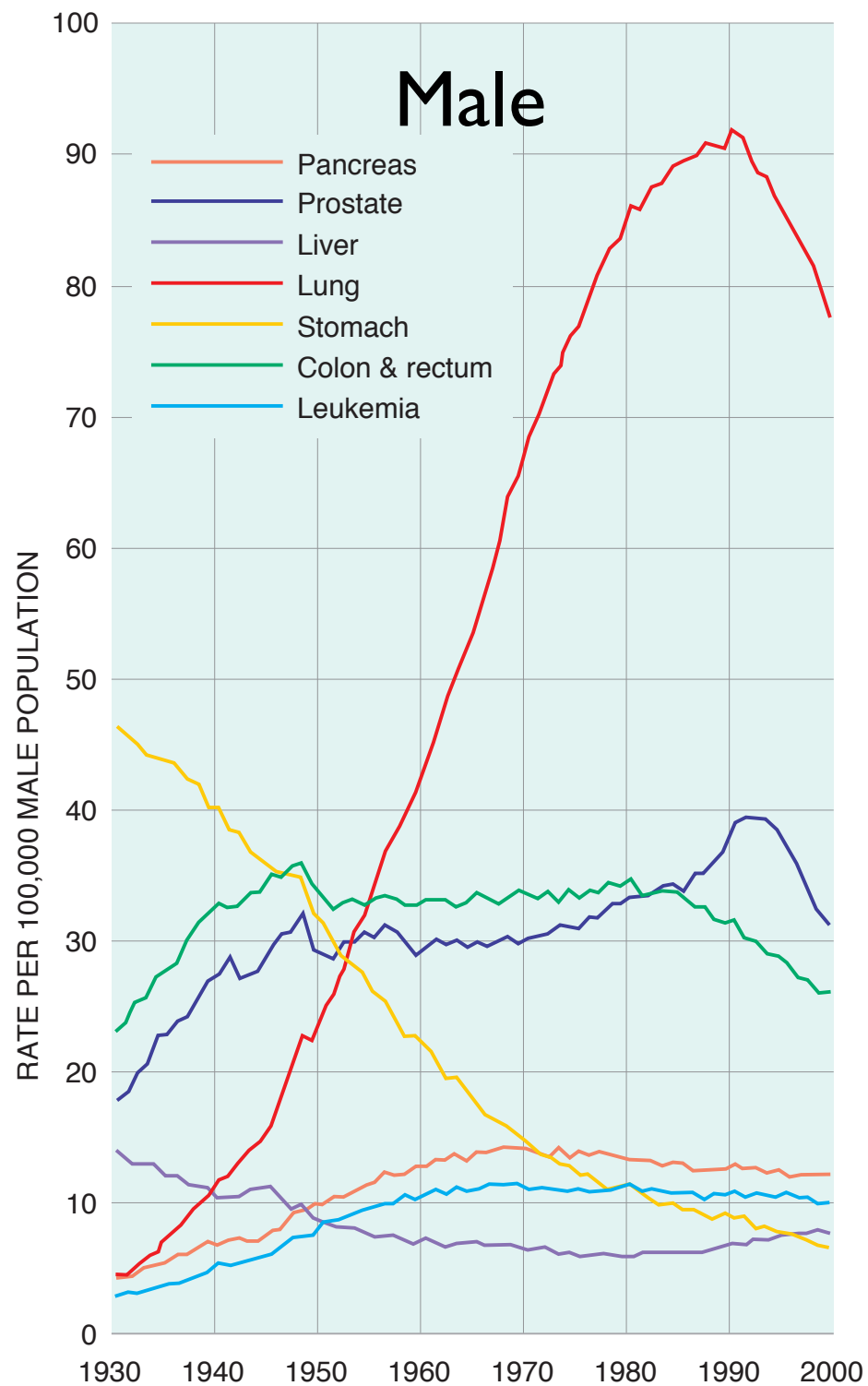
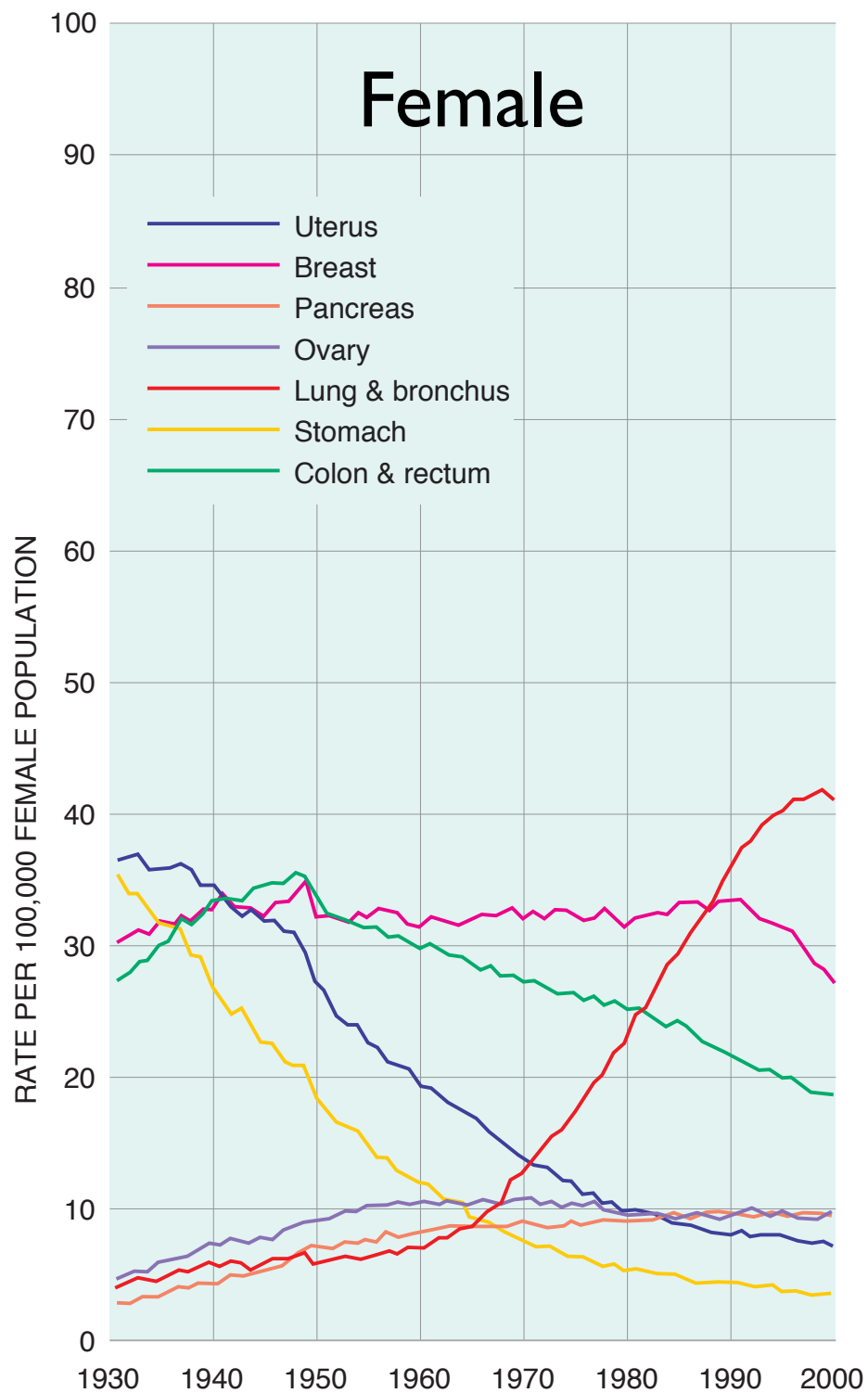
Epidemiology

- Second leading cause of death in the US in adults and children
- More than 1,685,540 estimated new cancer cases in 2016 (Female = 843,820 & Male = 841,390)
- More than 595,690 deaths in 2016 - 1 out of 4 deaths in US is due to cancer

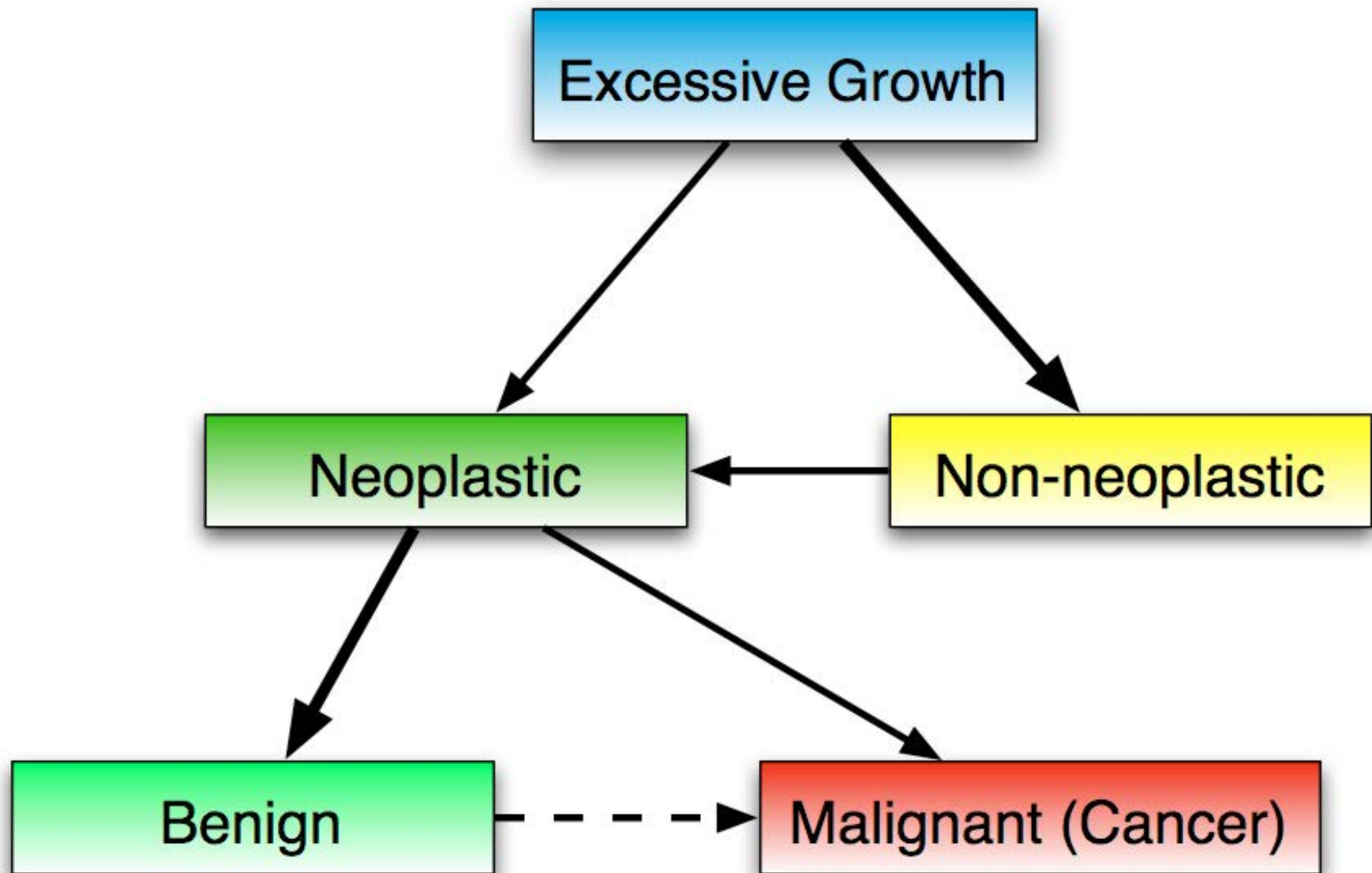
Figure 3. Leading Sites of New Cancer Cases and Deaths – 2016 Estimates



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.



Growth Disturbances



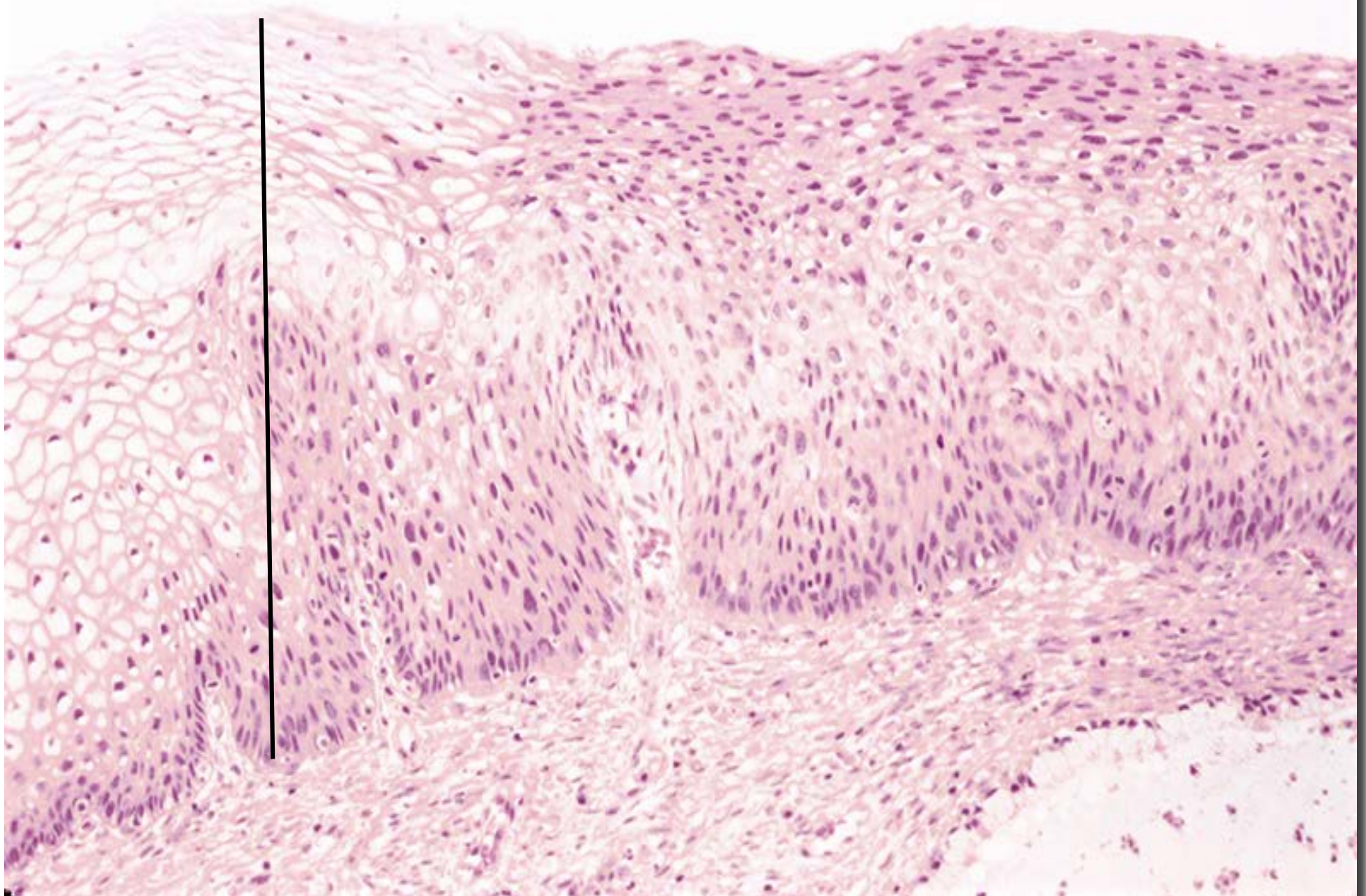
Non-Neoplastic Growth Disturbances

- Choristoma - ectopia, heterotopia
- Hamartoma - focal overgrowth of normal tissue
- Hyperplasia
- Hypertrophy
- Metaplasia
- Dysplasia - a type of dysfunctional proliferation

Cervix

Normal

Dysplasia



Nomenclature

- Benign

- “-oma”

- Examples: adenoma, squamous papilloma, lipoma, leiomyoma

- Malignant

- “carcinoma” - epithelial tissues

- Examples: adenocarcinoma, squamous cell carcinoma

- “sarcoma” - nonepithelial tissues

- Examples: fibrosarcoma, liposarcoma

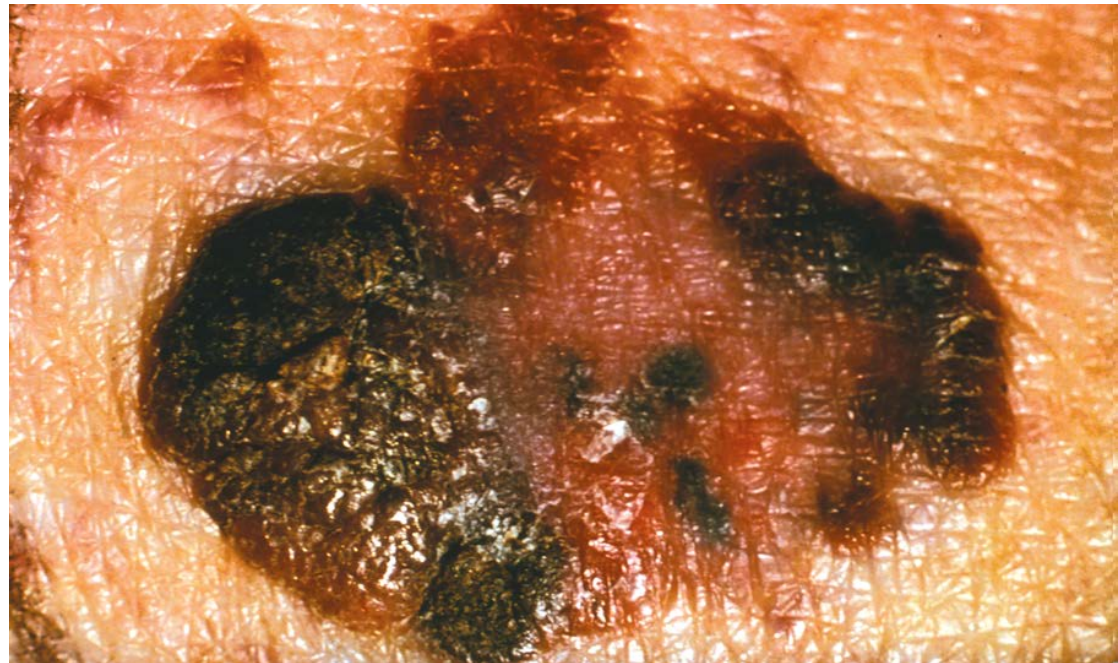
Nomenclature of Neoplasia

Germ Layer	Tissue	Cells	Benign	Malignant
Ectoderm	skin	squamous	squamous papilloma	squamous cell carcinoma
	basal	hair follicle		basal cell carcinoma
		melanocyte	nevus	malignant melanoma
	neural	glia		malignant gliomas
	neurons		ganglioneuroma	
Endoderm	gut	mucosa	adenomatous polyp	adenocarcinoma
	liver	hepatocyte	hepatic adenoma	hepatocellular carcinoma
	lung	epithelium		adenocarcinoma, squamous cell carcinoma
Mesoderm	fat	adipocyte	lipoma	liposarcoma
	bone	osteocyte	osteoma	osteosarcoma
	vessels	endothelium	angioma	angiosarcoma
	muscle	skeletal	rhabdoma	rhabdosarcoma
		smooth	leiomyoma	leiomyosarcoma
	lymphoid	lymphocyte		lymphoma
	blood marrow	lymphocyte		lymphocytic leukemia
		neutrophils		myelocytic leukemia
	kidney	tubules	tubular adenoma	renal cell carcinoma

Nevus (“birthmark”)



Malignant Melanoma



Important Generalizations

- 90% of all malignant tumors are carcinomas
- Leukemias and lymphomas are the most common forms of sarcoma
- Majority of benign tumors do not progress to malignancy

Benign Neoplasms

- Gross features
 - Expansile (compress adjacent tissue)
 - Encapsulated
 - Well-differentiated
 - Slow rate of growth (years)
 - Non-invasive
 - Never metastasize

Adenomatous Polyp



Adenomatous Polyp



Benign Neoplasms

- Microscopic features

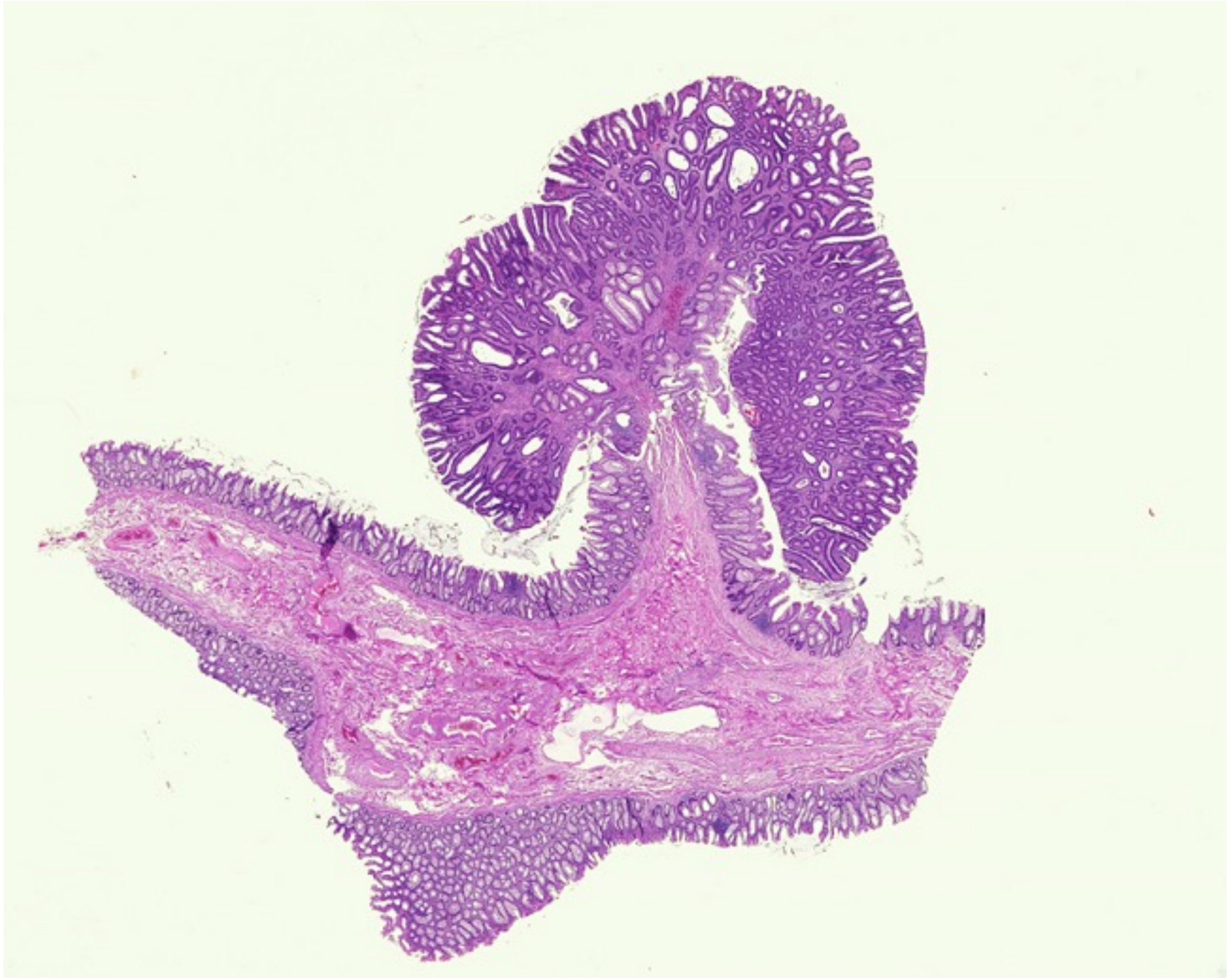
- Architecture

- Well circumscribed, encapsulated and expansile growth, no invasion

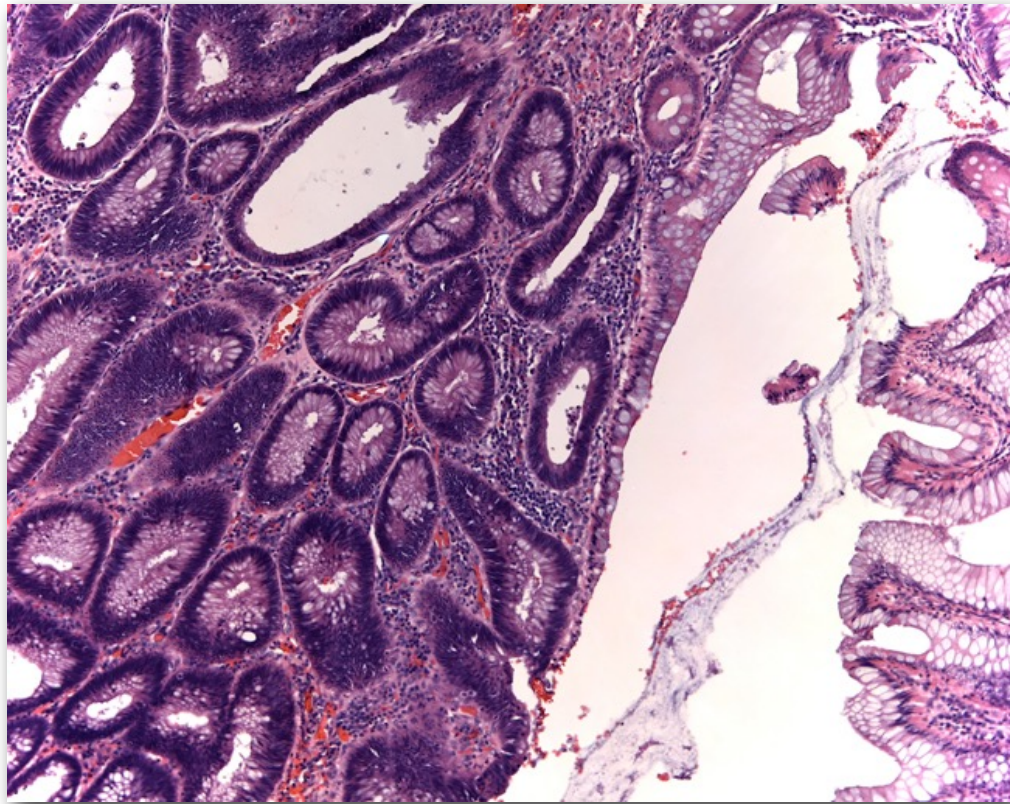
- Cytologic

- Close resemblance to its normal counterpart and usually diploid

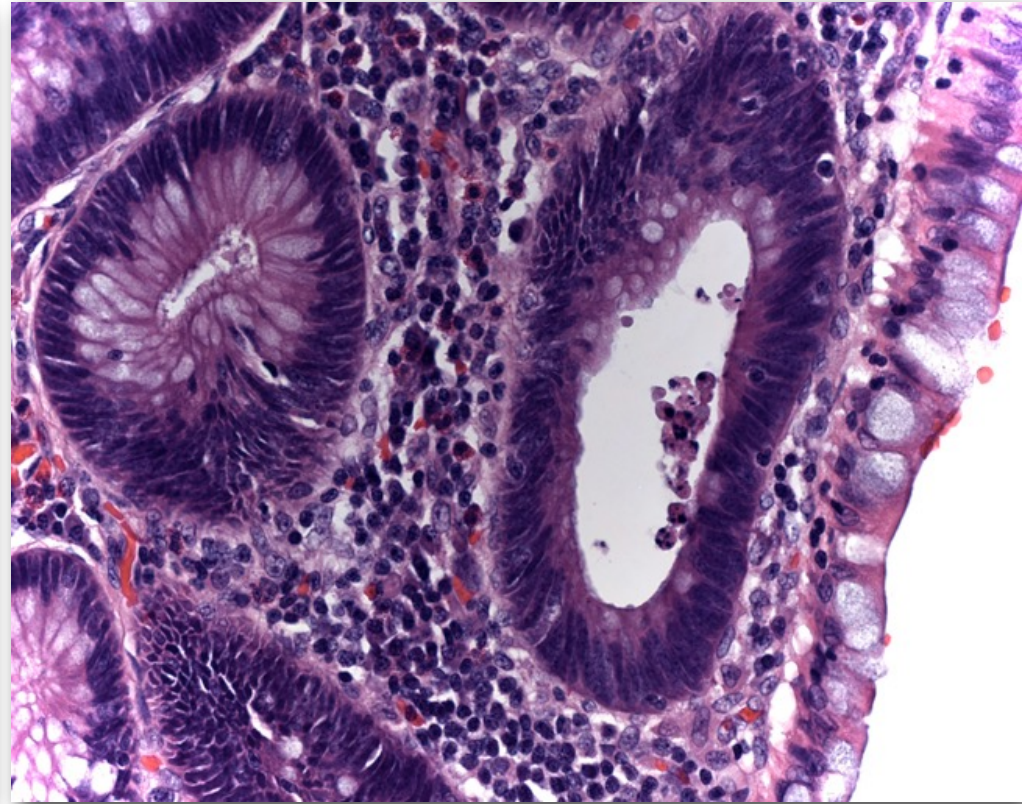
Colonic Adenomatous Polyp



Colonic Adenomatous Polyp



Medium Magnification



High Magnification

Malignant Neoplasms

- Gross features
 - Infiltrative
 - Necrosis
 - Hemorrhage
 - Rapid rate of growth (days to months)
 - Invasive
 - Metastasize

Invasive Colonic Adneocarconoma



Invasive Colonic Adneocarcinoma



Invasive Colonic Adneocarconoma



Malignant Neoplasms

- Microscopic features

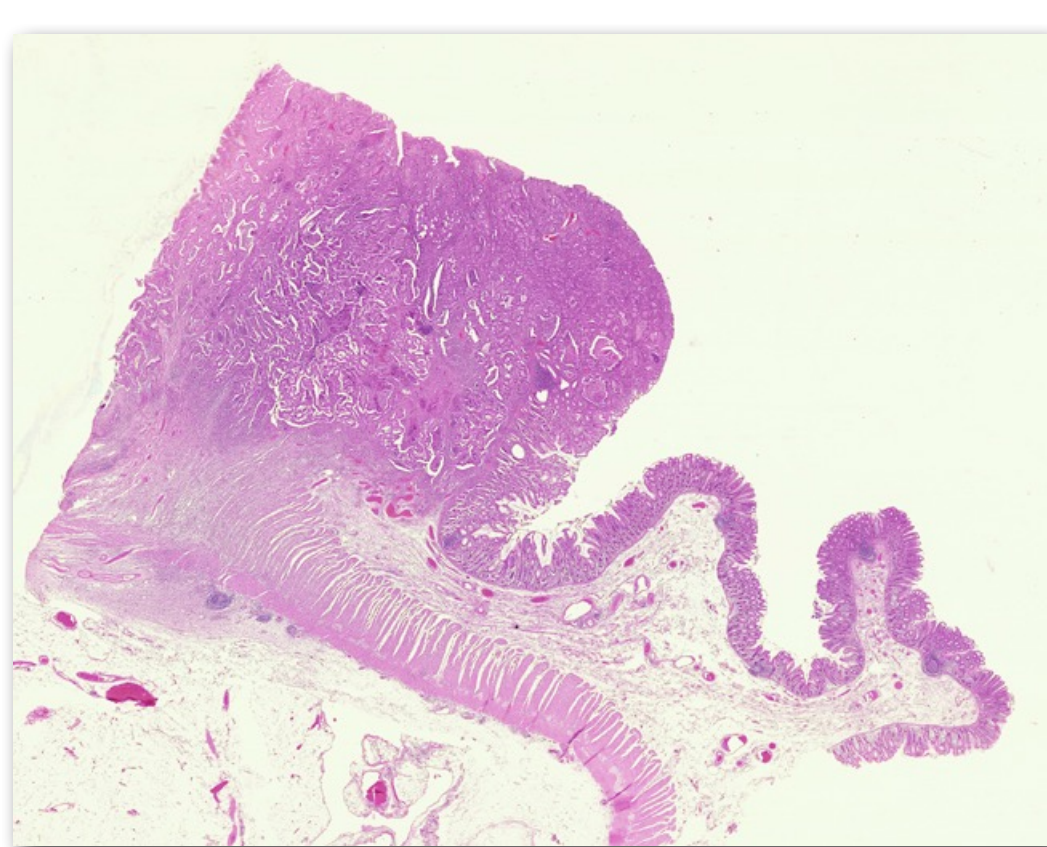
- Architecture

- Infiltrative, invasive, necrosis and destruction to normal architecture

- Cytologic

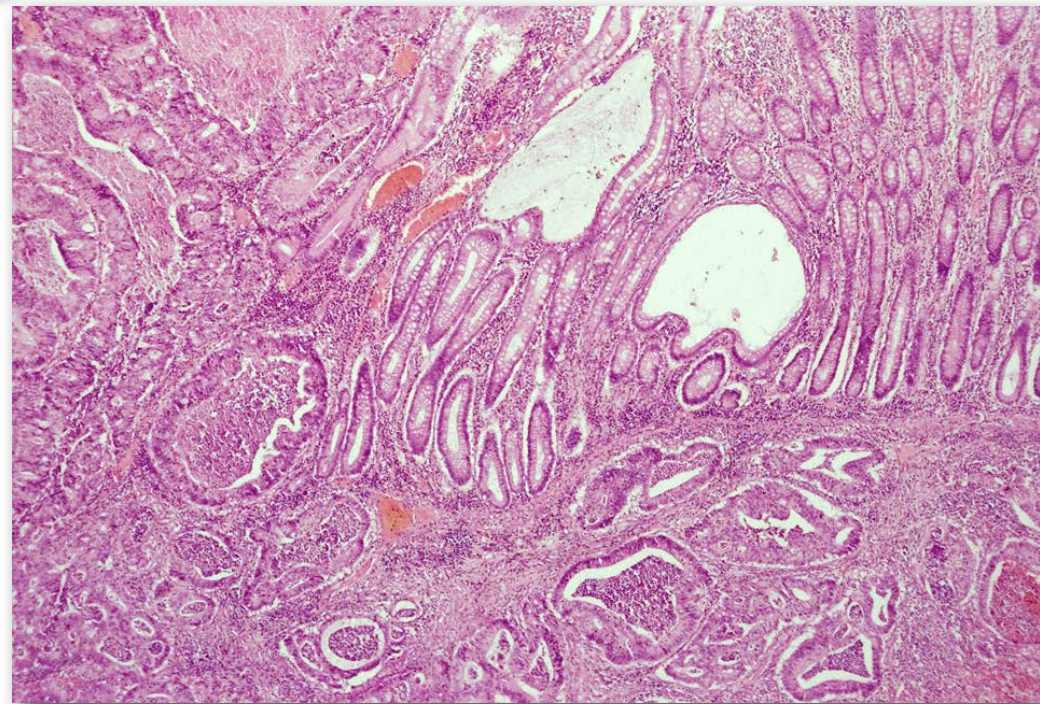
- Discohesion, pleomorphism, anaplasia, loss of polarity, increased nucleus/cytoplasm ratio, hyperchromasia, prominent nucleoli, tumor giant cells, increased or abnormal mitotic figures

Invasive Colonic Adenocarcinoma

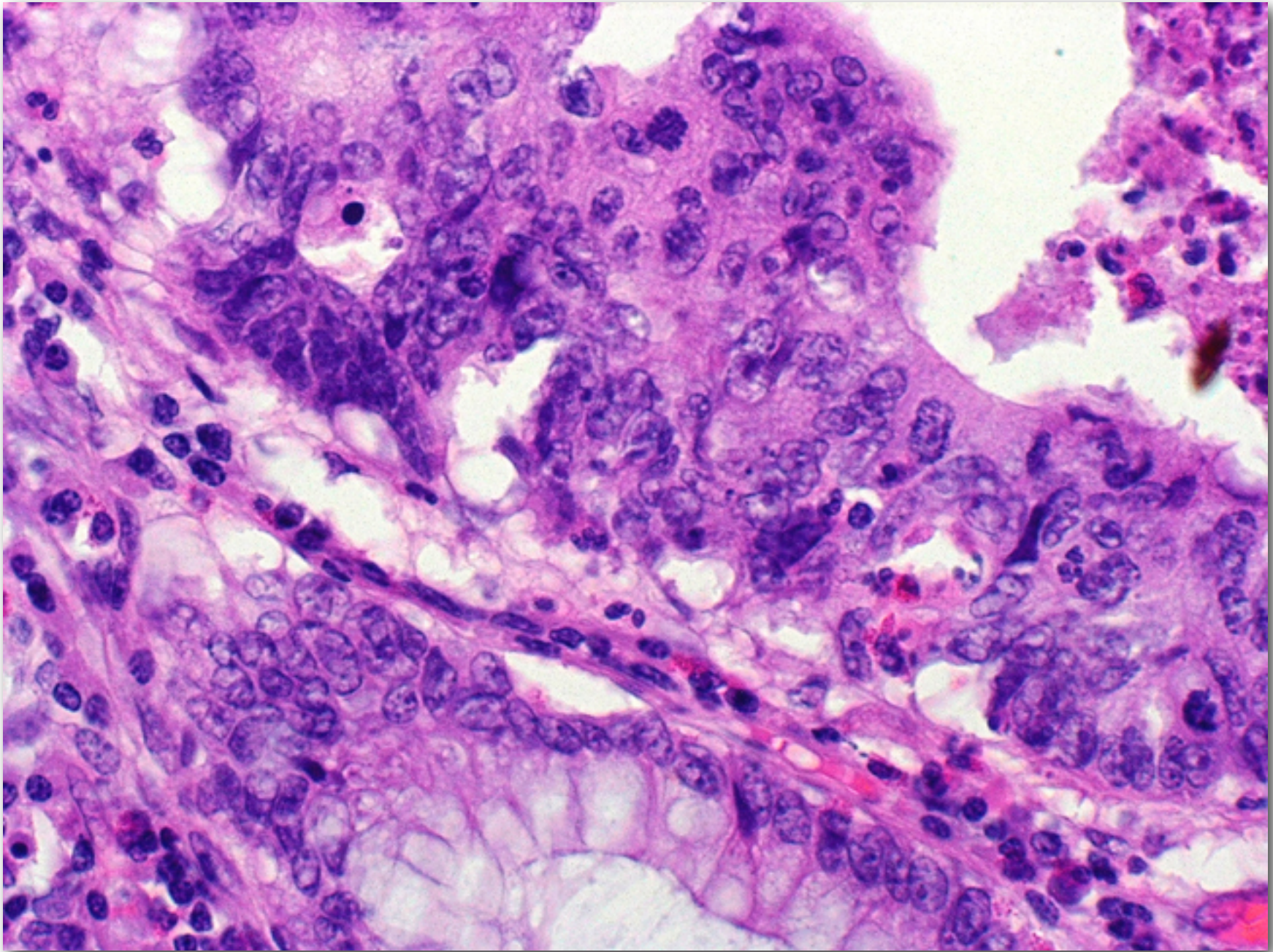


Low Magnification

Medium Magnification



Invasive Colonic Adenocarcinoma



High Magnification

Malignant Neoplasms

- Invasion
- Mechanism
 - Degradation of extracellular matrix by collagenases, plasmin and other proteolytic

Carcinoma-in-situ

vs.

Invasive Carcinoma

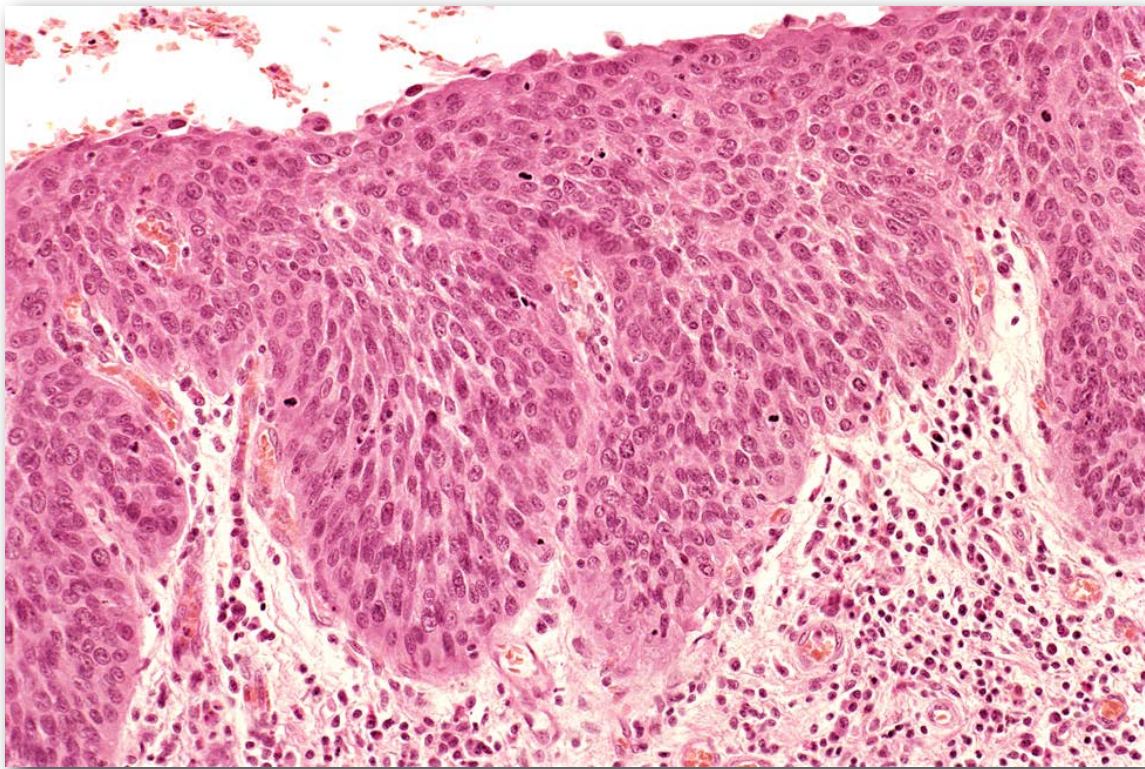
No invasion

Involves surrounding tissue

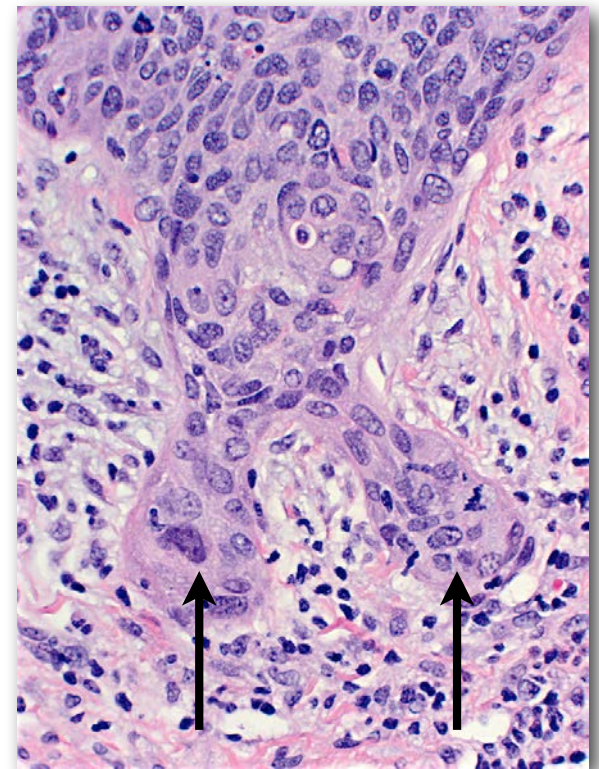
Limited to epithelial cells
above the basement membrane

Extends beyond the basement
membrane

Carcinoma-In-Situ



Microinvasion



Metastasis

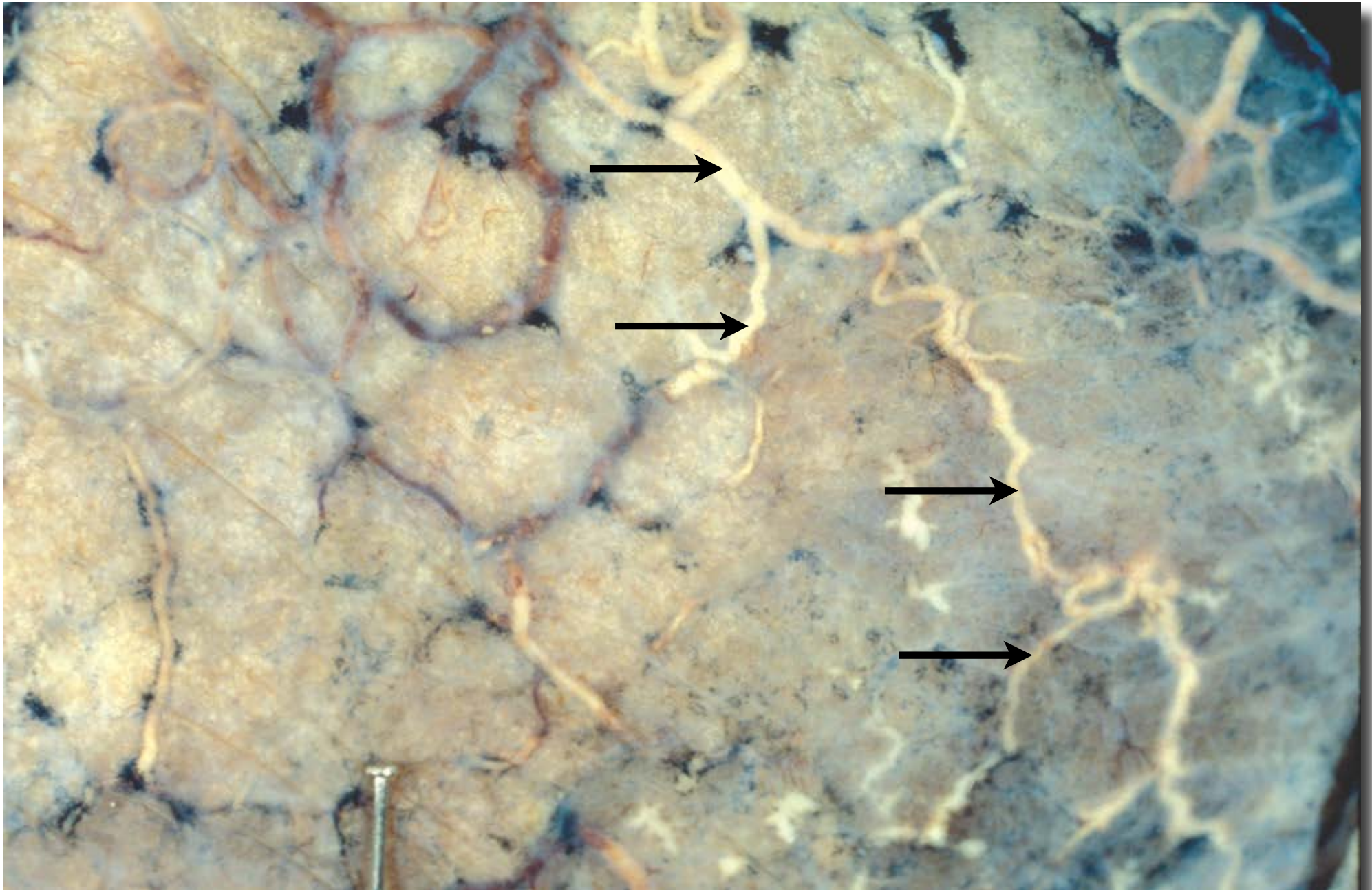
● Definition

- The process by which malignant cells migrate from the site of origin of the neoplasm to other site(s) in the body, where they resume growth and form new malignant lesions called metastases

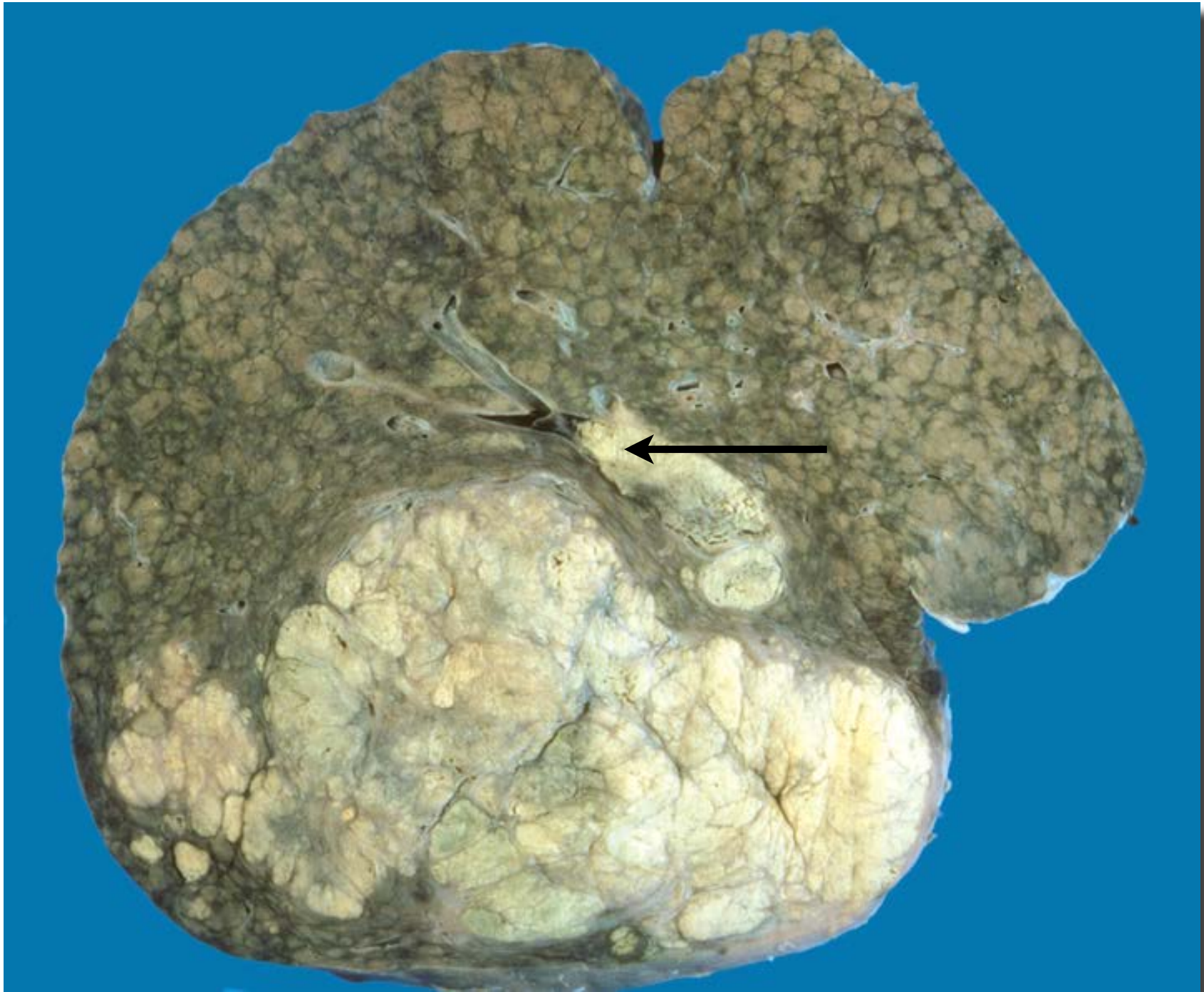
● Pathways of Spread

- Lymphatic spread
- Hematogenous spread
- Seeding of body cavities

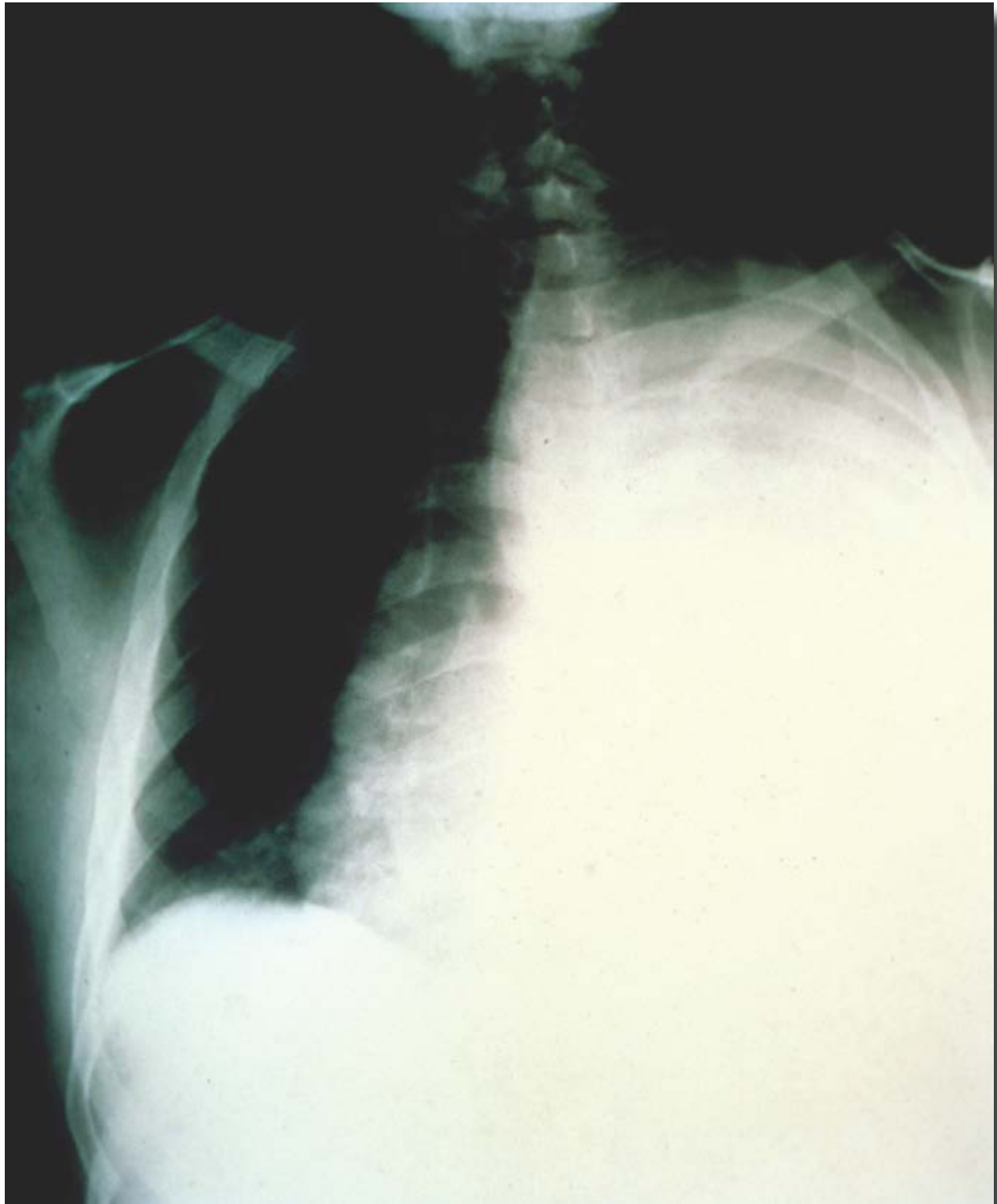
Lymphatic Spread: Pulmonary Squamous Cell Carcinoma



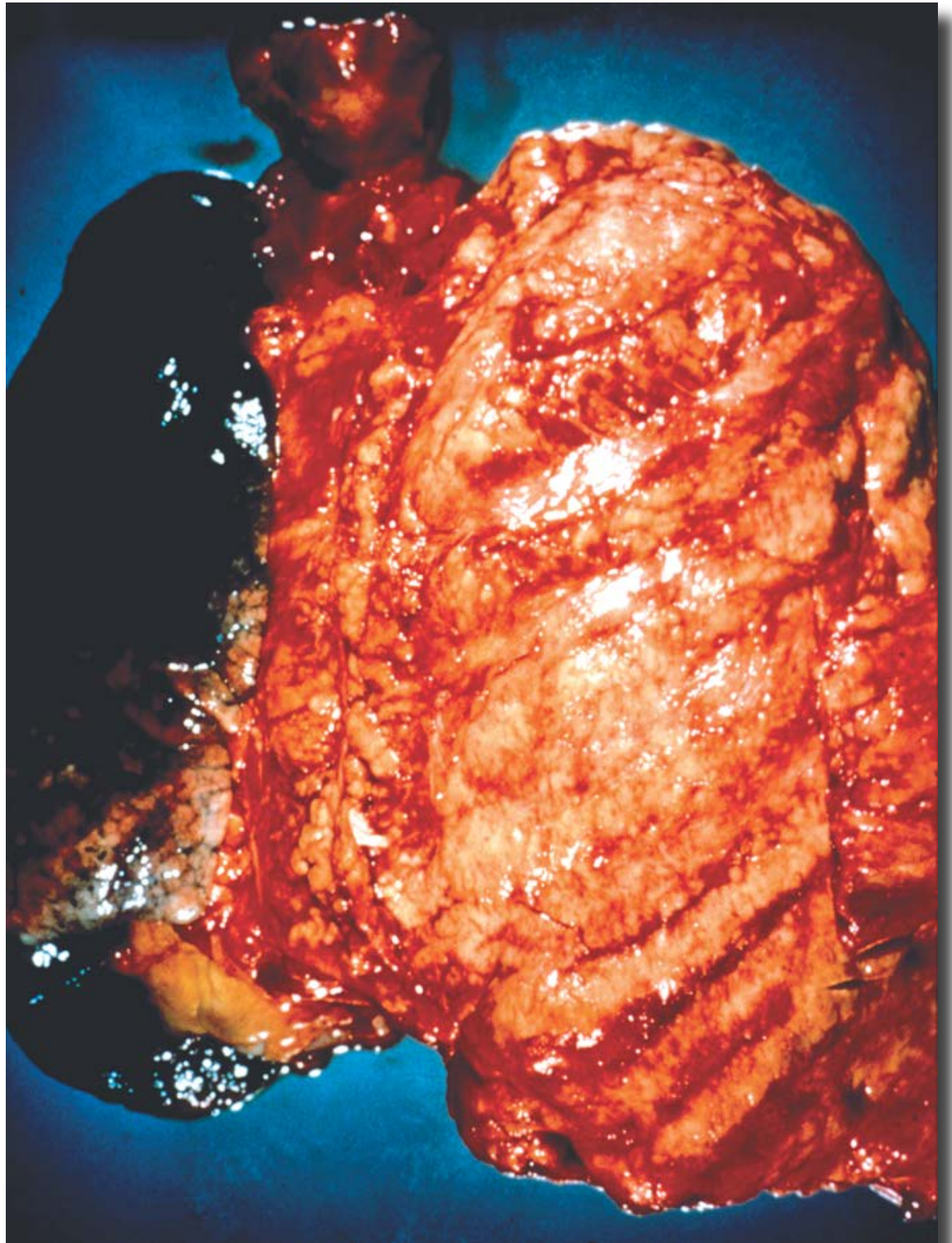
Hematogenous spread: Hepatocellular Carcinoma



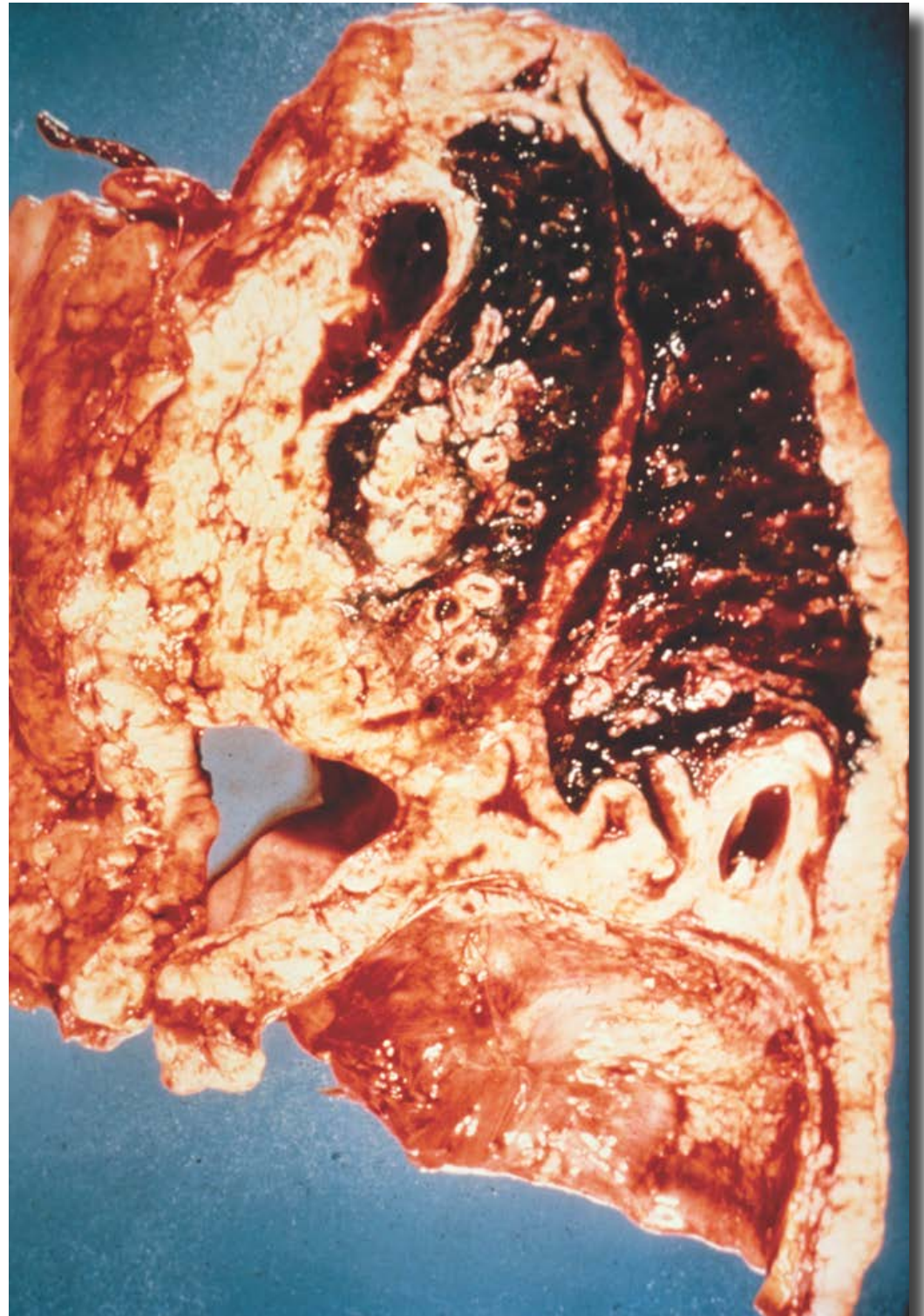
Seeding of body cavity:
Pulmonary Adenocarcinoma



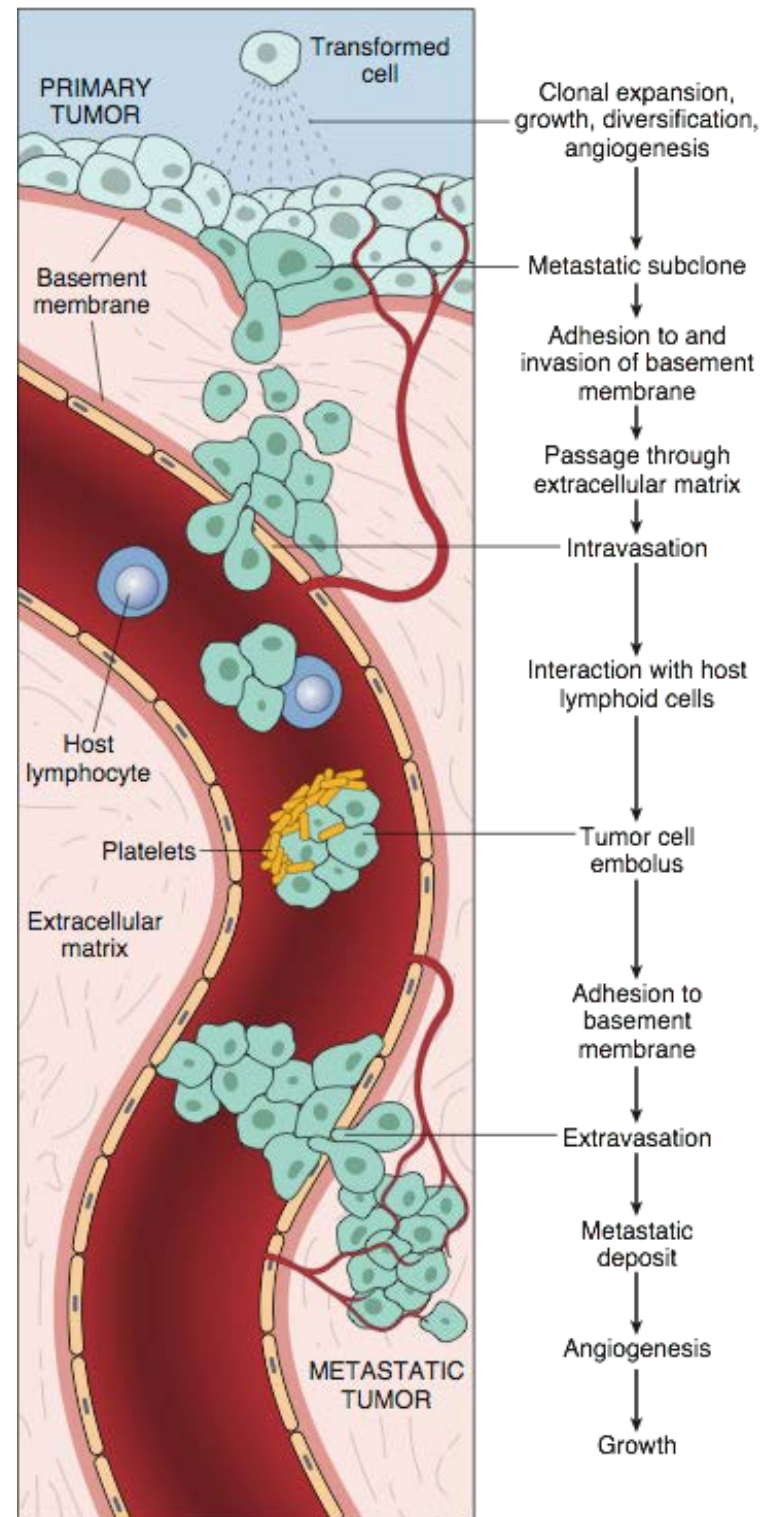
Seeding of body cavity:
Pulmonary Adenocarcinoma



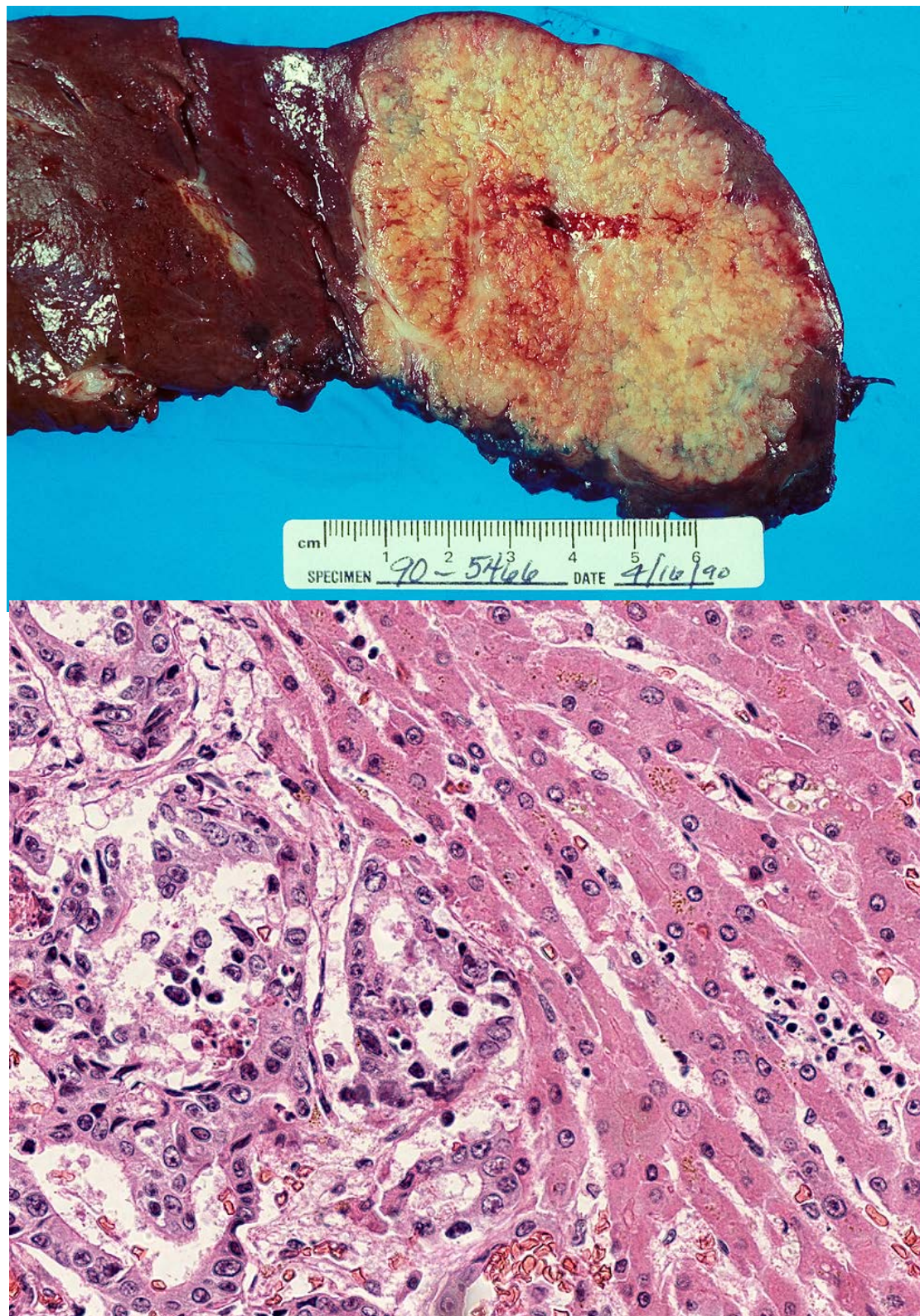
Seeding of body cavity:
Pulmonary Adenocarcinoma



Mechanism of Metastasis



Metastatic Colonic Adenocarcinoma

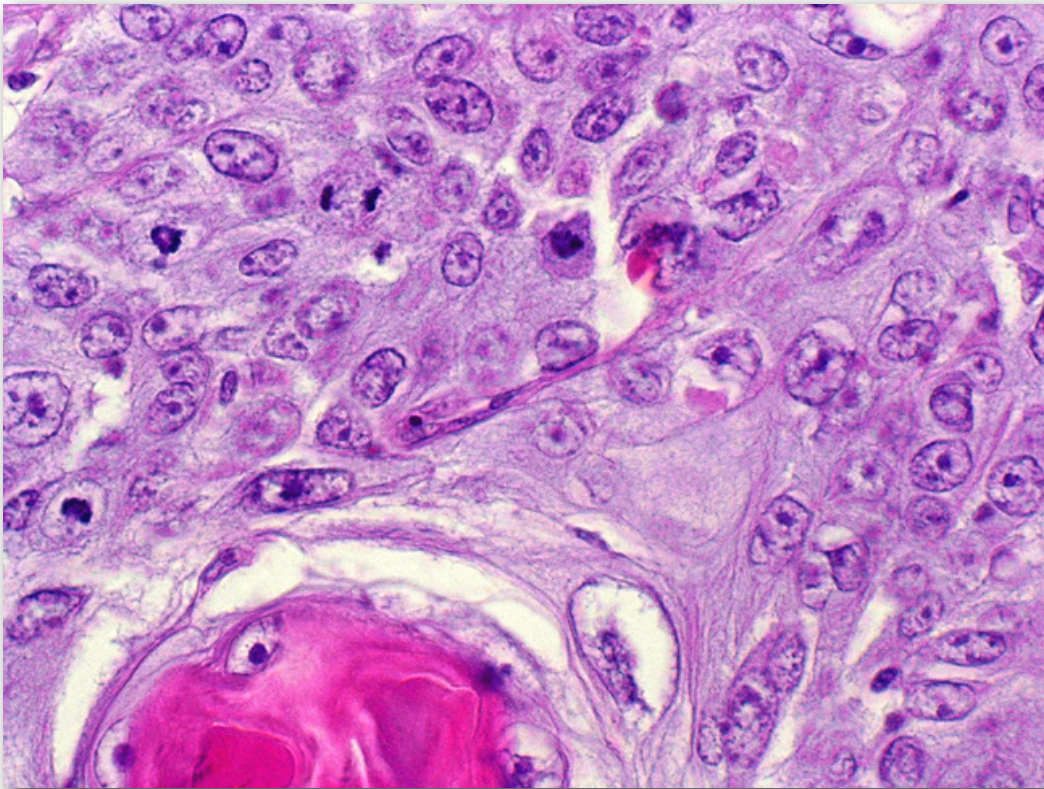


Grade and Stage of Malignant Neoplasms

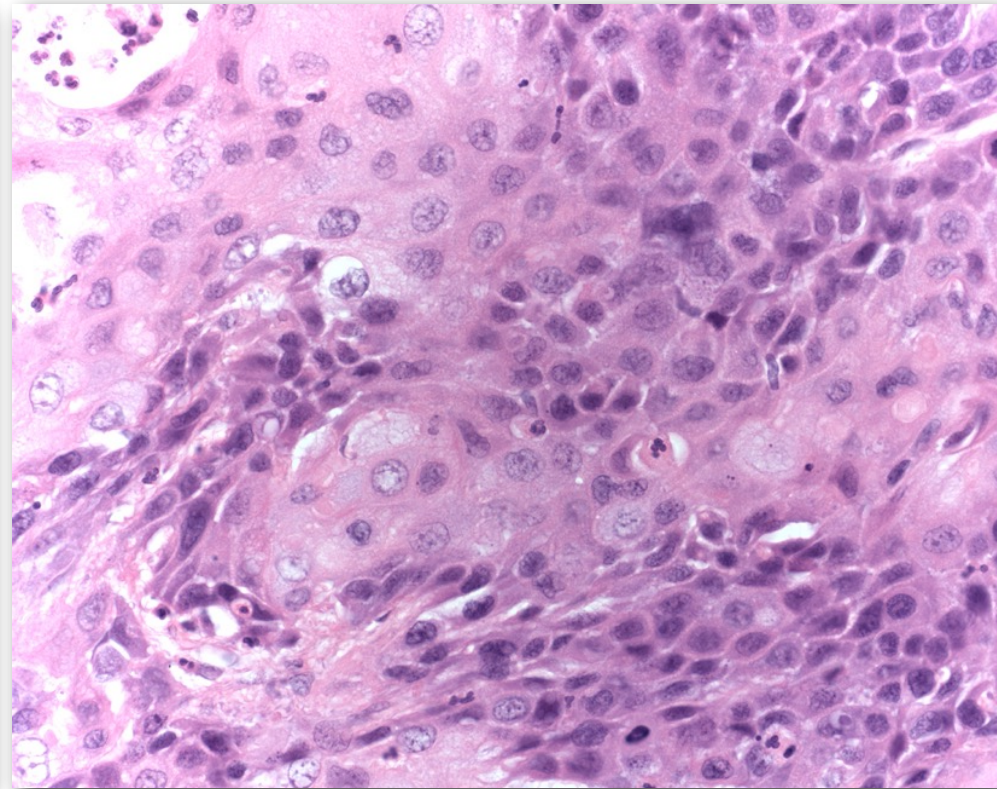
● Definitions

- Grade - the degree of anaplasia of a particular lesion; extent of cytologic abnormality
 - “Low-grade” = well-differentiated
 - “High-grade” = poorly-differentiated (anaplastic)
- Stage - based on the size of the primary lesion, its extent of spread to regional lymph nodes, and the absence or presence of blood-borne metastasis (TNM system)

Squamous Cell Carcinoma



Well-differentiated



Poorly-differentiated

Tumor Progression

- Definition

- Tendency of malignant/neoplastic cells to evolve over time by changing their biological behavior (e.g., rapid growth and metastasis) and phenotype (e.g., increased anaplasia)

- Dependent upon two factors

- Natural selection - evolution of a more malignant clone over time due to a selective growth advantage
- Genetic instability - malignant cells are more prone to mutate and accumulate additional genetic defects

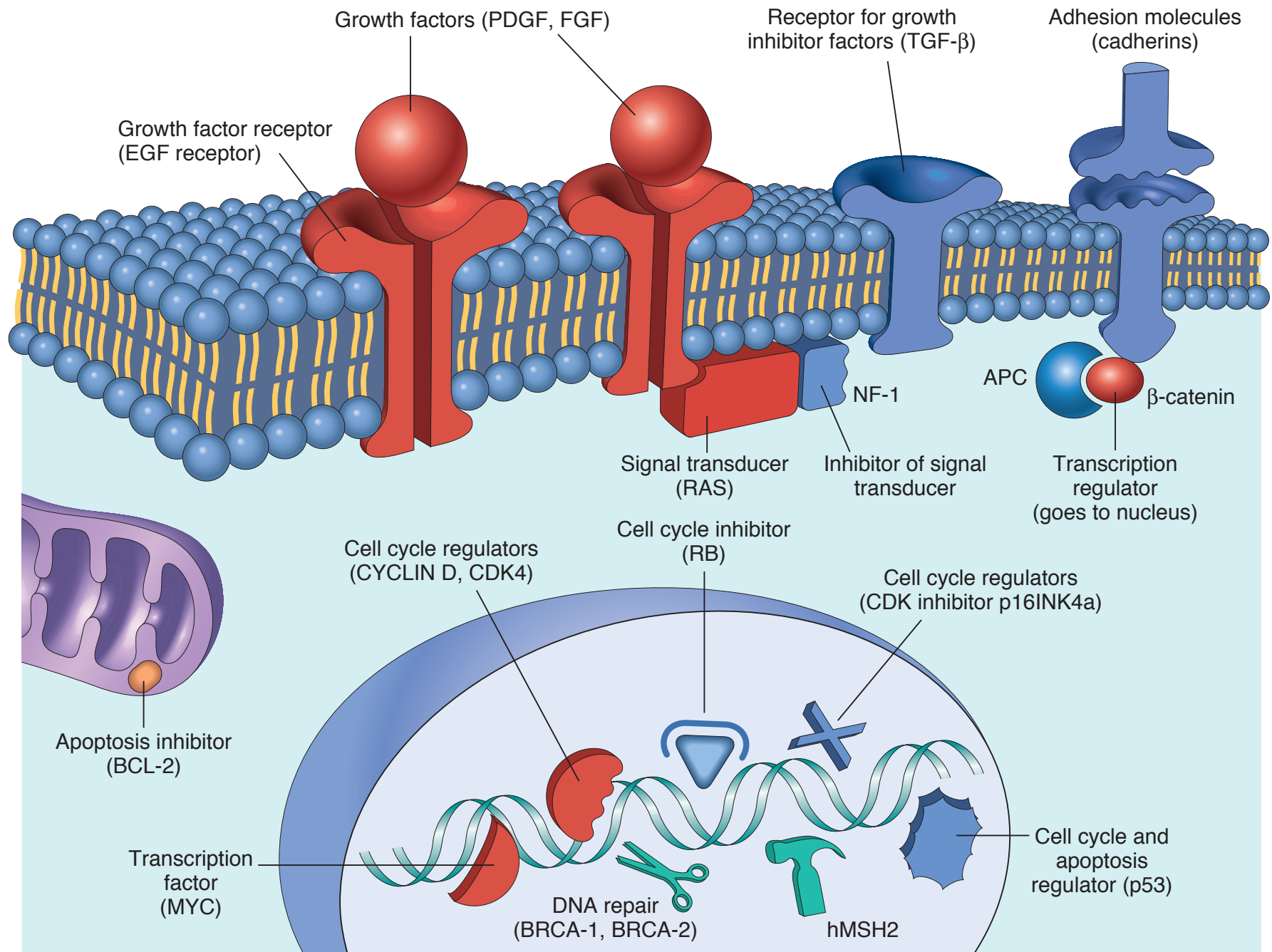
Complications of Cancer

- Mass effects (e.g., right-sided colonic adenocarcinoma)
- Pain (e.g., gastric carcinoma)
- Pathologic fractures (e.g., metastatic colon cancer)
- Infection (e.g., opportunistic infections)
- Anemia (e.g., anemia of chronic disease)
- Fever (e.g., Hodgkin lymphoma)
- Jaundice (e.g., carcinoma of the head of the pancreas)
- Obstruction of viscera (e.g., invasive esophageal cancer)
- Cachexia - general wasting (e.g., many malignant tumors)

Tumor Progression

- A multistep process involving genes that control cell proliferation and death
- Mutations in Two Broad Categories
 - Proto-oncogenes - promote cell proliferation or survival - growth factor receptor, intracellular signaling molecules, etc.
 - Tumor suppressor genes - promote cell death, inhibit cell growth, invasion, or other aspects of the malignant phenotype - apoptosis, etc.
- In general, multiple different mutations must occur in a cell to become malignant

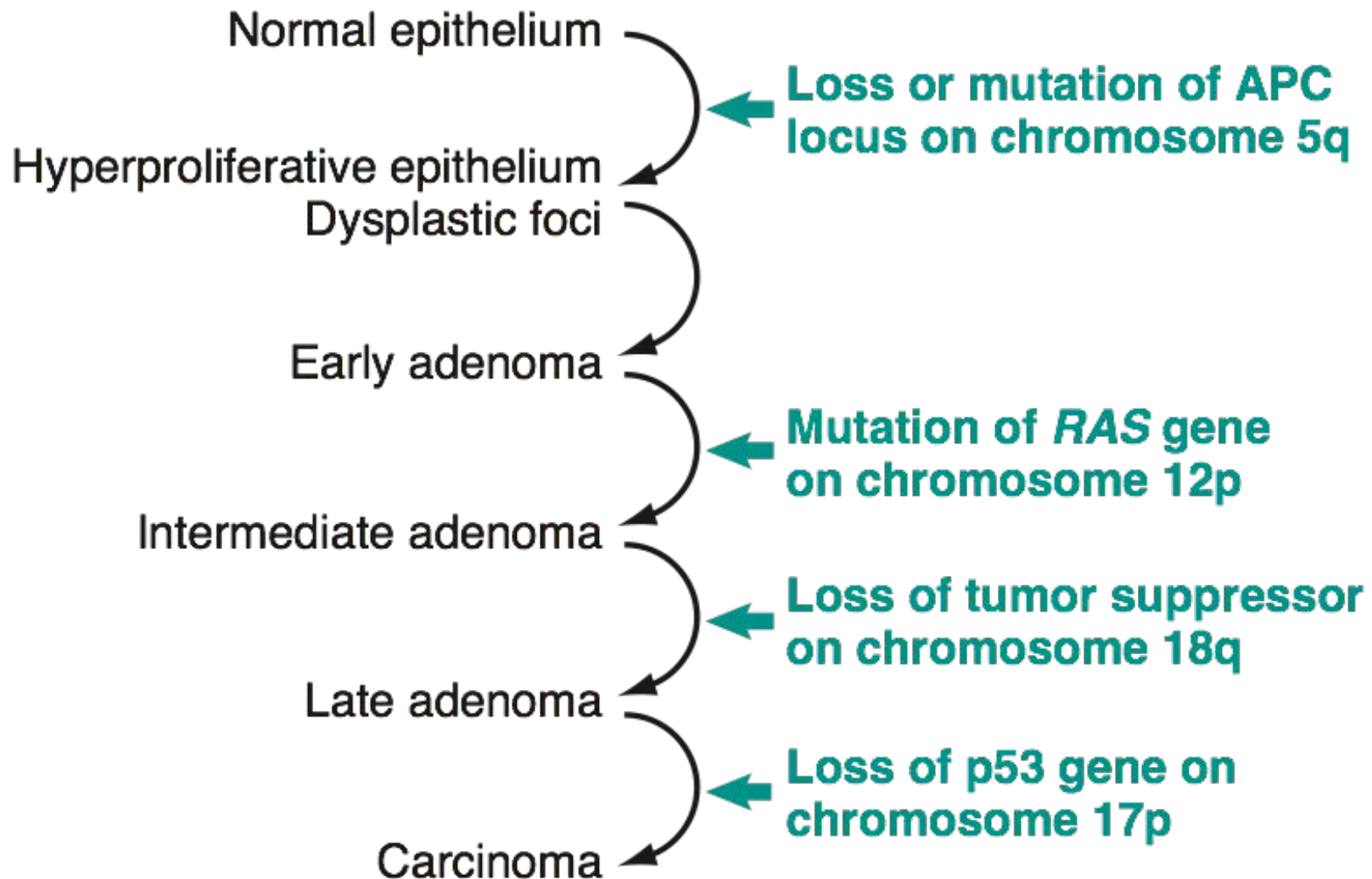
Proto-oncogenes and Tumor Suppressor Genes



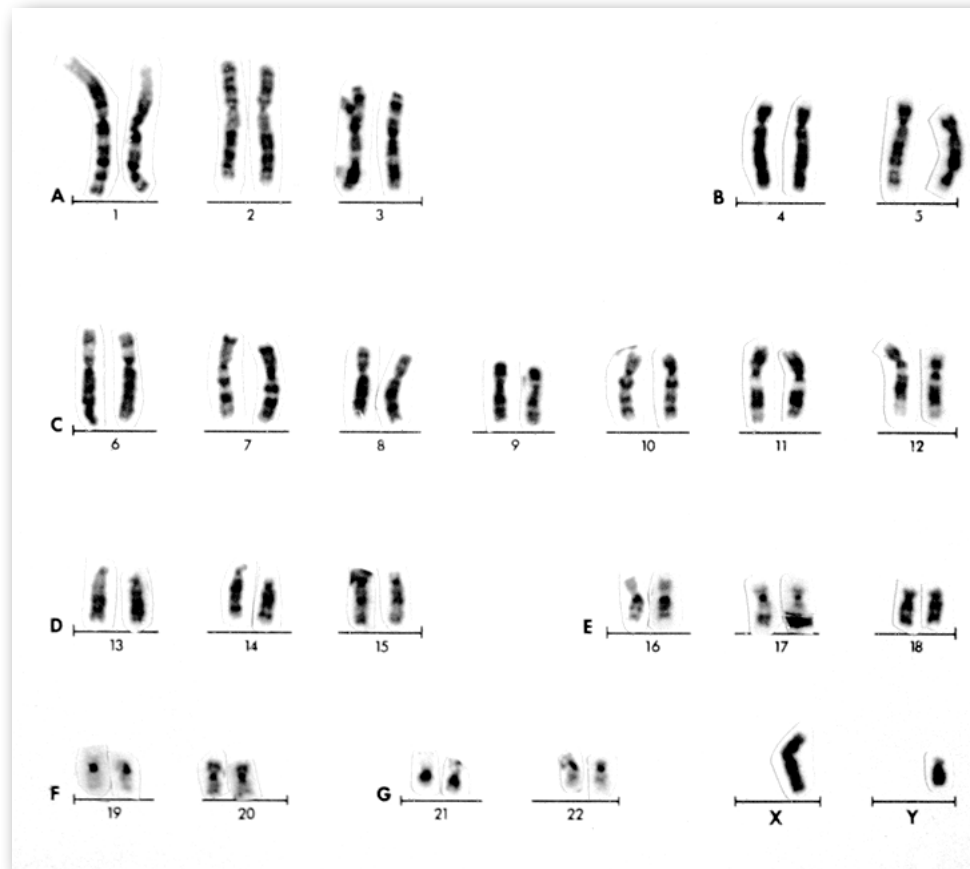
Tumor Progression for Colon Adenocarcinoma

MORPHOLOGIC APPEARANCE

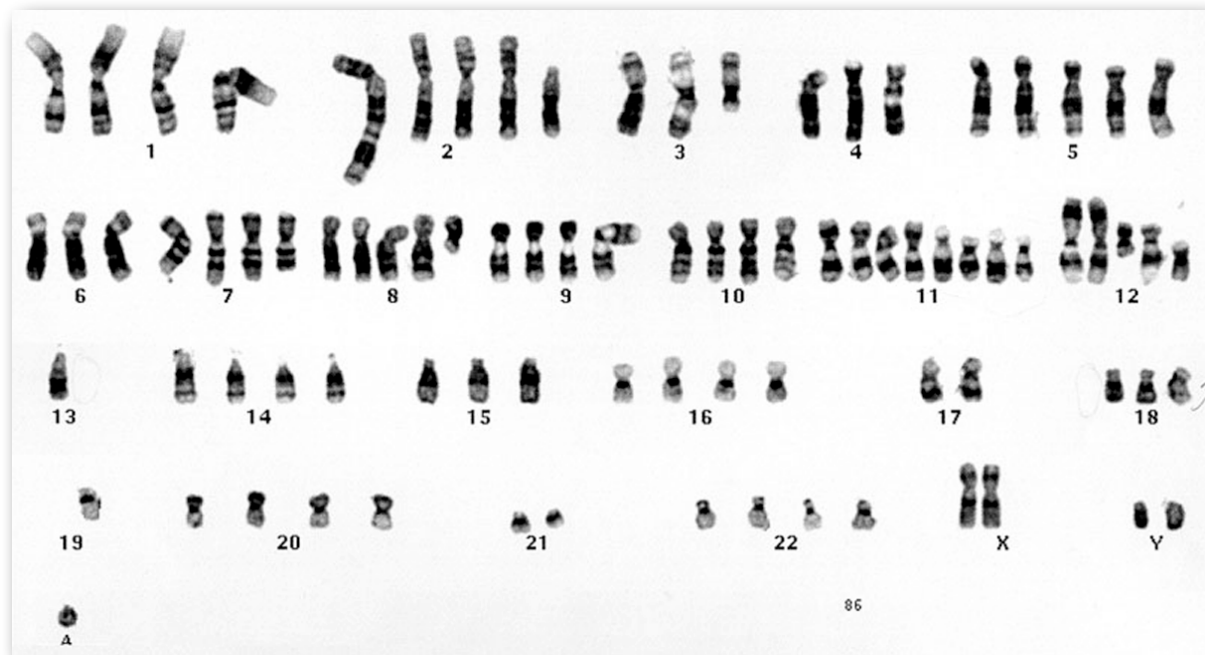
MOLECULAR CHANGE



Normal Karyotype



Malignant Karyotype



Years



Diagnosis of Malignancy

- Diagnosis of cancer absolutely requires microscopic evaluation of the lesion (tissue diagnosis) or individual cells (cytologic diagnosis) by a trained pathologist
- Diagnostic features of malignancy
 - Metastasis
 - Invasion of adjacent normal tissue
 - Loss of normal tissue architecture/abnormal cytologic features

Causes of Cancer

- Chemical carcinogens
- Physical carcinogens/Ionizing radiation
- Viruses
- Inflammation and cancer
- Familial gene alterations

Summary

- Neoplasia is a genetic disease
- Tumorigenesis is a multistep process
- Diagnosis of cancer is based upon unique gross and microscopic features