Neoplasia review

Neoplasia

Abnormality of cellular differentiation, maturation, and control of growth

- Rupert Willis,
- British Pathologist
- Early 1950s

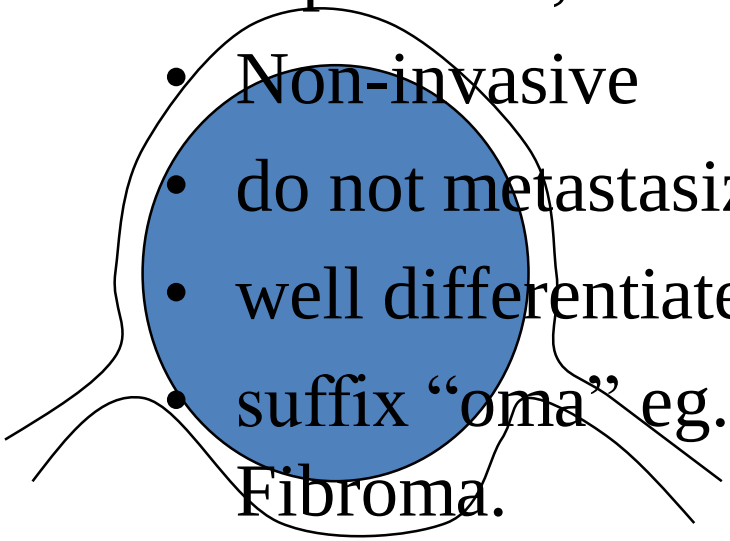
- "A neoplasm is an abnormal mass of tissue,
- The Growth Of Which Exceeds and is Uncoordinated with that of the surrounding normal tissues and
- Persists In The Same Excessive Manner After Cessation Of The Stimuli That Evoked The Change.”

Approaches to Classification of Neoplasms

Basis for Classification	Historical Aspect	Current Clinical Usefulness
Site	Egyptian embalmers, who realized that tumors of the breast, uterus, soft parts, and so forth were different from one another.	The basis for all clinical classifications; neoplasms of any given site may incude many different pathologic types.
Biologic behavior	Hippocrates recognized 2 broad groups: (1) "carcinos": innocuous, which included some inflammatory lesions and benign neoplasms; and (2) "carcinomas": dangerous, often causing death.	The distinction between benign and malignant is the most important form of clinical classification and the one on which treatment is based
Gross or microscopic features	Used throughout history to classify neoplasms; ulcerating, fungating, polypoid, gelatinous, scirrhous, medullary, etc.	Of little value

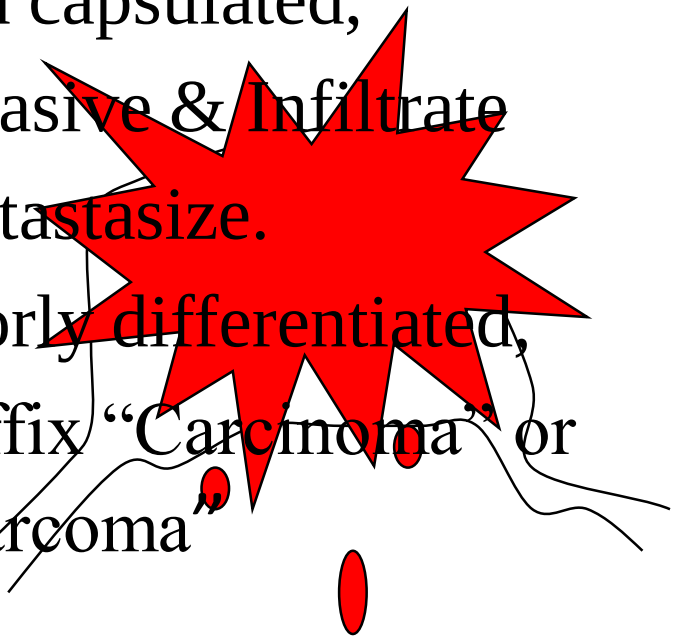
Benign

- Slow growing,
- capsulated,
- Non-invasive
- do not metastasize,
- well differentiated,
- suffix “oma” eg. Fibroma.

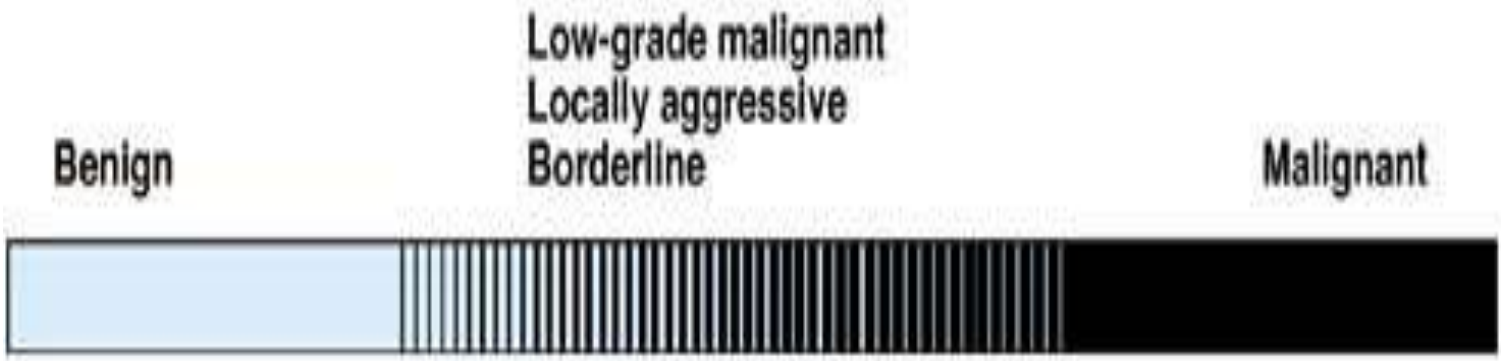


Malignant:

- Fast growing,
- non capsulated,
- Invasive & Infiltrate
- Metastasize.
- poorly differentiated,
- Suffix “Carcinoma” or “Sarcoma”



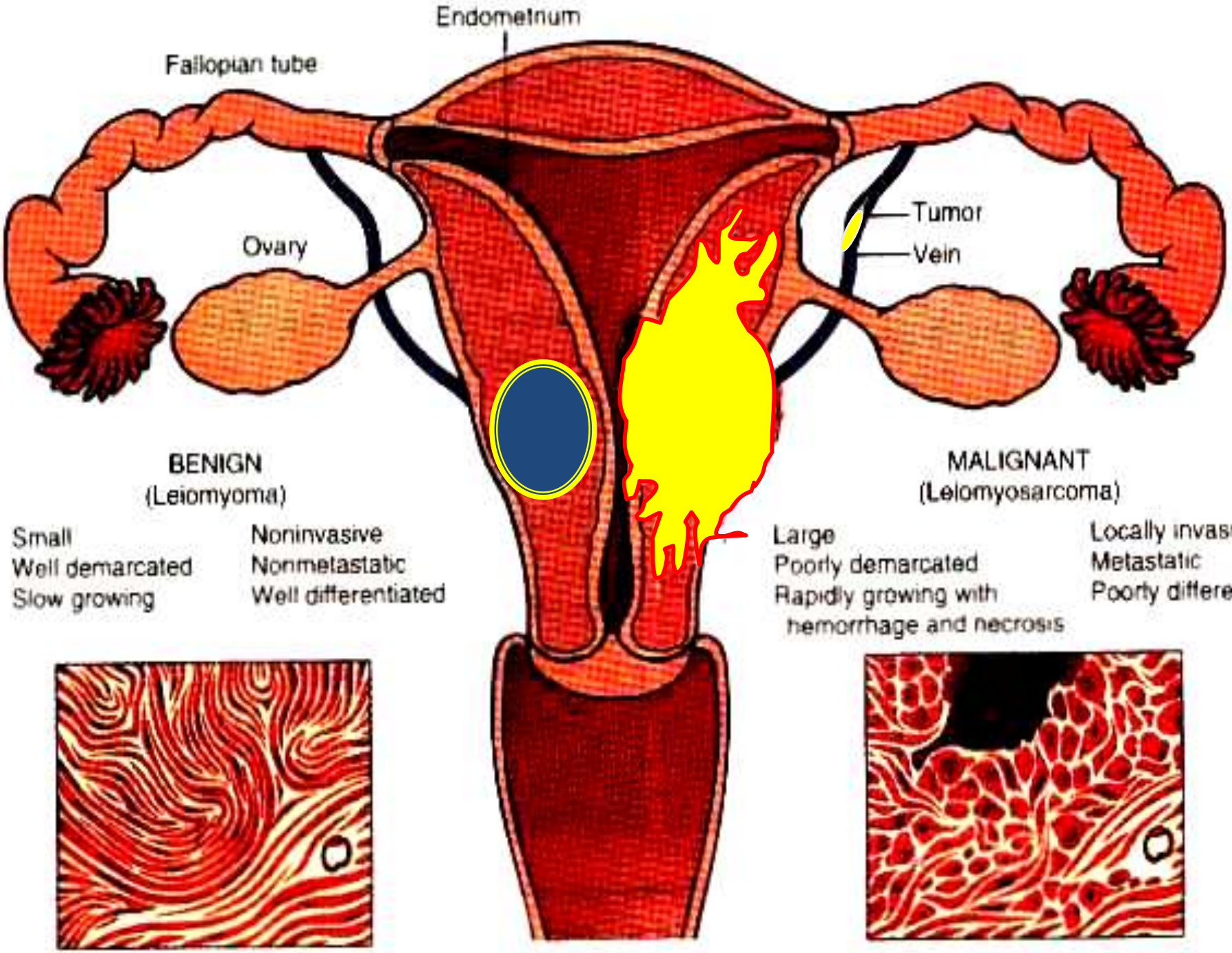
Biologic Behavior of Neoplasms
Spectrum with two extremes:



- Slow growth rate
- No infiltration
- No metastasis
- High patient survival rates after successful surgical removal

- Variable growth rate
- Locally infiltrative
- Low or no metastatic potential
- Intermediate patient survival rates; tendency for local recurrence after successful surgical removal

- Rapid growth rate
- Infiltrative
- Metastasizing
- Poor patient survival rates; tendency for local and distant recurrence (metastasis)


Endometrium
Fallopian tube
Ovary
Tumor
Vein
BENIGN
(Leiomyoma)
Small
Well demarcated
Slow growing
Noninvasive
Nonmetastatic
Well differentiated
MALIGNANT
(Leiomyosarcoma)
Large
Poorly demarcated
Rapidly growing with hemorrhage and necrosis
Locally invasive
Metastatic
Poorly differentiate

Summary of Features Differentiating Benign and Malignant Neoplasms

Benign	Malignant
Gross features	
Smooth surface with a fibrotic capsule; compressed surrounding tissues.	Irregular surface without encapsulation; destruction of surrounding tissues.
Small to large, sometimes very large.	Small to large.
Slow rate of growth.	Rapid rate of growth.
Rarely fatal (except in central nervous system) even if untreated.	Usually fatal if untreated.

Microscopic features	
Growth by compression of surrounding tissue.	Growth by invasion of surrounding tissue.
Highly differentiated, resembling normal tissue of origin microscopically.	Well or poorly differentiated. Most malignant neoplasms do not resemble the normal tissue of origin (anaplasia).
Cells similar to normal and resembling one another, presenting a uniform appearance.	Cytologic abnormalities,including enlarged, hyperchromatic, irregular nuclei with large nucleoli; marked variation in size and shape of cells (pleomorphism).
Few mitotic figures; those present are normal.	Increased miotic activity; abnormal, bizarre mitotic figures often present.

Well–formed blood vessels.	Blood vessels numerous and poorly formed; some lack endothelial lining.
Necrosis unusual; other degenerative changes may be present.	Necrosis and hemorrhage common.
Distant spread (metastasis) does not occur.	Metastasis to distant sites.
Investigative techniques	
DNA content usually normal.	DNA content of cells increased, additional chromosomes commonly present.
Karyotype usually normal.	Aneuploidy, polyploidy, clonal genetic abnormalities.

Before I got married I had six theories about raising children; now, I have six children and no theories.

JOHN WILMOT

Benign

- Rarely life-threatening but may become so because of hormone secretion or critical location,

  eg, a benign neoplasm can cause death if it arises in a cranial nerve and compresses the medulla.

Malignant

- Grow rapidly, infiltrate and destroy surrounding tissues, and metastasize throughout the body, often lethal.

Intermediate

- Locally invasive but have low metastatic potential. Locally aggressive neoplasms or low-grade malignant neoplasms. Basal cell carcinoma of the skin.

Prediction of Biologic Behavior by Pathologic Examination

Treatment of neoplasms is based upon their biologic behavior.

- *Benign neoplasms* ;excision of the tumor.
- *Locally aggressive* ;
- *Malignant neoplasms*

The pathologist classifies a neoplasm as benign or malignant on the basis

- Histologic and cytologic features in association with the cumulative clinicopathologic experience gained with various types of neoplasms.

- There are no absolute criteria for distinguishing benign from malignant neoplasms

Rate of Growth

- No critical rate that distinguishes
- Assessment of the growth rate is based upon clinical information (eg, change in size of the mass in serial examinations).
- The number of mitotic figures and the metabolically active appearance of nuclei (enlarged, dispersed chromatin, large nucleoli)

Size

- Many benign neoplasms become very large; conversely, highly malignant neoplasms may be lethal by virtue of extensive dissemination even though the original primary tumor is still small.
- In a few neoplasms, however, size is the deciding factor in distinguishing benign from malignant growths.
- A carcinoid tumor of the appendix is considered benign unless it is larger than 2 cm,
- Benign and malignant carcinoid tumors are histologically identical

Degree of Differentiation

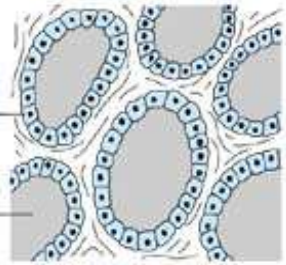
- The degree to which a neoplastic cell resembles the normal mature cells of the tissue in question
- Benign neoplasms are usually fully (well) differentiated, ie, they closely resemble normal tissue

- Malignant neoplasms, on the other hand, show variable degrees of differentiation and frequently demonstrate little resemblance to normal tissue (ie, they are poorly differentiated).
- In **anaplasia,** the neoplastic cells have no morphologic resemblance whatsoever to normal tissue.

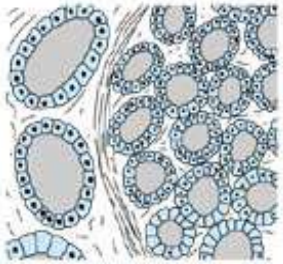
The importance of these individual criteria varies with different neoplasms

- For example, the mitotic rate is the major factor distinguishing benign from malignant smooth muscle neoplasms in the uterus; in many other neoplasms, the mitotic rate is of little relevance.

- Similarly, pheochromocytoma, a neoplasm of the adrenal medulla, may show extreme cytologic abnormalities without demonstrating malignant behavior.

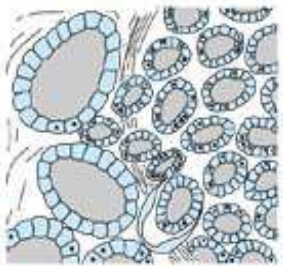


Normal thyroid



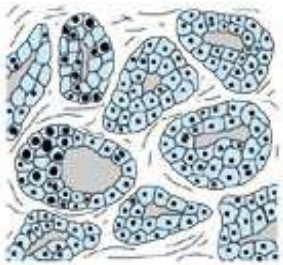
Does not metastasize

Benign neoplasm of thyroid (follicular adenoma)
Neoplasm differs from normal thyroid in that it displays an area of increased growth that forms an encapsulated nodular mass within the gland. Microscopically, it is similar to normal thyroid tissue.



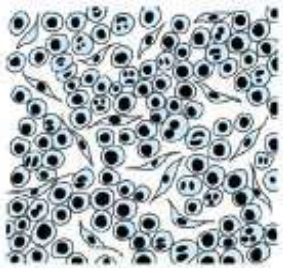
Metastatic potential +

Well-differentiated malignant neoplasm of thyroid (follicular carcinoma)
Differs from benign neoplasm in that it invades surrounding normal thyroid tissue and blood and lymph vessels. Microscopically, it may be similar to normal thyroid tissue.



Metastatic potential ++

Poorly differentiated follicular carcinoma
Nuclear abnormalities and pleomorphism; some mitotic figures; follicular structure and colloid are barely recognizable. Thyroglobulin can be demonstrated by immunologic methods.



Metastatic potential +++

Anaplastic carcinoma of thyroid
No resemblance to normal tissue (anaplastic); no follicles or colloid; marked cytologic abnormalities, spindle cells, giant cells, frequent mitotic figures.

Degree of differentiation and anaplasia

Changes in Deoxyribonucleic Acid (DNA)

- Associated with abnormalities in their DNA content;
- This abnormality increases with the degree of malignancy.
- The degree of **hyperchromatism** provides a crude assessment of DNA content on microscopic examination
- When measured precisely by flow cytometry, the DNA content of malignant cells correlates well with the degree of malignancy in malignant lymphoma, bladder neoplasms, and astrocytic neoplasms.
- Cytogenetic studies demonstrating **aneuploidy and polyploidy** also are indicative of malignancy.

Infiltration and Invasion

- Benign neoplasms are generally noninfiltrative and are surrounded by a capsule of compressed and fibrotic normal tissue.
- Malignant neoplasms, on the other hand, have infiltrating margins.

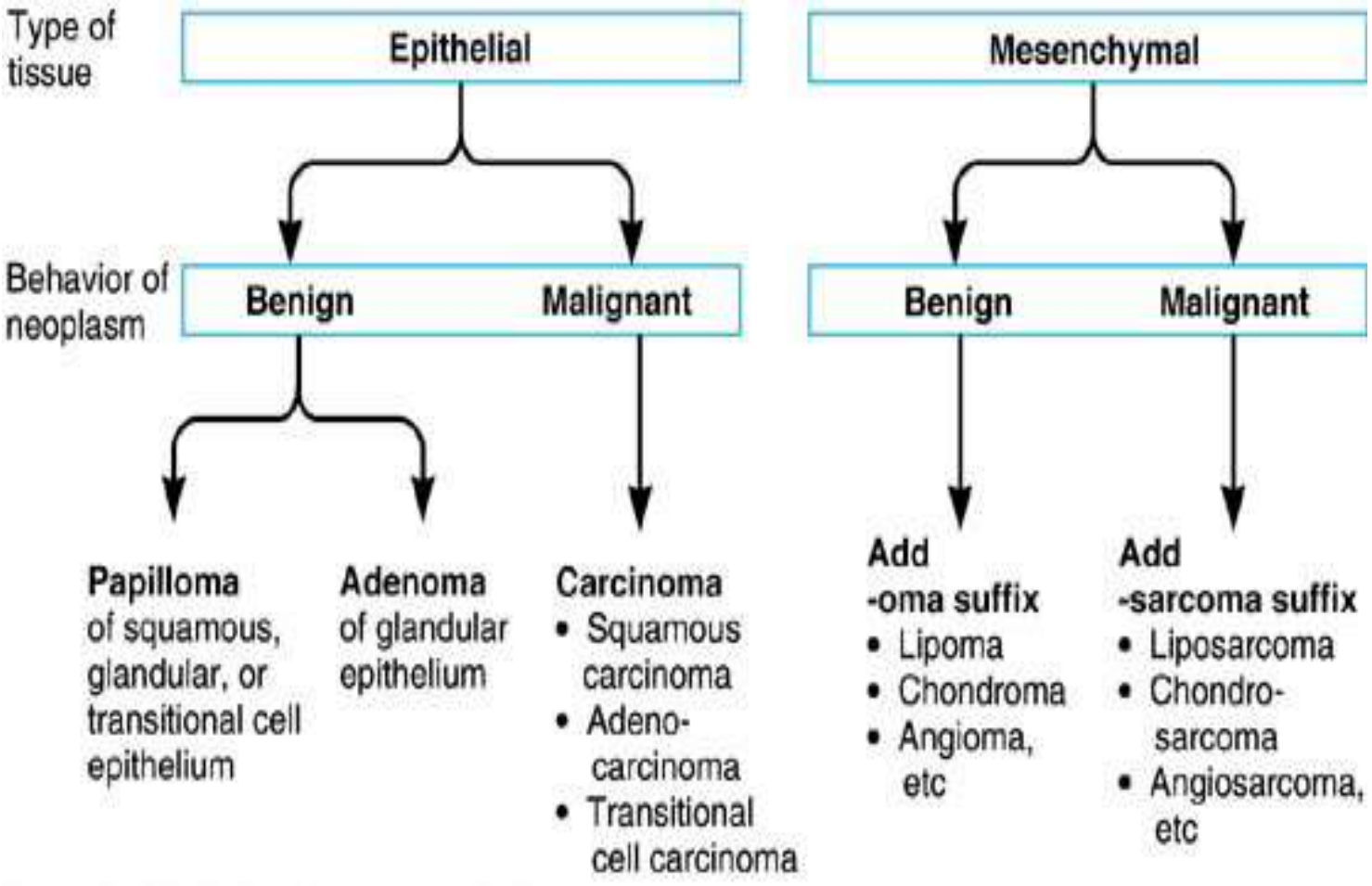
- Many exceptions to this rule exist, and some benign neoplasms—eg, granular cell tumor, dermatofibroma, and carcinoid tumors—lack a capsule and have an infiltrative margin.

Metastasis

- Absolute evidence of malignancy.

- The major reason for distinguishing benign from malignant neoplasms is to be able to predict their ability to metastasize before they do so.

Nomenclature of Neoplasms of Differentiated Cells



Epithelial Neoplasms

- A benign epithelial neoplasm is called an
- **adenoma** if it arises within a gland (eg, thyroid adenoma, colonic adenoma) or a
- **papilloma** (Latin, *papilla* = nipple) when arising from an epithelial surface.

- Papillomas may arise from squamous, glandular, or transitional epithelium (eg, squamous papilloma, intraductal papilloma of the breast, and transitional cell papilloma, respectively

Malignant epithelial neoplasms are called

- **Carcinomas** (adenocarcinomas if derived from glandular epithelia; squamous carcinoma and transitional cell carcinoma if originating in those kinds of epithelia).

- Names may also include the organ of origin and often an adjective as well, eg, clear cell adenocarcinoma of the kidney, papillary adenocarcinoma of the thyroid, verrucous squamous carcinoma of the larynx.

Benign mesenchymal neoplasms

- Named after the cell of origin (a greek or latin word is used)
- Followed by the suffix -*oma*.
- Lipoma
- Fibroma
- leomyoma
- Hemangioma

Malignant mesenchymal neoplasms

- Named after the cell of origin, to which is added the suffix -*sarcoma*.
- Liposarcomas
- Fibrosarcoma
- Leomyosarcoma
- Rhabdomyosarcoma
- Osteosarcoma

Classification of Normal Cells on the Basis of Their Ability to Differentiate into Different Tissues.

Cell Type	Occurrence in Normal Development	Differentiation Capabilities Displayed in Derived Neoplasms
Totipotent cell	Zygote (fetal) Germ cells (gonads usually, extragonadal rarely)	Able to develop into any cell type (capability similar to that of zygote) germ cell tumors; teratomas.
Pluripotent cell	Found in primitive cells that constitute organ anlagen (fetal). Persists in some organs (eg, cerebellum, kidney, adrenal, retina, pineal) in the first few years of postnatal life.	Able to develop into multiple cell types having a maximum of 2 germ layers. These neoplasms occur in the first few years of life. Blastomas.
Differentiated cell	Adult labile and stable cell: usually differentiates into one cell type only but retains limited ability to differentiate into related cells (as in metaplasia).	Most human neoplasms arise from these cells. Common in older patients. Neoplasm composed of one cell type (may have metaplastic elements).
Permanent cell	End–stage functional cells of epithelia and permanent cells in muscle and brain. Unable to divide (postmitotic).	Does not produce neoplasms (few if any exceptions).

Differentiated cells

Epithelial cells			
Squamous	Skin, esophagus, vagina, mouth, metaplastic epithelium	Squamous papilloma	Squamous carcinoma Basal cell carcinoma
Glandular	Gut, respiratory tract, secretory glands, bile ducts, ovary, endometrium of uterus	Adenoma Cystadenoma	Adenocarcinoma Cystadenocarcinoma
Transitional	Urothelium	Papilloma	Transitional cell carcinoma
Hepatic	Liver cell	Adenoma	Hepatocellular carcinoma
Renal	Tubular epithelial cell	Adenoma	Adenocarcinoma
Endocrine	Thyroid, parathyroid, pancreatic islets	Adenoma	Adenocarcinoma
Mesothelium	Mesothelial cells	Benign mesothelioma	Malignant mesothelioma
Placenta	Trophoblast cells	Hydatidiform mole	Choriocarcinoma

Mesenchymal cells

Fibrous tissue	Fibroblast	Fibroma	Fibrosarcoma
Cartilage	Chondrocyte	Chondroma	Chondrosarcoma
Nerve	Schwann cell	Schwannoma	Malignant peripheral–nerve–sheath tumor
	Neural fibroblast	Neurofibroma	Malignant peripheral–nerve–sheath tumor
Bone	Osteoblast	Osteoma	Osteosarcoma
Fat	Lipocyte	Lipoma	Liposarcoma
Notochord	Primitive mesenchyme		Chordoma
Vessels	Endothelial cells	Hemangioma Lymphangioma	Hemangiosarcoma, Kaposi's sarcoma Lymphangiosarcoma
Pia and arachnoid	Meningeal cells	Meningioma	Malignant meningioma
Muscle	Smooth muscle cells Striated muscle cells	Leiomyoma Rhabdomyoma	Leiomyosarcoma Rhabdomyosarcoma
Melanocytes	Melanocytes[1]	Nevi (various types)	Melanoma (malignant)

Exceptions to These Rules

Neoplasms That Sound Benign But Are Malignant

- Lymphoma (lymphocyte),
- Plasmacytoma (plasma cell),
- Melanoma (melanocyte),
- Glioma (glial cell), and
- Astrocytoma (astrocyte).
- The adjective malignant should be used—malignant lymphoma, malignant melanoma—but if it is not, these neoplasms are assumed to be malignant because there is no benign lymphoma, melanoma, glioma, etc.

Neoplasms That Sound Malignant But Are Benign

- Two rare bone neoplasms, osteoblastoma and chondroblastoma, present in adult bone.

Leukemias

- Neoplasms of blood-forming organs are called leukemias.
- Malignant, although some exhibit a slower clinical course than others.

- Clinical course (acute or chronic) and cell of origin (lymphocytic, granulocytic [myelocytic], monocytic, etc).

- Neoplastic cells in bone marrow and peripheral blood; they rarely produce localized tumors.

Mixed Tumors

More than one neoplastic cell type.

- Malignant mixed tumors may have two epithelial components, as in adenosquamous carcinoma;
- Two mesenchymal components, as in malignant fibrous histiocytoma; or
- An epithelial and a mesenchymal component, as in carcinosarcoma of the lung and malignant mixed müllerian tumor of the uterus.

Common Eponymous Neoplasms.

Eponym	Cell of Origin
Neoplasms of uncertain histogenesis	
Ewing's sarcoma	Primitive neuroepithelial cell
Hodgkin's lymphoma	?Early lymphoid cell
Brenner tumor	Celomic epithelium covering ovary
Neoplasms of known histogenesis	
Burkitt's lymphoma	B lymphocyte
Kaposi's sarcoma	Vascular endothelial cell
Krukenberg tumor	Metastatic adenocarcinoma cell involving ovary
Wilms' tumor	Pluripotent embryonic renal cell (nephroblastoma)
Grawitz's tumor	Renal tubular cell (renal adenocarcinoma)
Hürthle cell tumor	Thyroid follicular cell

Hamartomas & Choristomas

Tumor-like growths thought to be the result of developmental anomalies

- Not true neoplasms
- Abnormal, disorganized, proliferating masses of several different adult cell types

- A **hamartoma** is composed of tissues that are normally present in the organ in which the tumor arises;

- A hamartoma of the lung consists of a disorganized mass of bronchial epithelium and cartilage that may become so large that it presents as a lung mass. Its growth is coordinated with that of the lung itself.

Choristoma

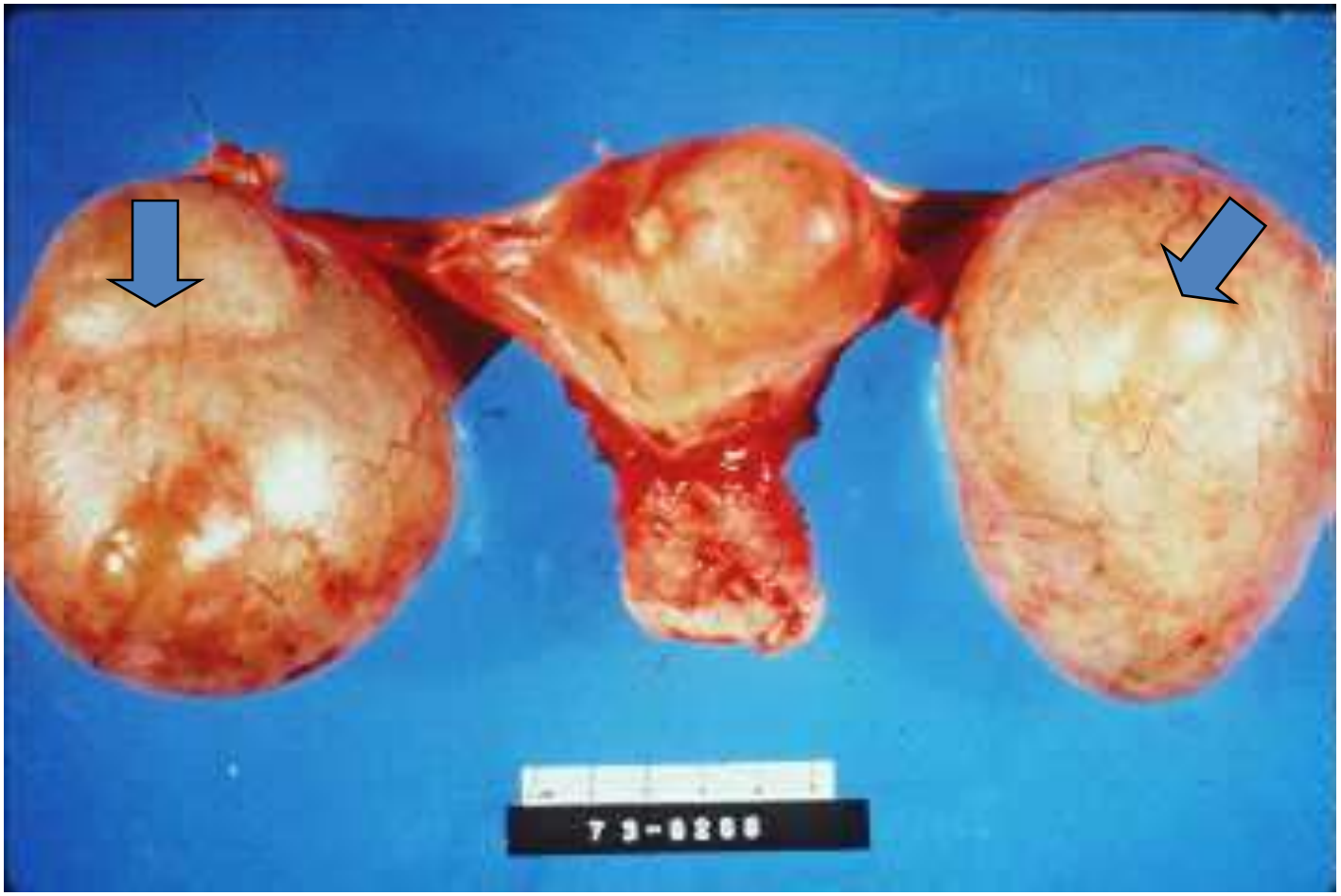
- A disorderly mass of smooth muscle and pancreatic acini and ducts in the wall of the stomach is properly called a choristoma.

- A gastric choristoma such as this may present as an intramural mass that is clinically indistinguishable from a benign neoplasm

Common Childhood Neoplasms.

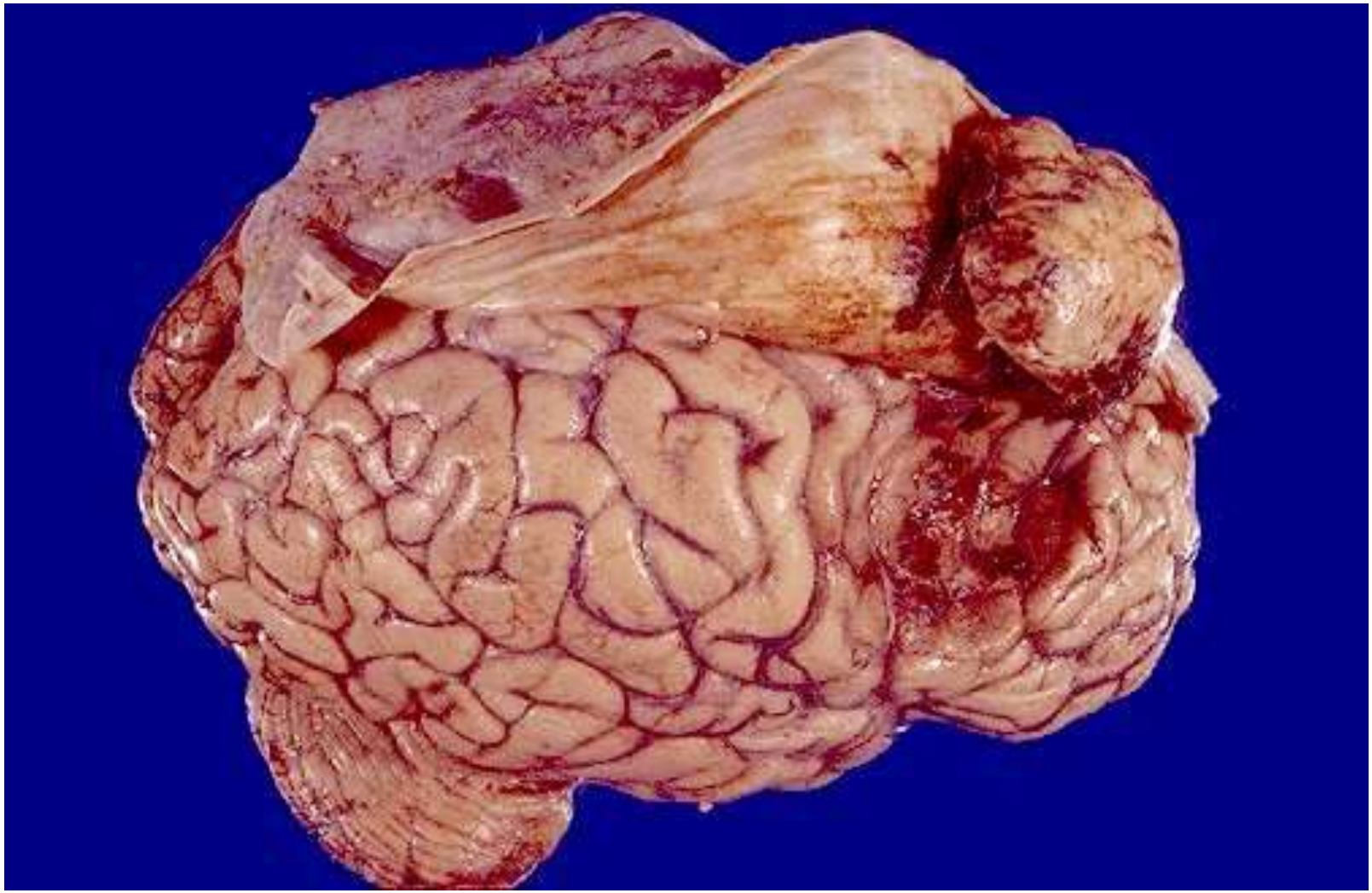
Neoplasm	Site	Proposed Progenitor Cell
Acute lymphocytic leukemia	Blood or marrow	Embryonic lymphoblasts (nonmarking, B or T)
Lymphoblastic lymphoma	Lymph nodes or lymphoid tissue	Embryonic T lymphoblasts
Burkitt's lymphoma (B cell)	Lymph nodes or lymphoid tissue	Embryonic B lymphoblasts
Medulloblastoma	Cerebellum	Embryonic cerebellar neuroectodermal cells
Retinoblastoma	Retina	Embryonic retinal blast cells
Neuroblastoma	Adrenal medulla; sympathetic ganglia	Embryonic neuroblasts
Nephroblastoma (Wilms' tumor)	Kidney	Embryonic metanephric cells
Hepatoblastoma	Liver	Embryonic liver cells
Osteosarcoma	Bone	Osteoblasts

Bilateral Cystadenoma Ovary:

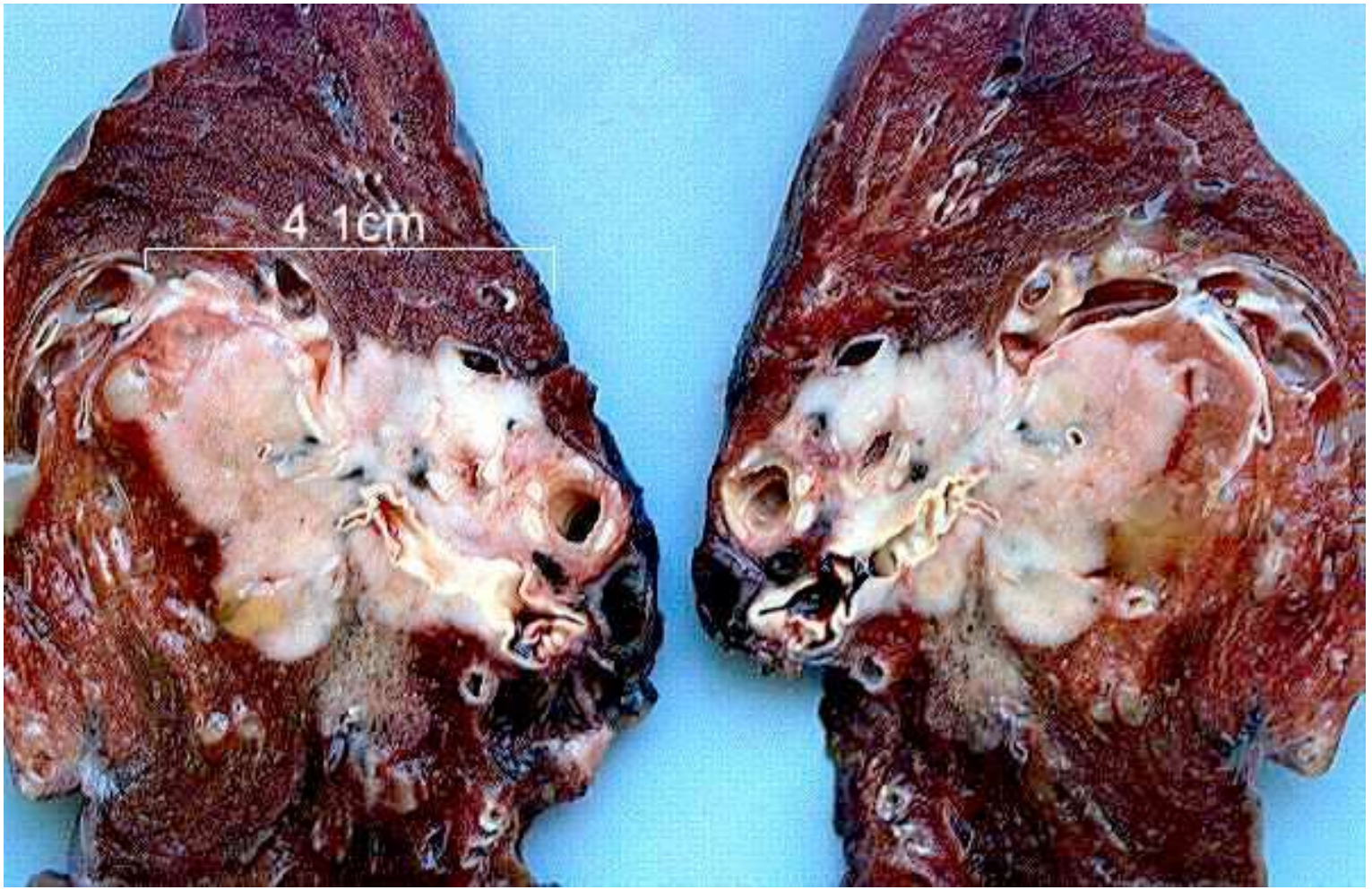


Lipoma Intestine:

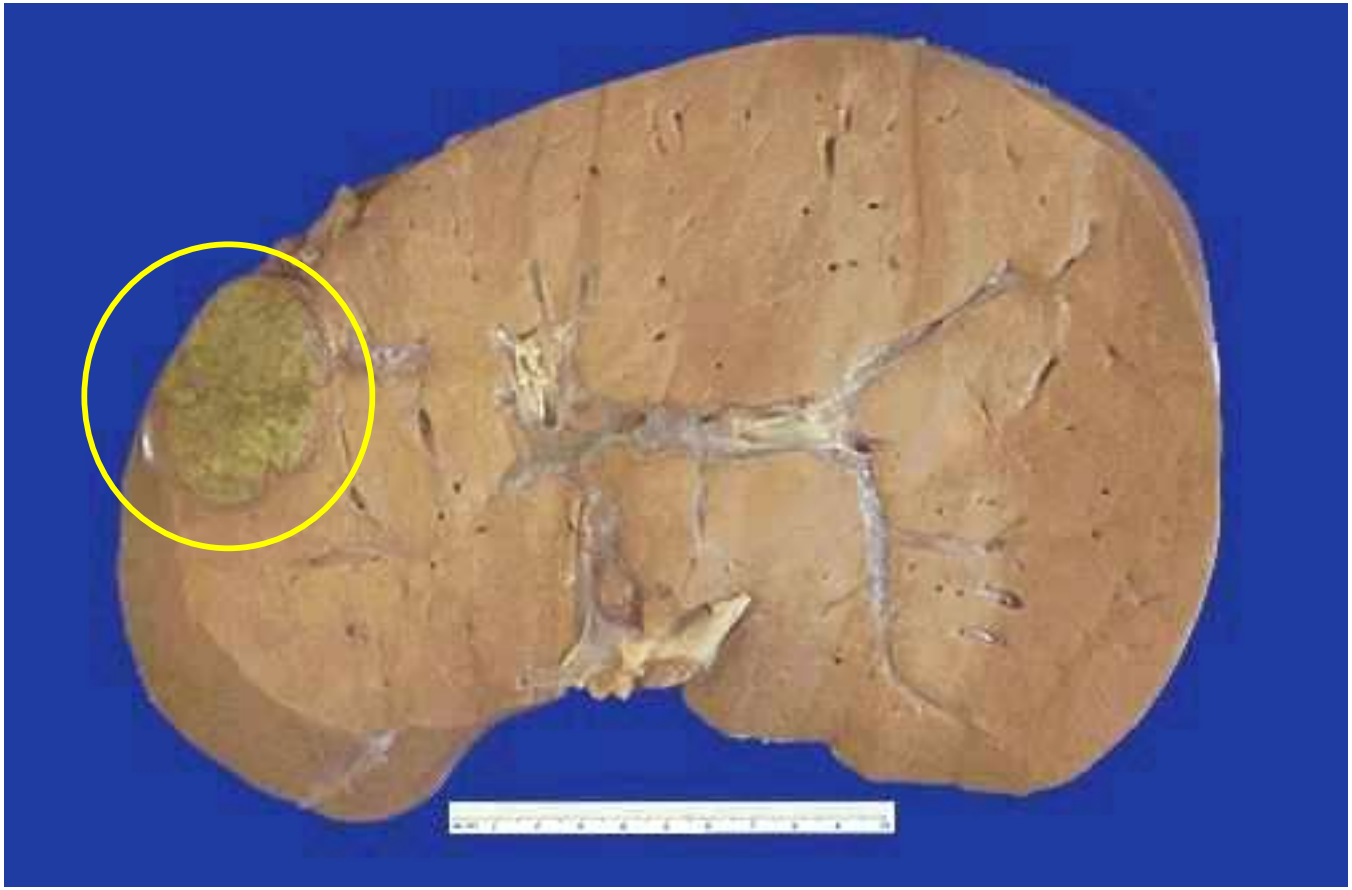
meningioma



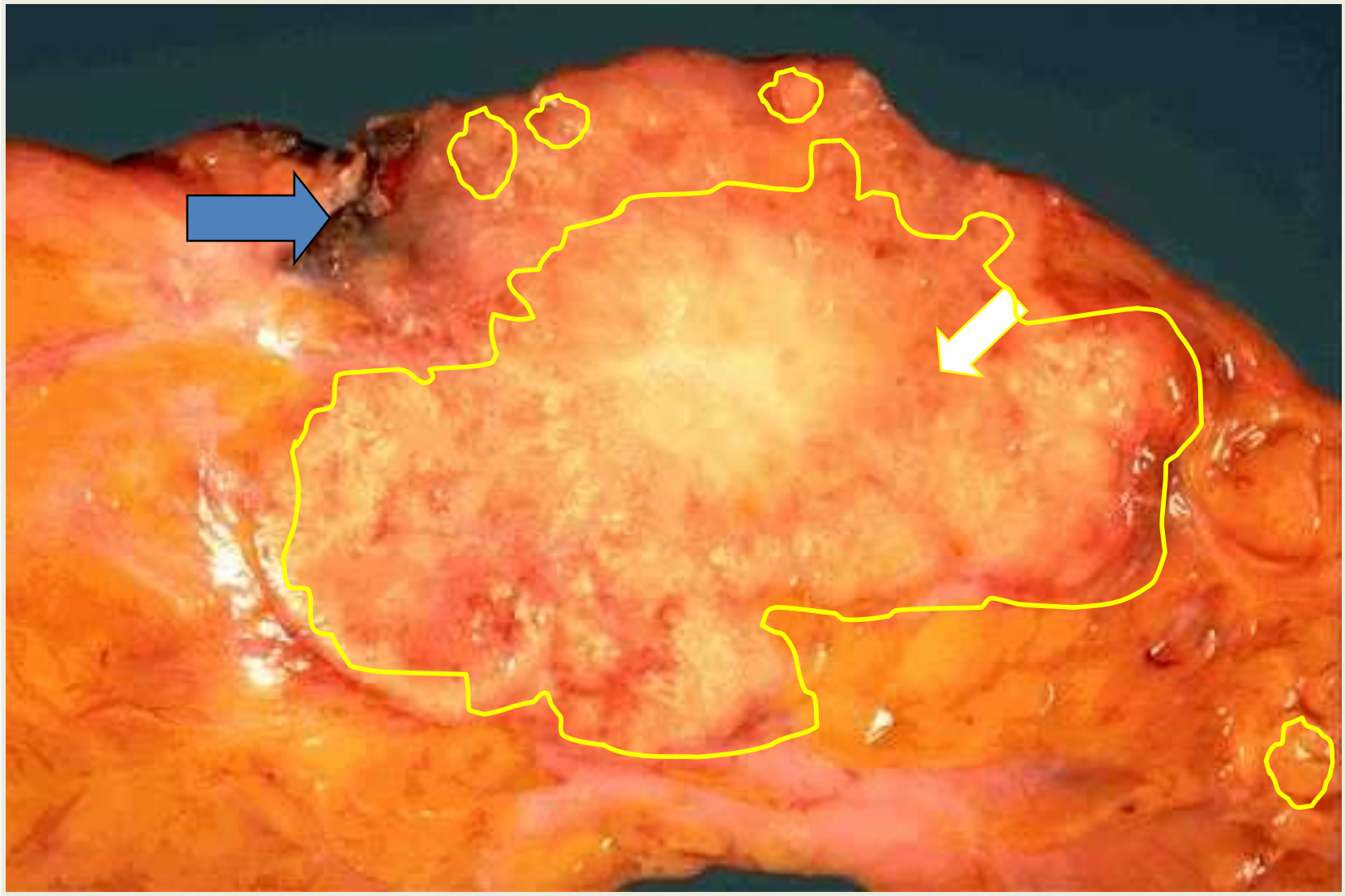
Lung carcinoma



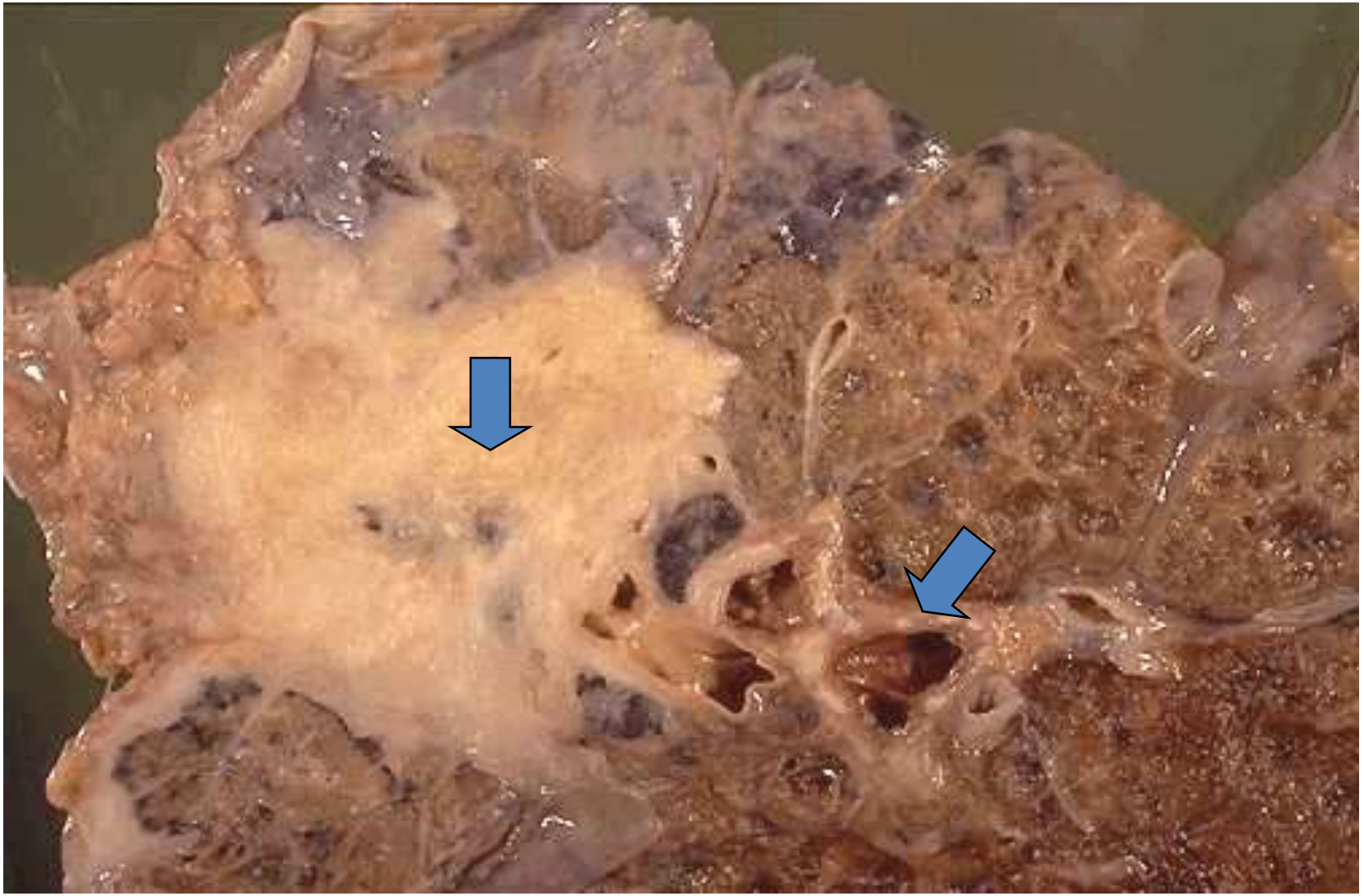
Hepatic Adenoma:



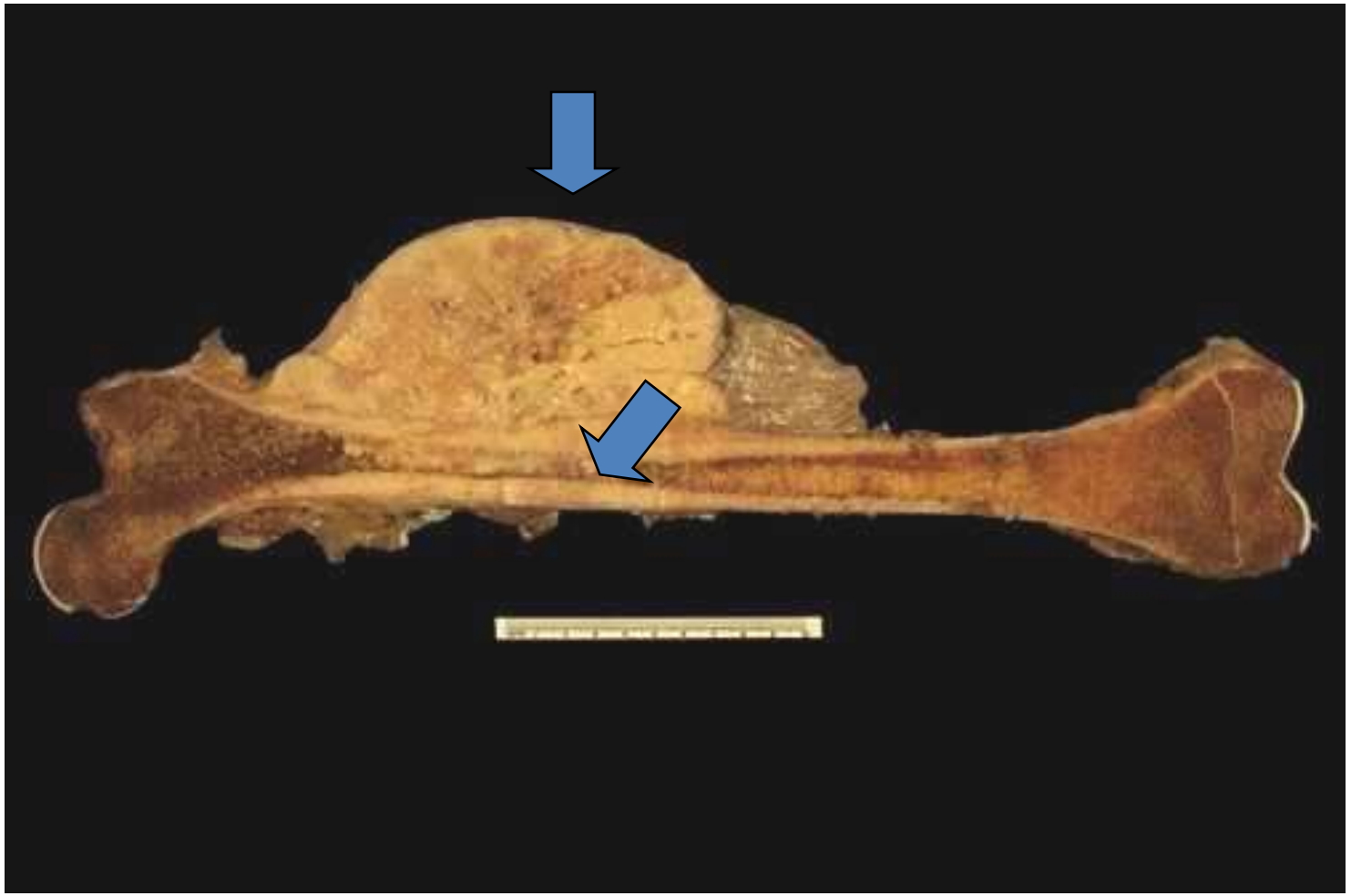
Carcinoma Breast:



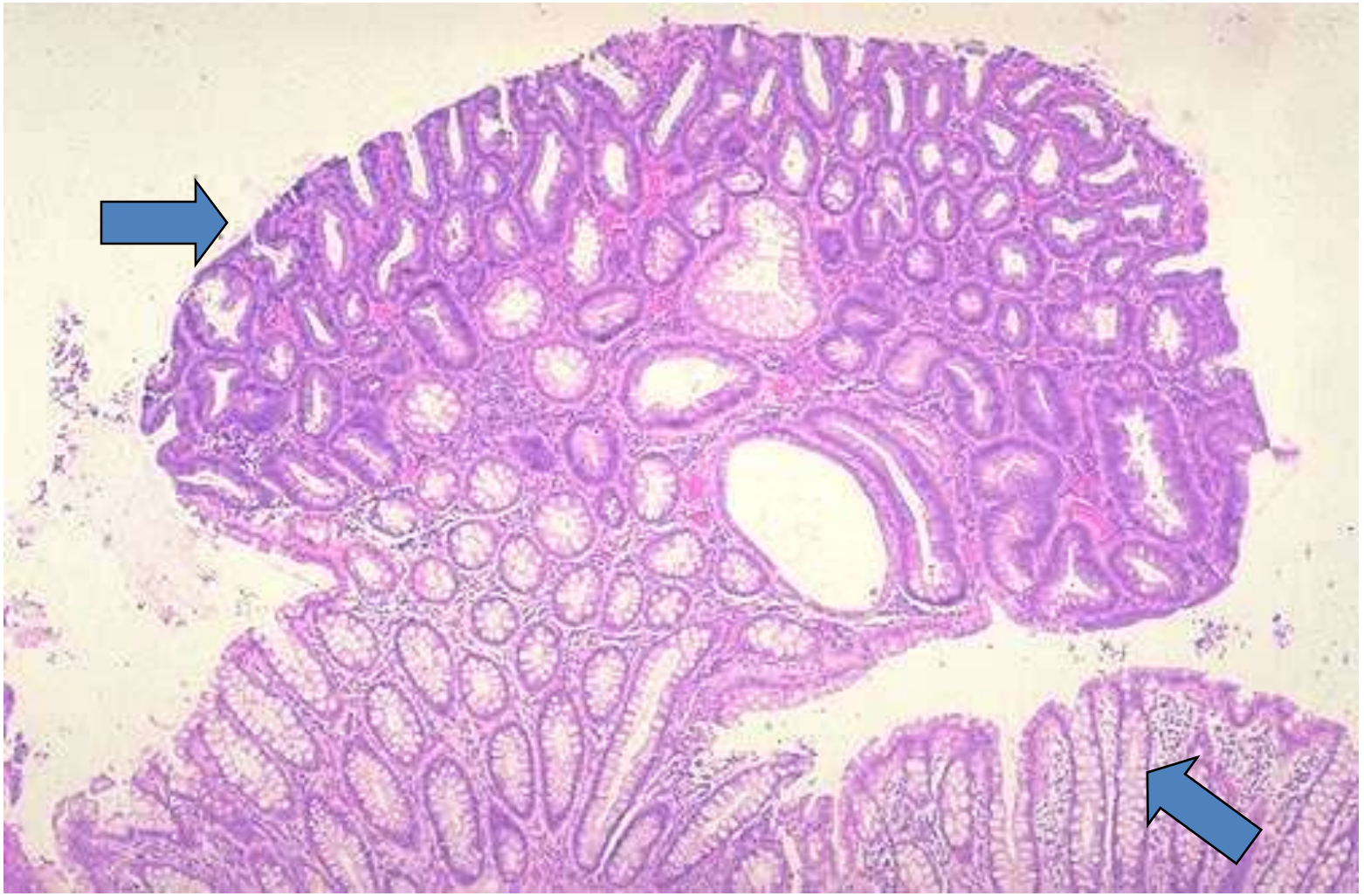
Carcinoma Lung:



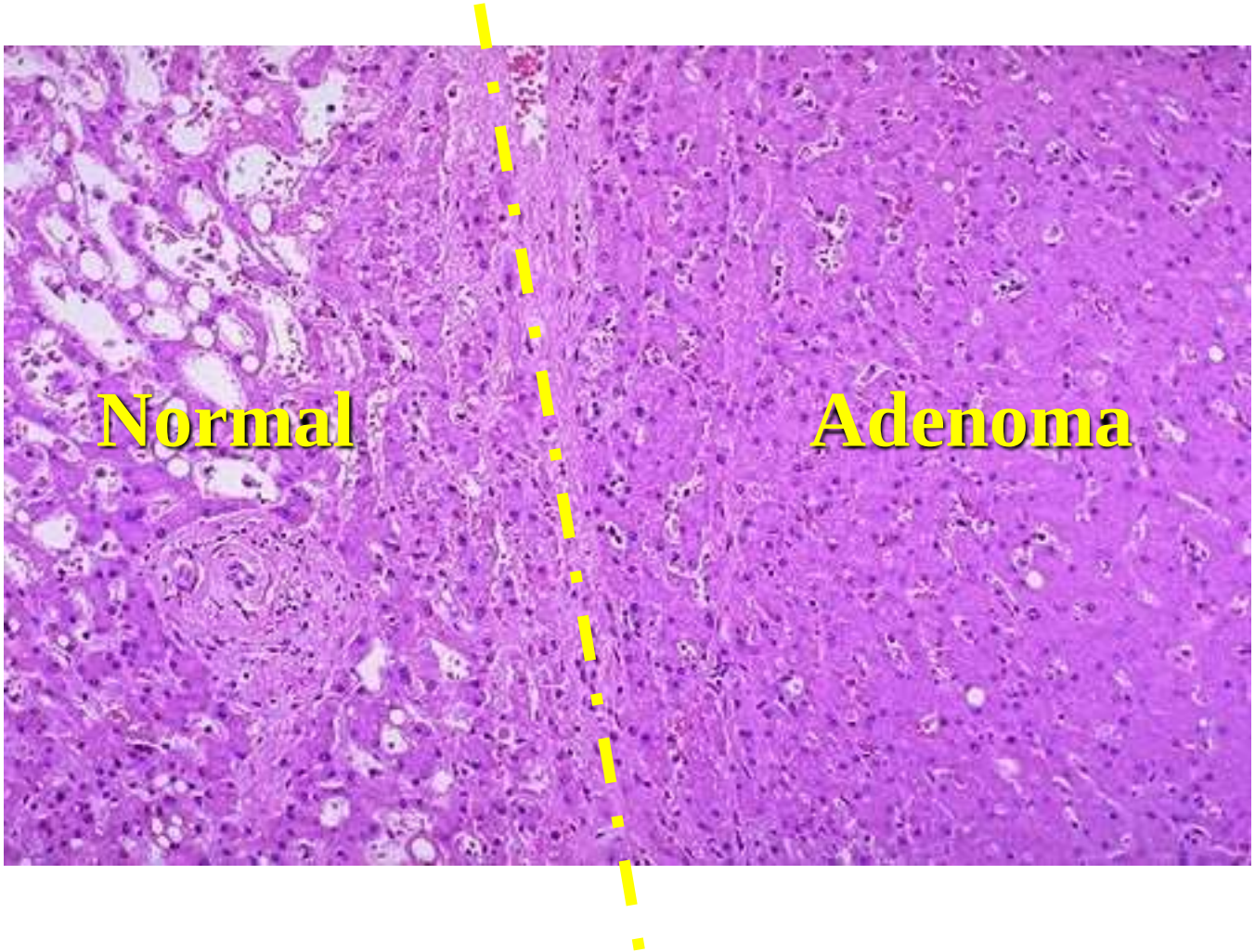
Osteo - sarcoma:



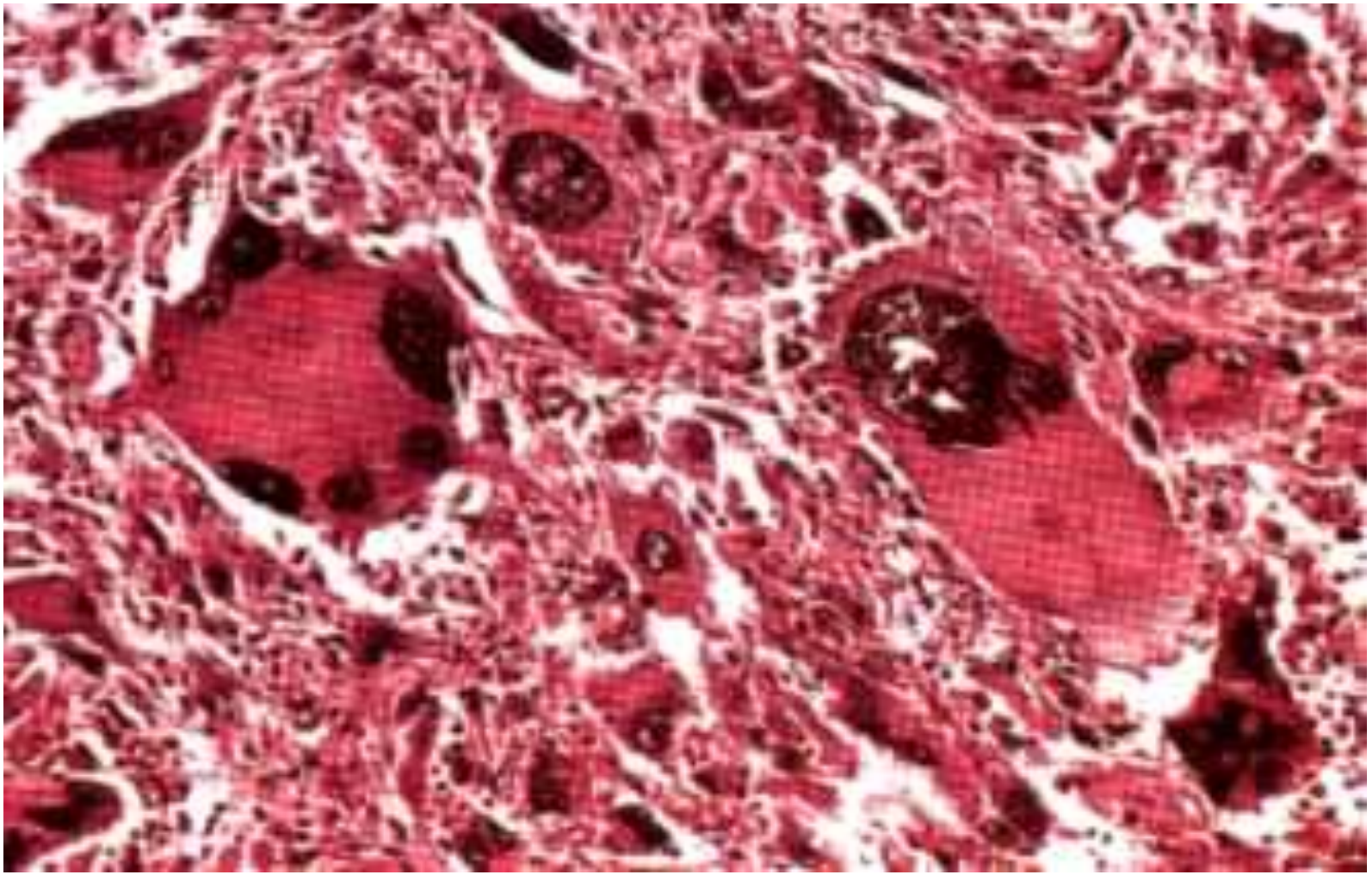
Colon Polyp:



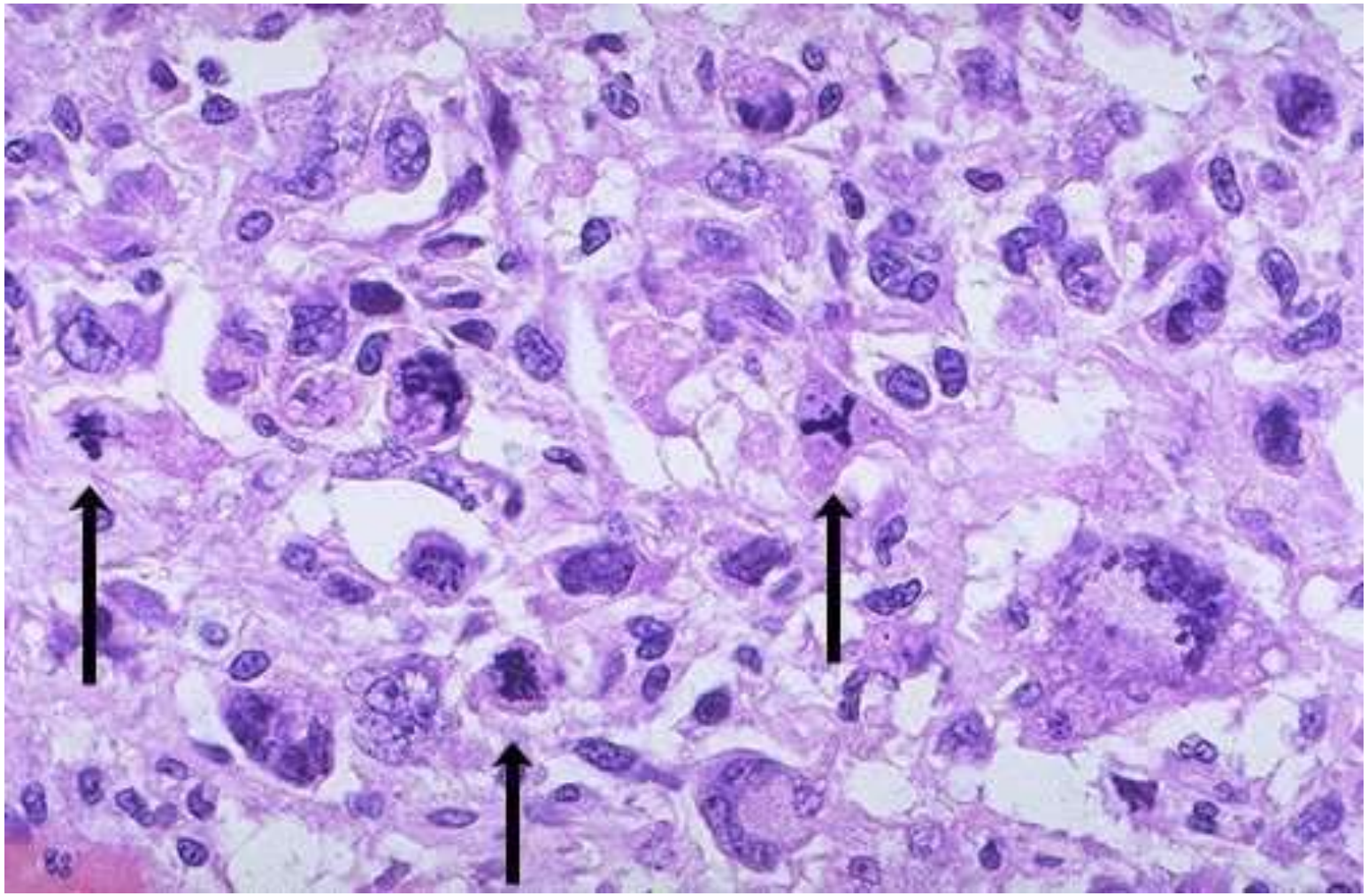
Hepatic Adenoma:



Anaplasia in Sarcoma:

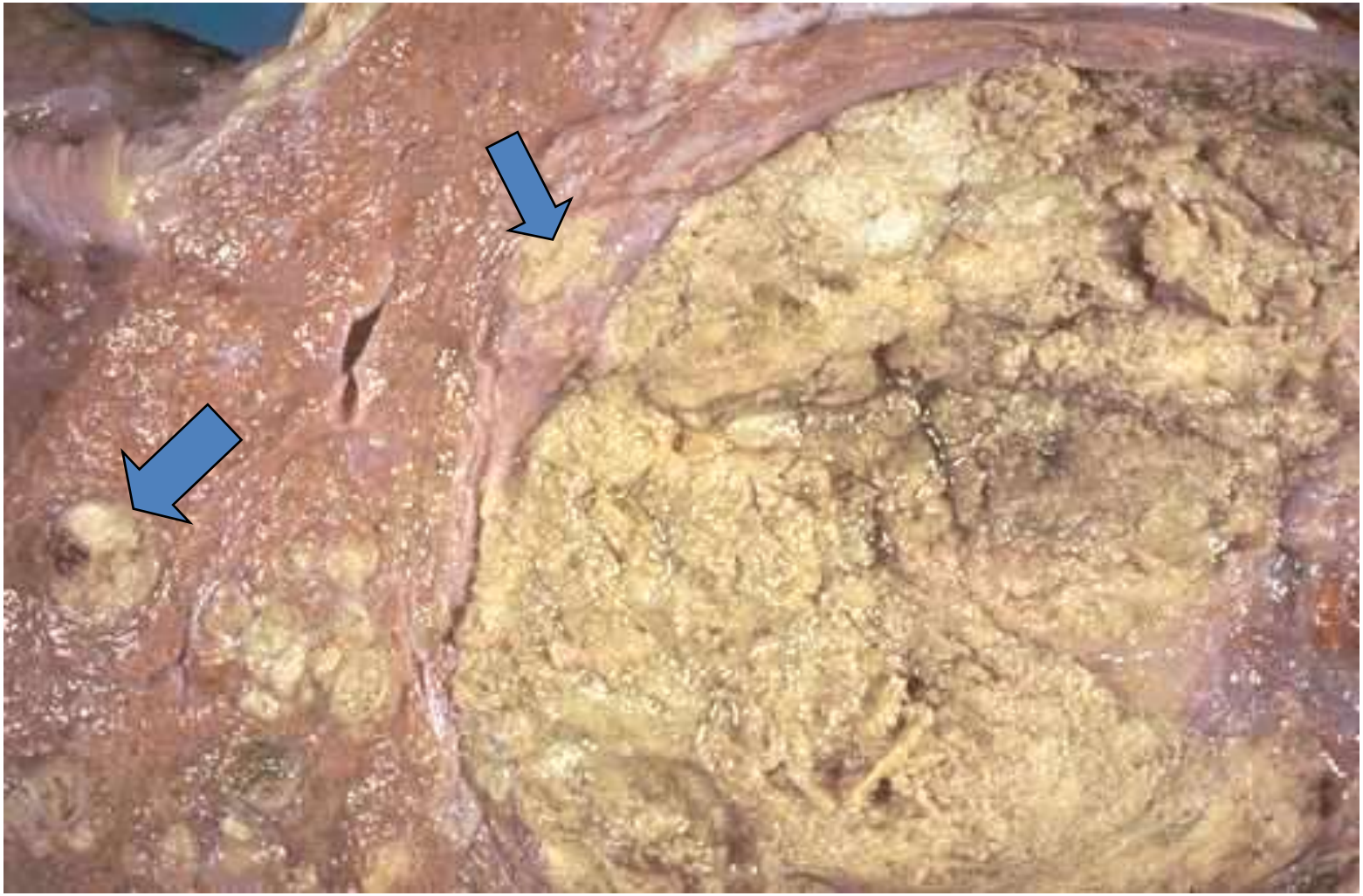


Anaplasia:

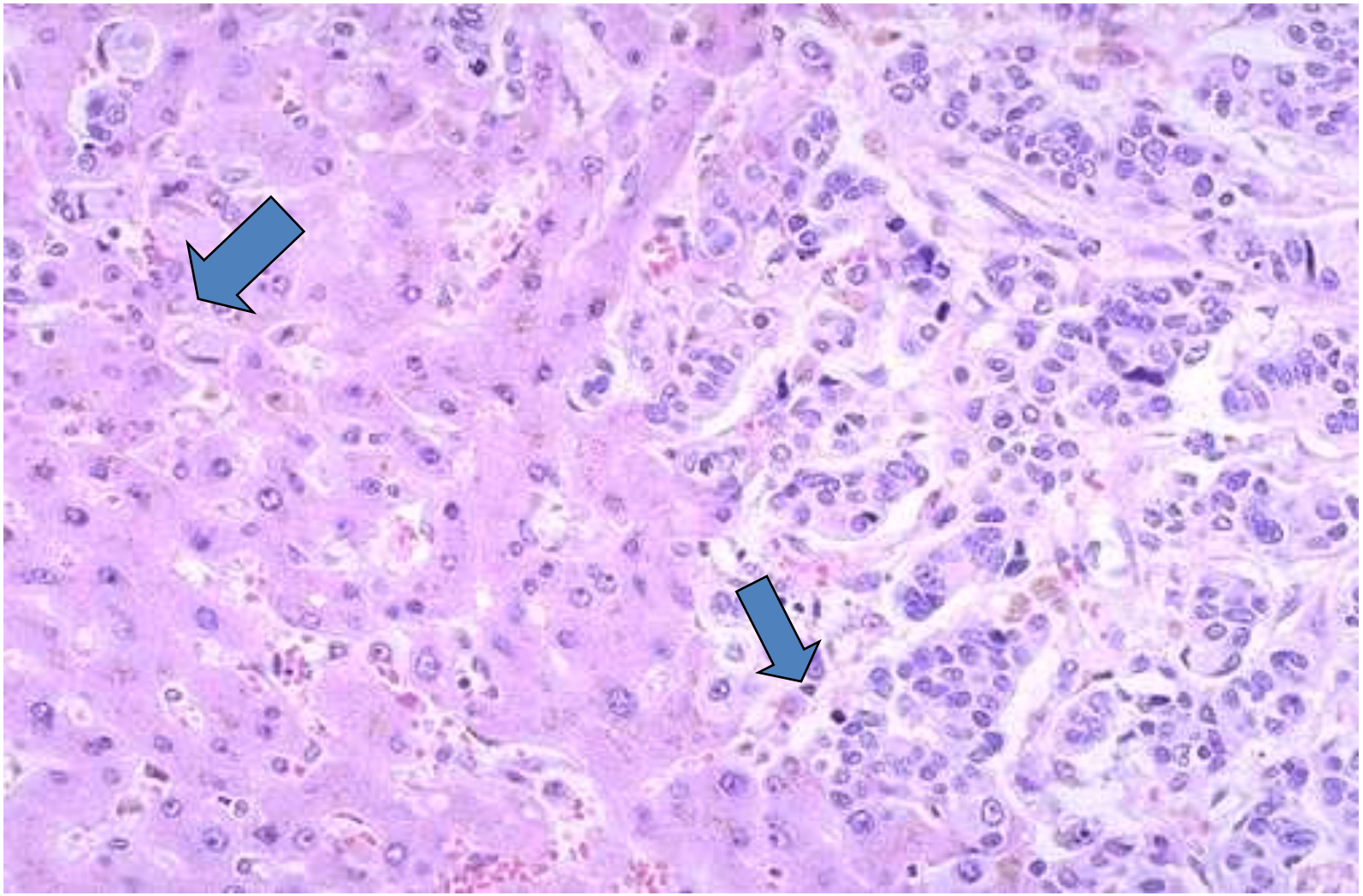


Hepatic Adenocarcinoma:

Hepatic Adenocarcinoma:



Liver Metastasis:



In the end, it's not going to matter how many breaths you took, but how many moments took your breath away.