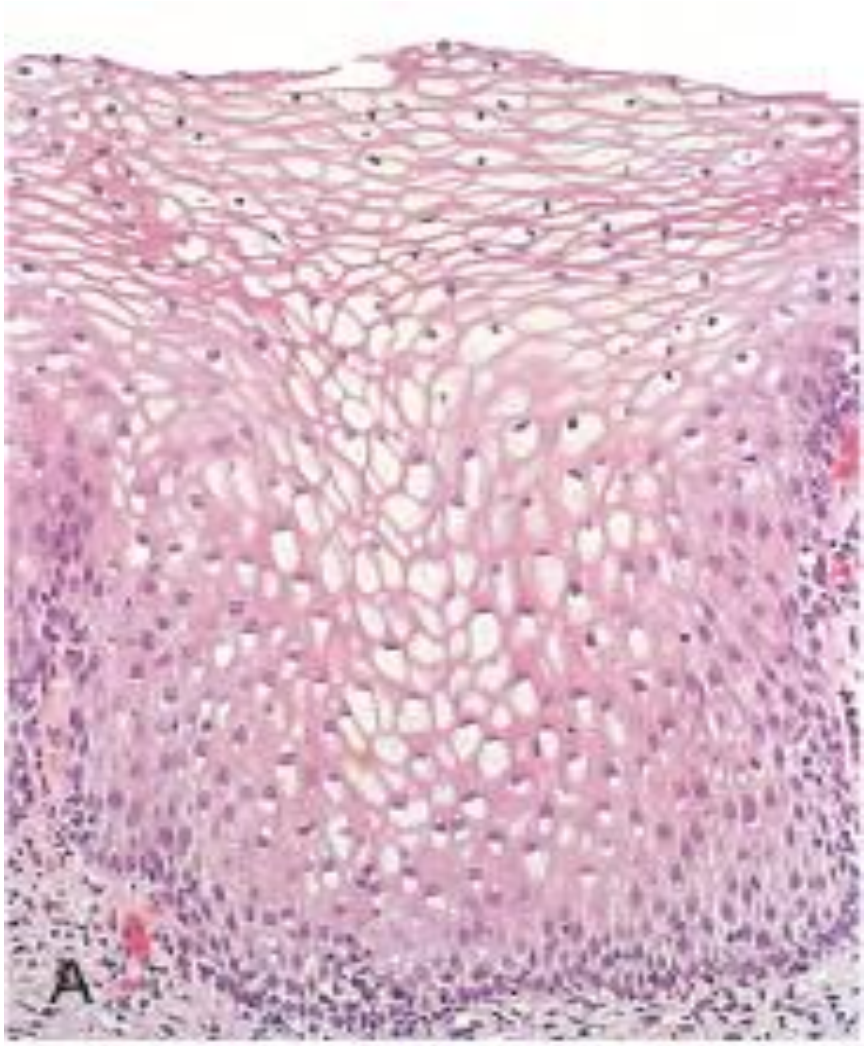
Neoplasia

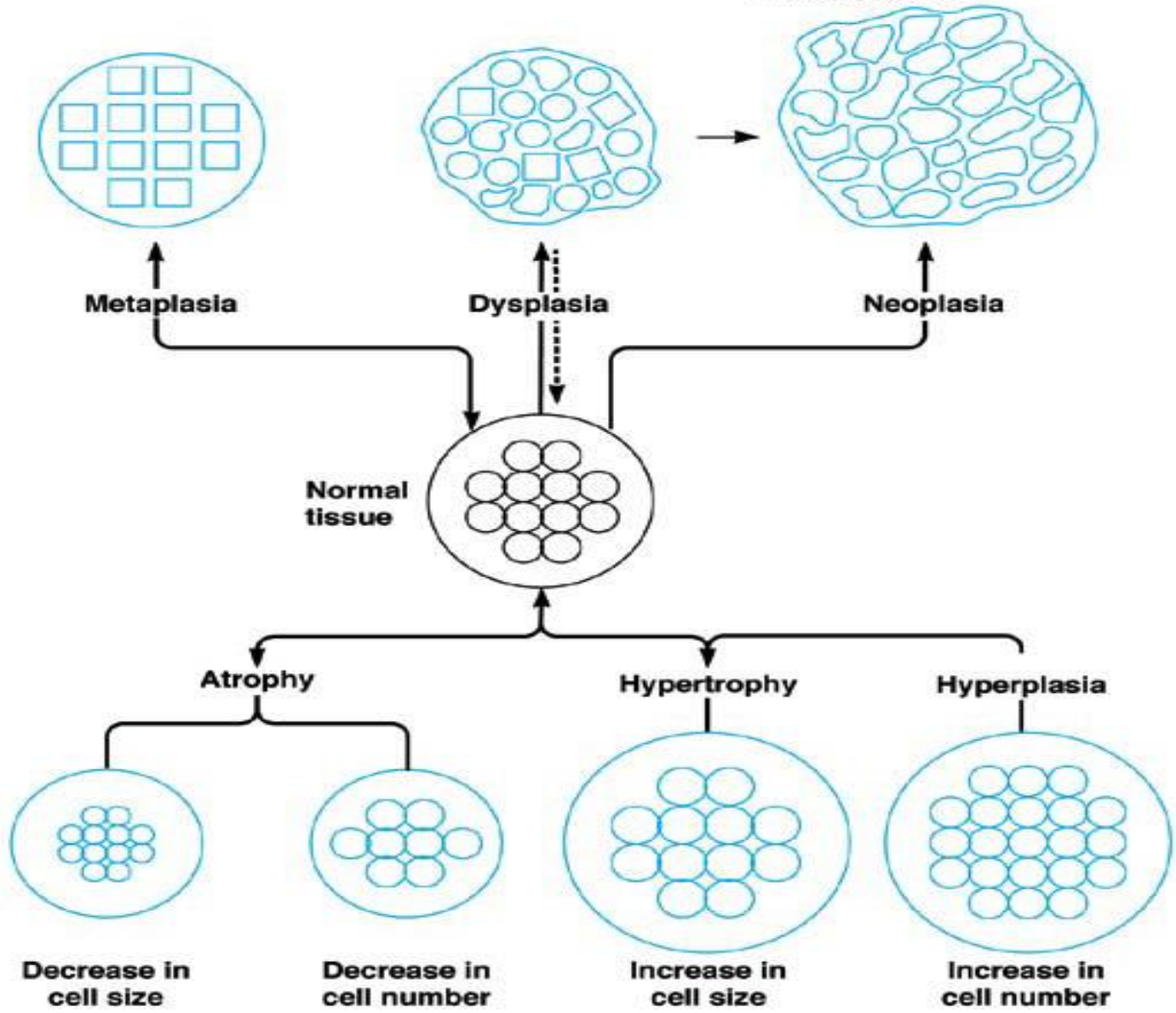
Dysplasia

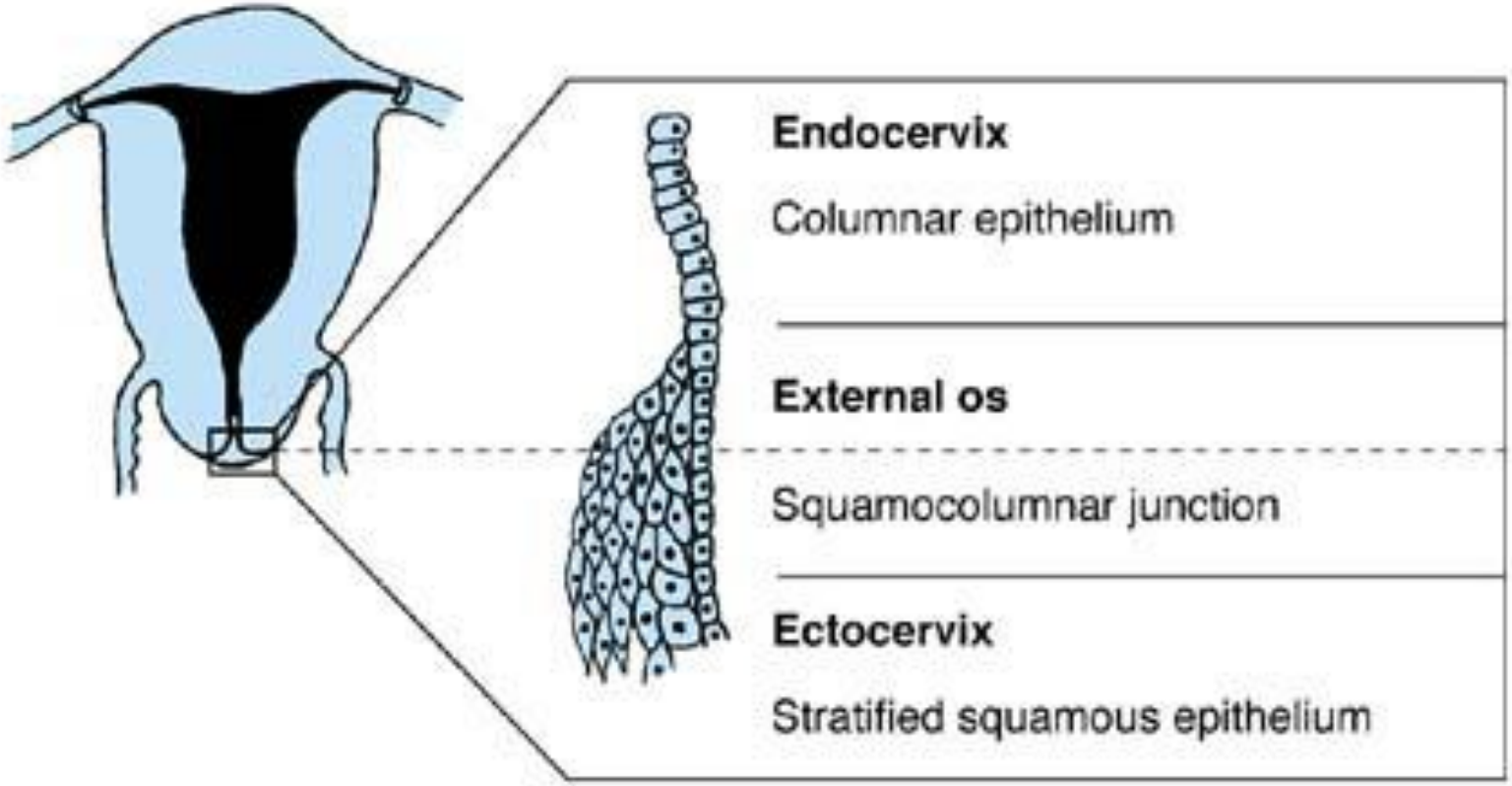

A

- Abnormal differentiation
- Replacement of mature cells of one type with cells of another type
- Regular organization of tissue maintained
- Reversible

- Abnormal differentiation and maturation
- Partial loss of control and organization
- Slight increase in cell number
- Cytologic abnormalities
- **Partially reversible**

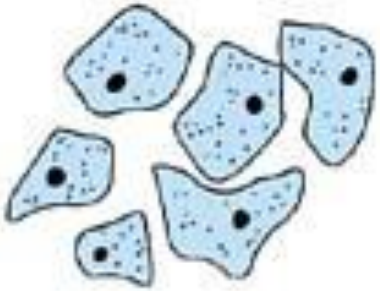
- Abnormal differentiation and maturation
- Marked increase in cell number
- Complete loss of control
- Variable loss of organization
- Cytologic abnormalities
- **Irreversible**





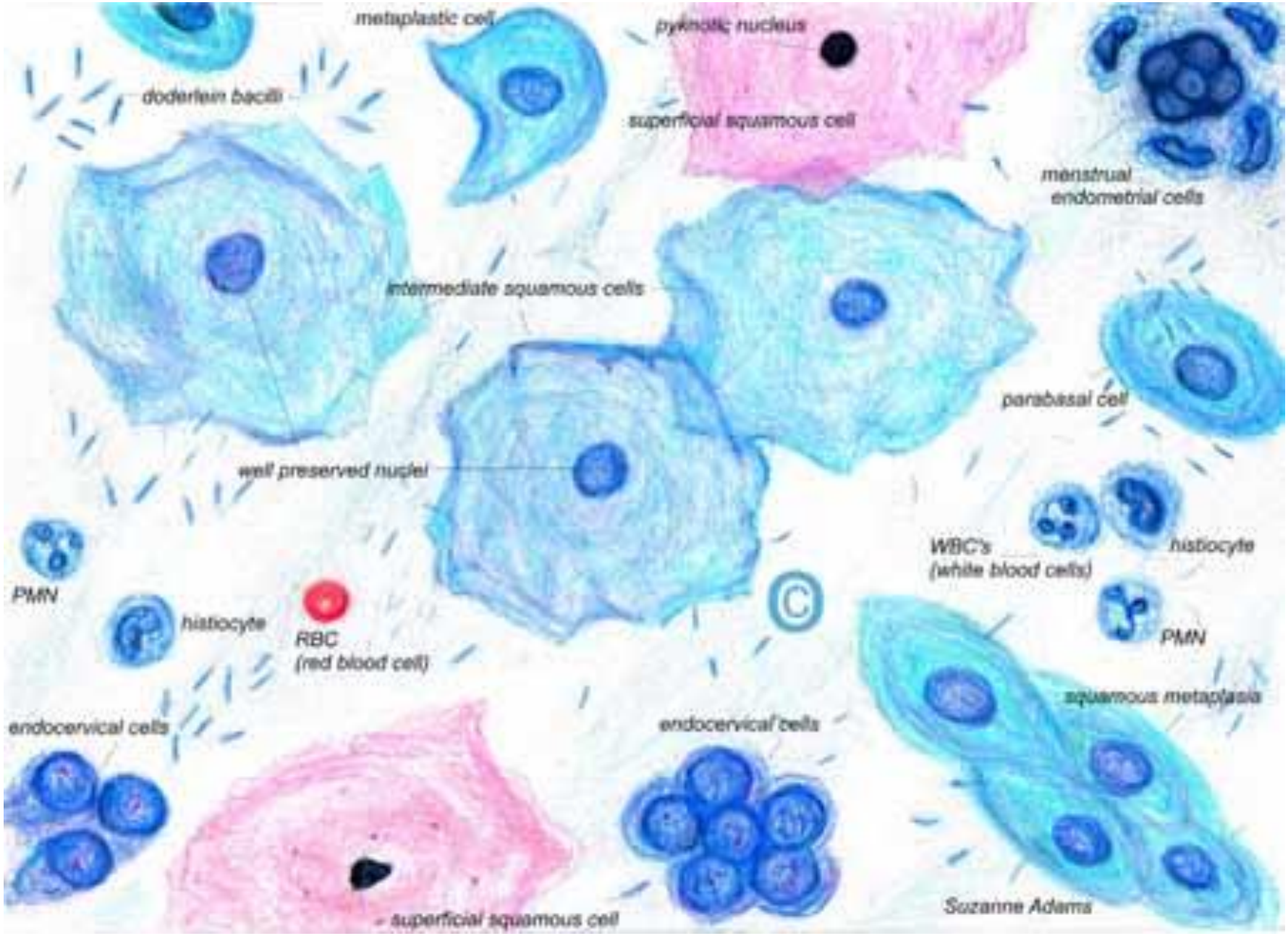
Papanicolaou smear

NORMAL
Large, surface-type squamous cells with small pyknotic nuclei



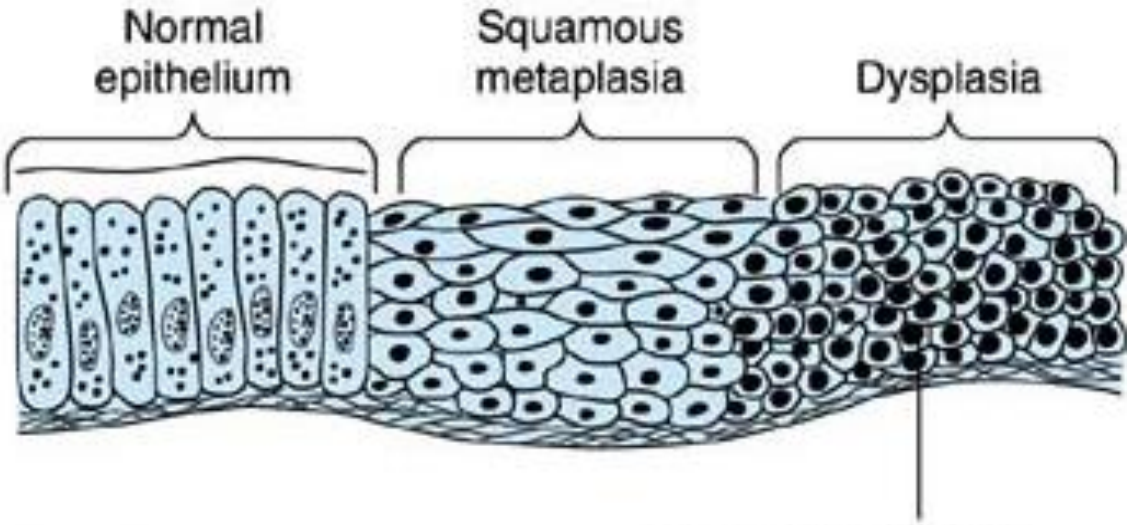
Tissue biopsy

Regular, orderly maturation from dividing basal cells to flattened surface squames


metaplastic cell
pyknotic nucleus
doderlein bacilli
superficial squamous cell
menstrual endometrial cells
intermediate squamous cells
parabasal cell
well preserved nuclei
WBC's (white blood cells)
histiocyte
PMN
histiocyte
RBC (red blood cell)
PMN
squamous metaplasia
endocervical cells
endocervical cells
superficial squamous cell
Suzanne Adams

Dysplasia

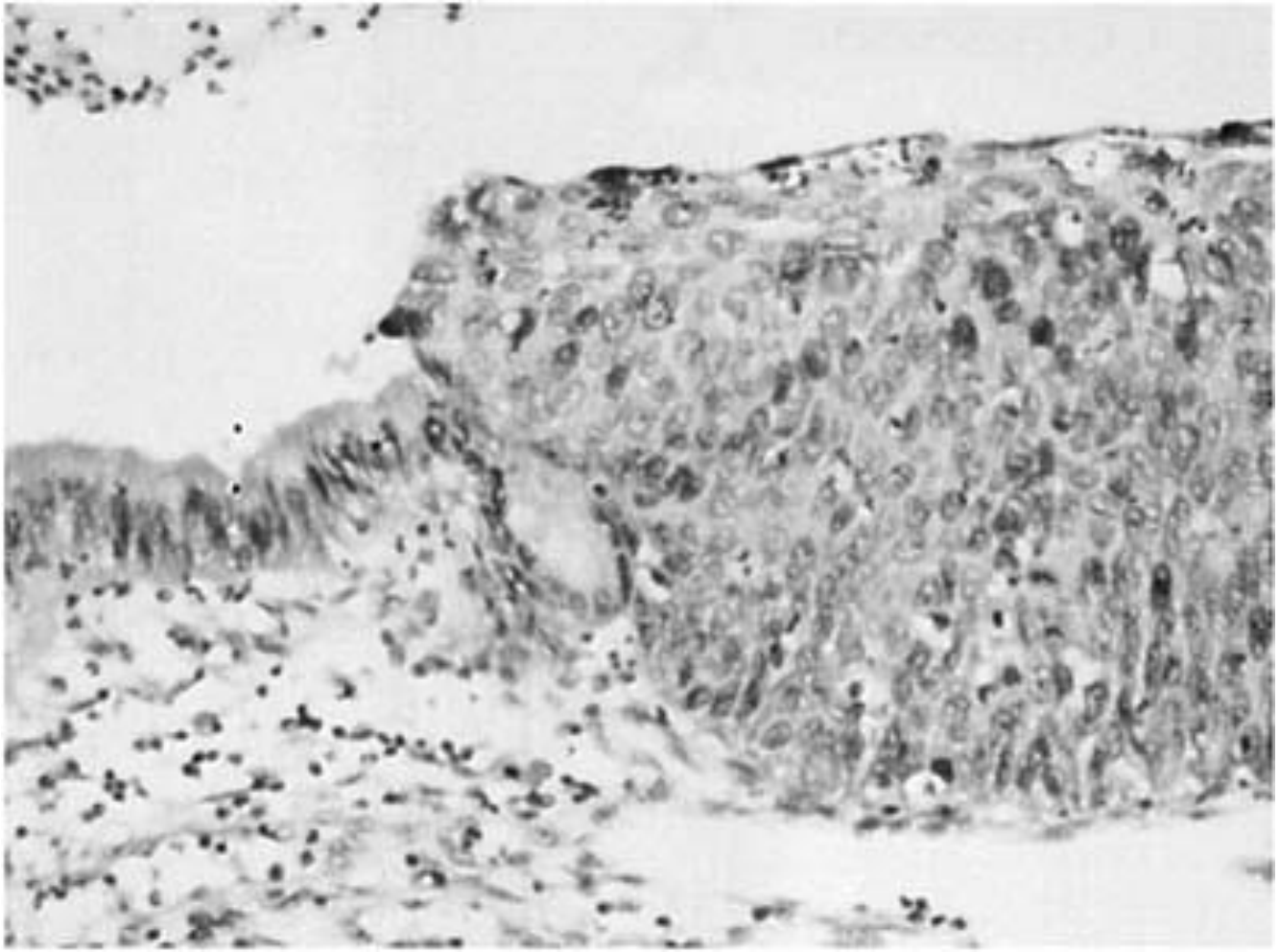
- Abnormality of both differentiation and maturation.
- Principally in epithelia



Dysplasia

Squamous epithelial cells show abnormal maturation and cytologic abnormalities.

Endocervix, showing squamous metaplasia with severe dysplasia. The normal columnar epithelium has been replaced by a squamous epithelium, which in turn shows cytologic features of dysplasia and loss of normal maturation.



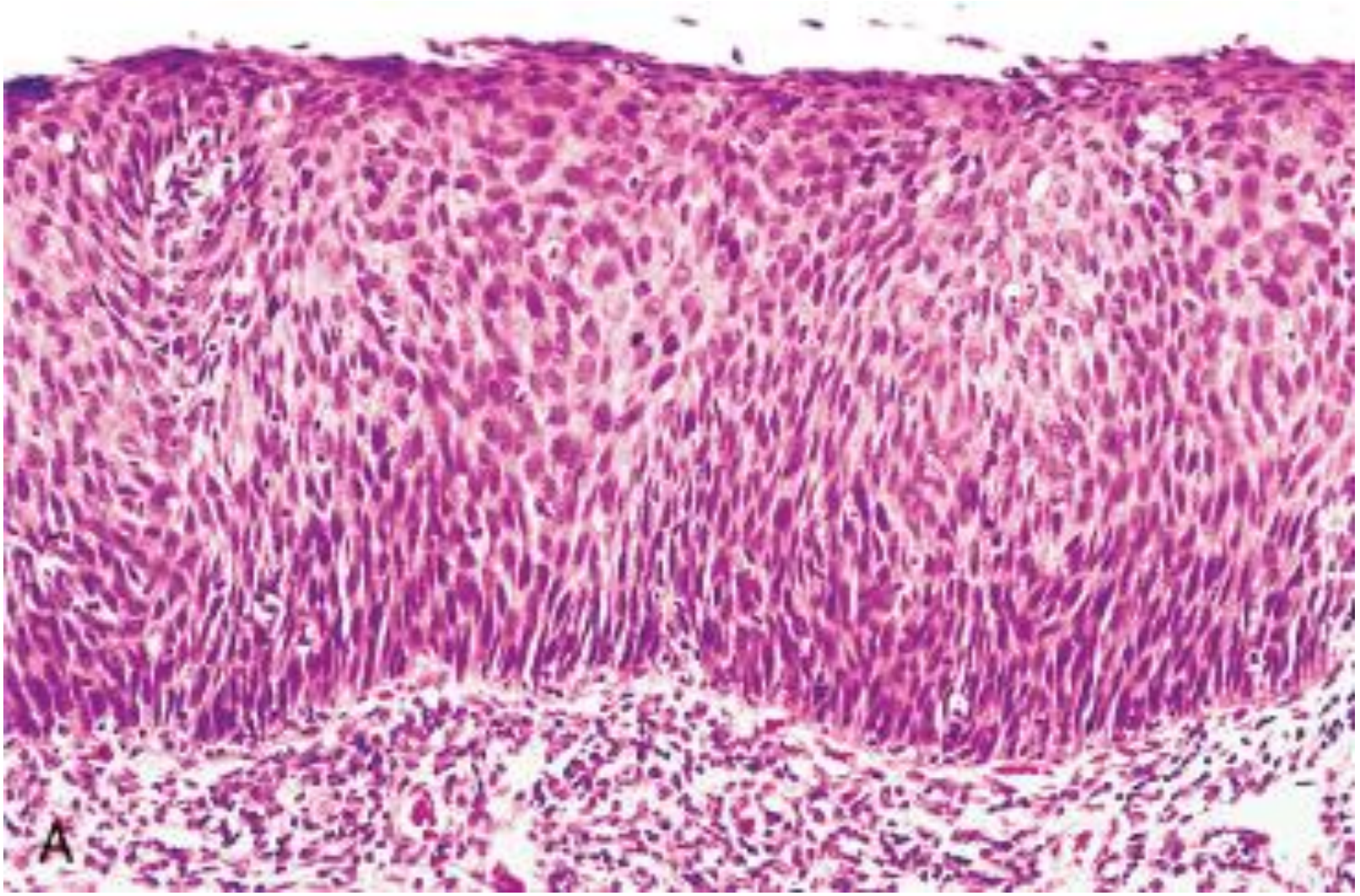
Constellation of changes that include

- *A loss in the uniformity of the individual cells as well as a loss in their architectural orientation*.
- Pleomorphism
- Hyperchromatic nuclei that are abnormally large for the size of the cell.
- Abundant mitotic figures
- Appear in abnormal locations may appear at all levels and even in surface cells.

- Disorderly architecture of the tissue
- The usual progressive maturation of tall cells in the basal layer to flattened squames on the surface may be lost and replaced by a scrambling of dark basal-appearing cells throughout the epithelium.

- When dysplastic changes are marked and involve the entire thickness of the epithelium, but the lesion remains confined to the normal tissue, it is considered a preinvasive neoplasm and is referred to as ***Carcinoma In Situ***

Carcinoma in situ. entire thickness of the epithelium is replaced by atypical dysplastic cells. There is no orderly differentiation of squamous cells



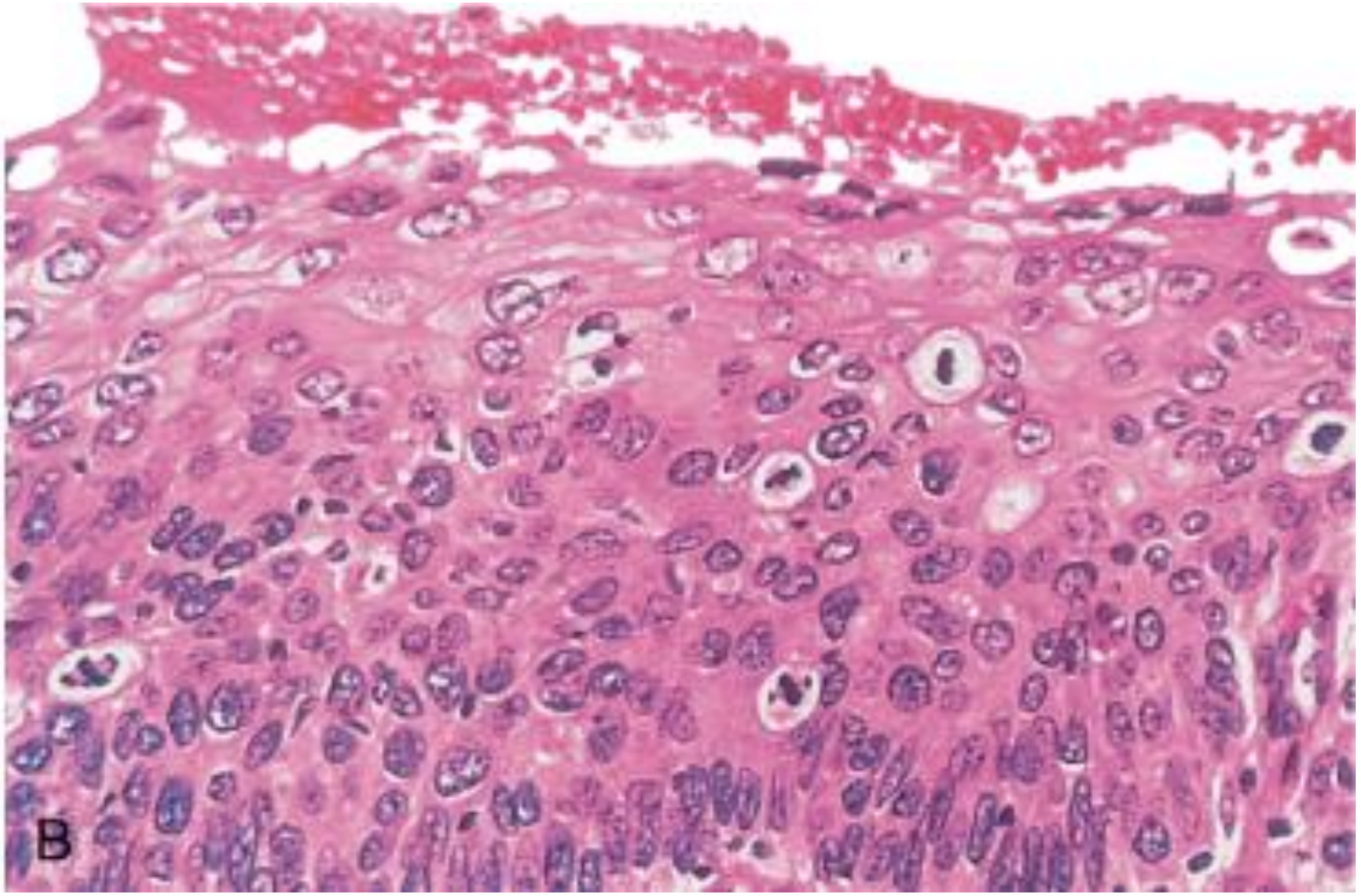
- Once the tumor cells move beyond the normal confines, the tumor is said to be *invasive.*
- Dysplastic changes are often found adjacent to foci of invasive carcinoma,

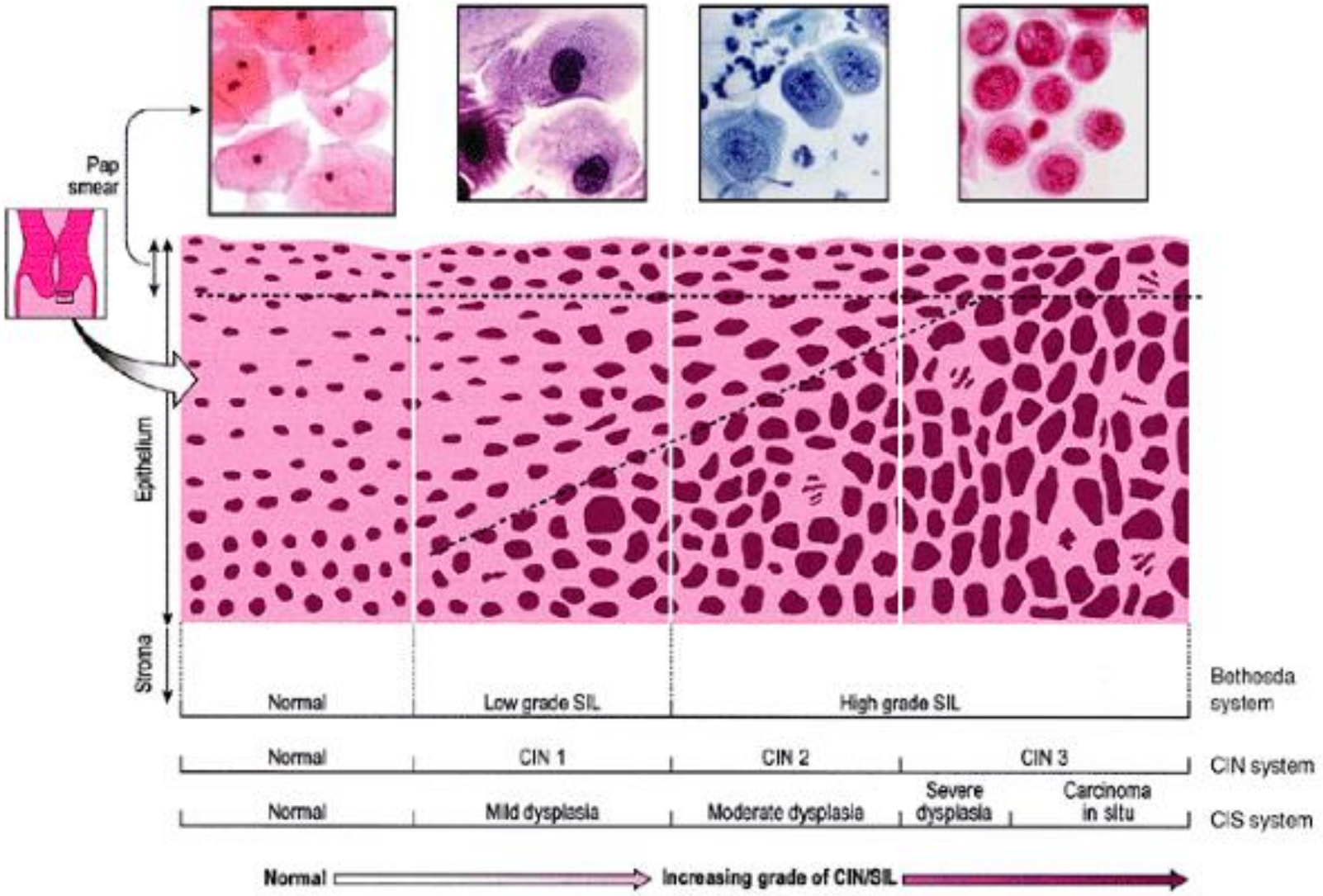
- In long-term cigarette smokers and Barrett esophagus, severe epithelial dysplasia frequently antedates the appearance of cancer.

- Mild to moderate changes that do not involve the entire thickness of epithelium may be reversible,

- With removal of the inciting causes, the epithelium may revert to normal.

Failure of normal differentiation, marked nuclear and cellular pleomorphism, and numerous mitotic figures extending toward the surface.




Pap smear
Epithelium
Stroma
Normal
Low grade SIL
High grade SIL
Bethesda system
Normal
CIN 1
CIN 2
CIN 3
CIN system
Normal
Mild dysplasia
Moderate dysplasia
Severe dysplasia
Carcinoma in situ
CIS system
Normal
Increasing grade of CIN/SIL
Moving from left (low grade) to right (high grade) there is differentiation, maturation and stratification taking place higher in the epithelium but absent at extreme right
↓Cytoplasm
↑Nuclear size
↑Pleomorphism
↑Nuclear anisokaryosis
↑Nuclear hyperchromasia
More mitotic figures
More abnormal mitotic figures
At all levels in epidermis

Abnormal Growth Involving Both Differentiation & Maturation: Dysplasia

Nuclear abnormalities

- Increased size of the nucleus, both absolute and relative to the amount of cytoplasm (increased nuclear:cytoplasmic ratio);
- Increased chromatin content (hyperchromatism);
- Abnormal chromatin distribution (coarse clumping); and
- Nuclear membrane irregularities such as thickening and wrinkling

Cytoplasmic Abnormalities
in dysplasia

Result from failure of normal differentiation

- Lack of keratinization in squamous cells
- Lack of mucin in glandular epithelium.

Increased rate of cell multiplication

- In squamous epithelium, an increased rate of cellular multiplication is characterized by the presence of mitotic figures in many layers of the epithelium—in contrast to the normal state, in which mitosis is limited to the basal layer.

- Individual mitoses are morphologically normal in dysplasia.

Disordered Maturation

- Dysplastic epithelial cells retain a resemblance to basal stem cells as they move upward in the epithelium;
- Normal differentiation (keratin production) fails to occur.

- Dysplasia grading as mild, moderate, or severe.

Significance of Dysplasia
premalignant lesion

- One step short of cancer

- With cancer a general term for invasive, aggressive growths that are more properly called malignant neoplasms.

- In the uterine cervix, the relationship of dysplasia to cervical cancer is so intimate that the term cervical intraepithelial neoplasia (CIN) is used synonymously with the term dysplasia

- **Carcinoma in situ** is a true neoplasm with all of the features of malignant neoplasms except invasiveness

The risk of developing invasive cancer varies

- (1) Grade
- (2) Duration
- (3) Site

Differences between Dysplasia & Cancer

Lack of Invasiveness

Reversibility

- Does not invade the basement membrane.
- Complete removal of the dysplastic area is therefore curative.

- Cancer, in contrast, invades the basement membrane and spreads from the local (primary) site via lymphatics and blood vessels, so that excision of the primary site may not be curative.

Diagnosis of Dysplasia

Gross Examination

- Usually asymptomatic,
- Many cases gross examination of the mucosa shows no abnormality
- Special examination techniques (colposcopy, fluorescent bronchoscopy)

- Lack of cellular differentiation of the dysplastic epithelium

Microscopic Examination

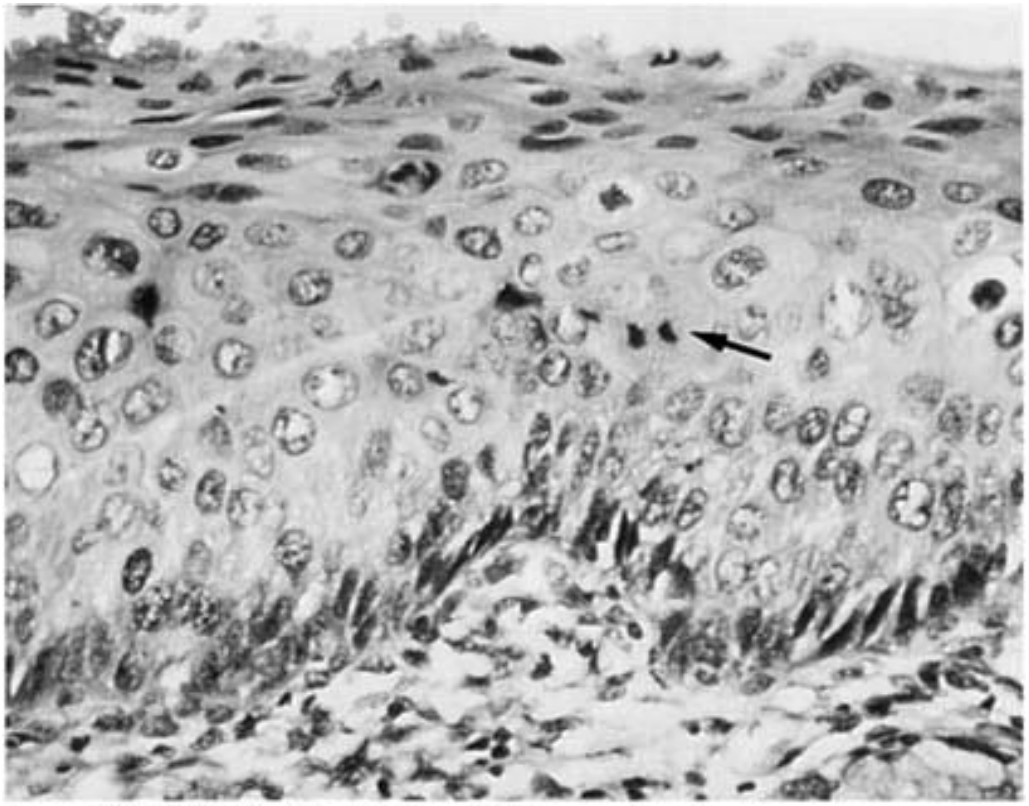
Cytologic findings (in cell smears) must be confirmed by biopsy

- Smears are made from material scraped from the epithelium for cytologic diagnosis ; tissue obtained by biopsy is necessary for histologic diagnosis .

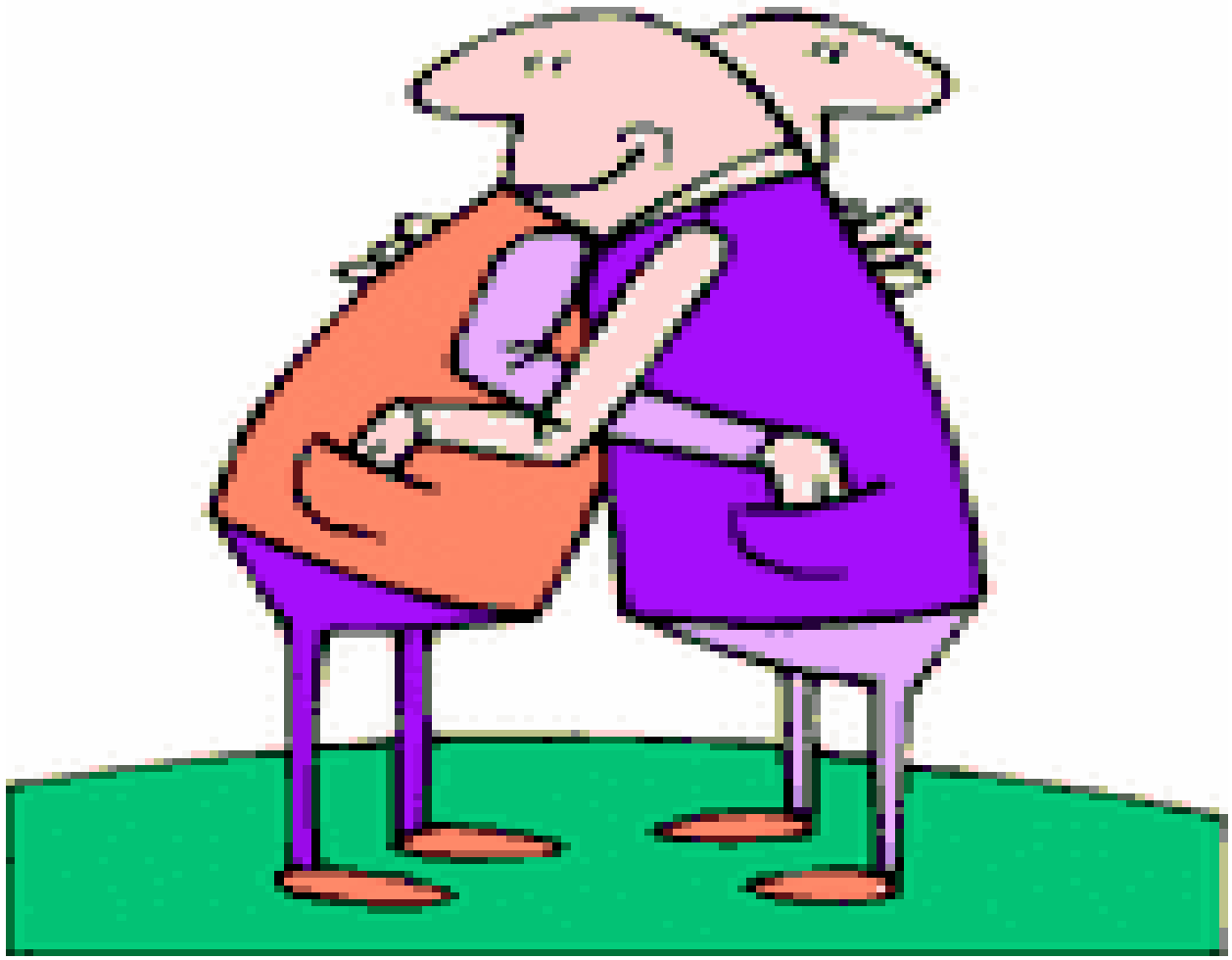
- Nuclear & cytoplasmic features of dysplastic tissue provides evidence for both diagnosis and grading of dysplasia.

- The criteria for cytologic diagnosis of dysplasia are well established for the cervix, urinary bladder, and lung.

Moderate dysplasia



- Routine cytologic screening of Papanicolaou cervical smears has permitted early detection and treatment of cervical dysplasia
- Striking decline in incidence of cancer of the uterine cervix
- The results of cytologic screening in other sites have not been as encouraging



Have a nice day!

- 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."

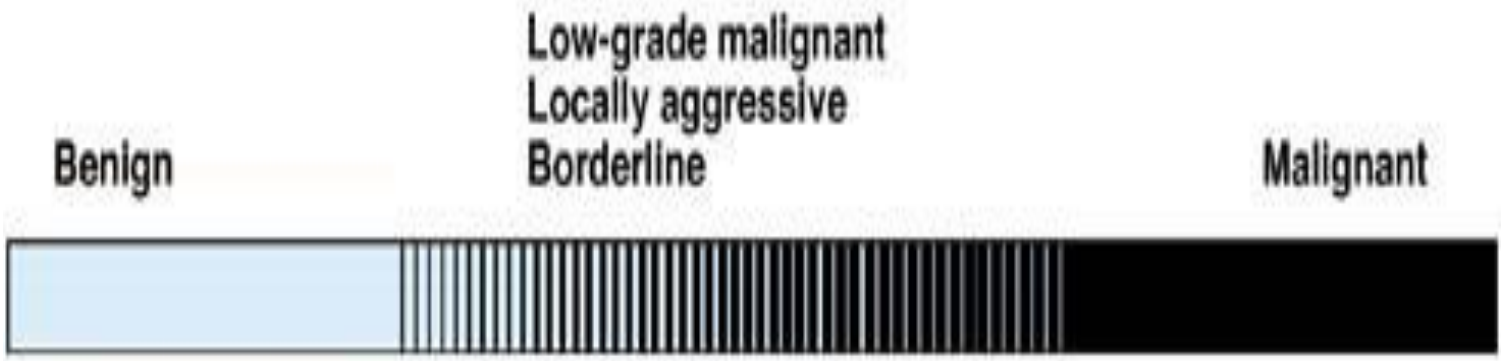
Neoplasia

Abnormality of cellular differentiation, maturation, and control of growth

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

Biologic Behavior of Neoplasms
Spectrum with two extremes:



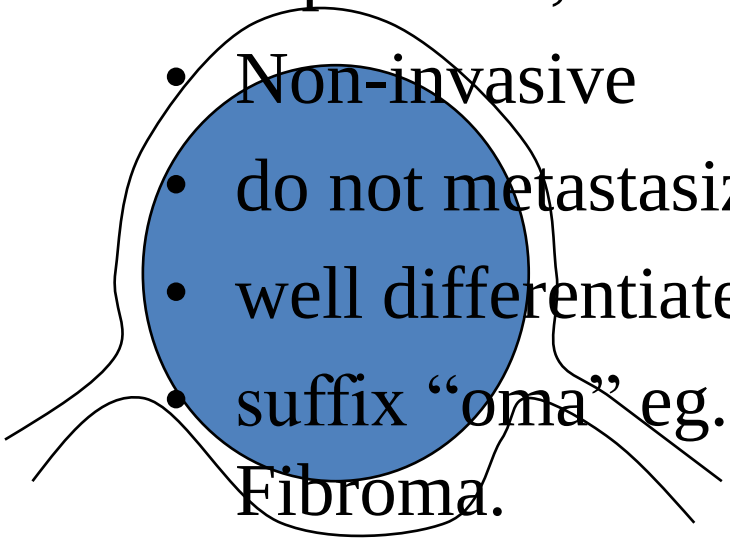
- Slow growth rate
- No infiltration
- No metastasis
- High patient survival rates after successful surgical removal

- 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)

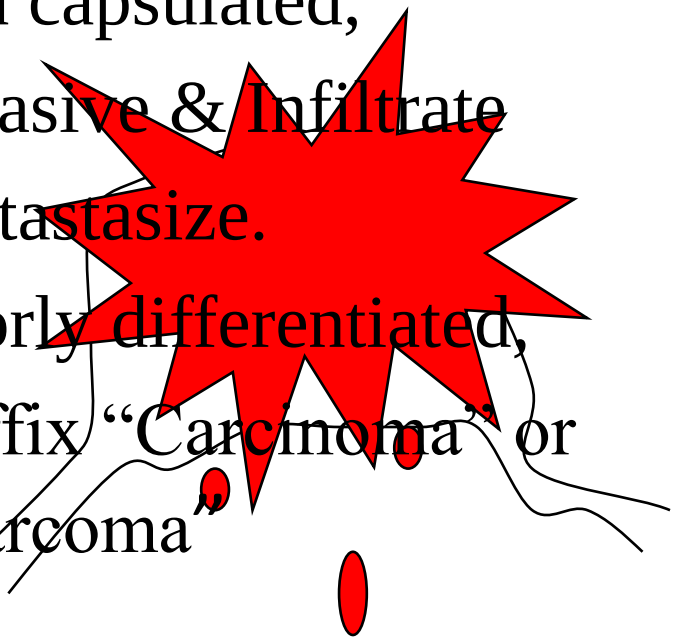
Benign

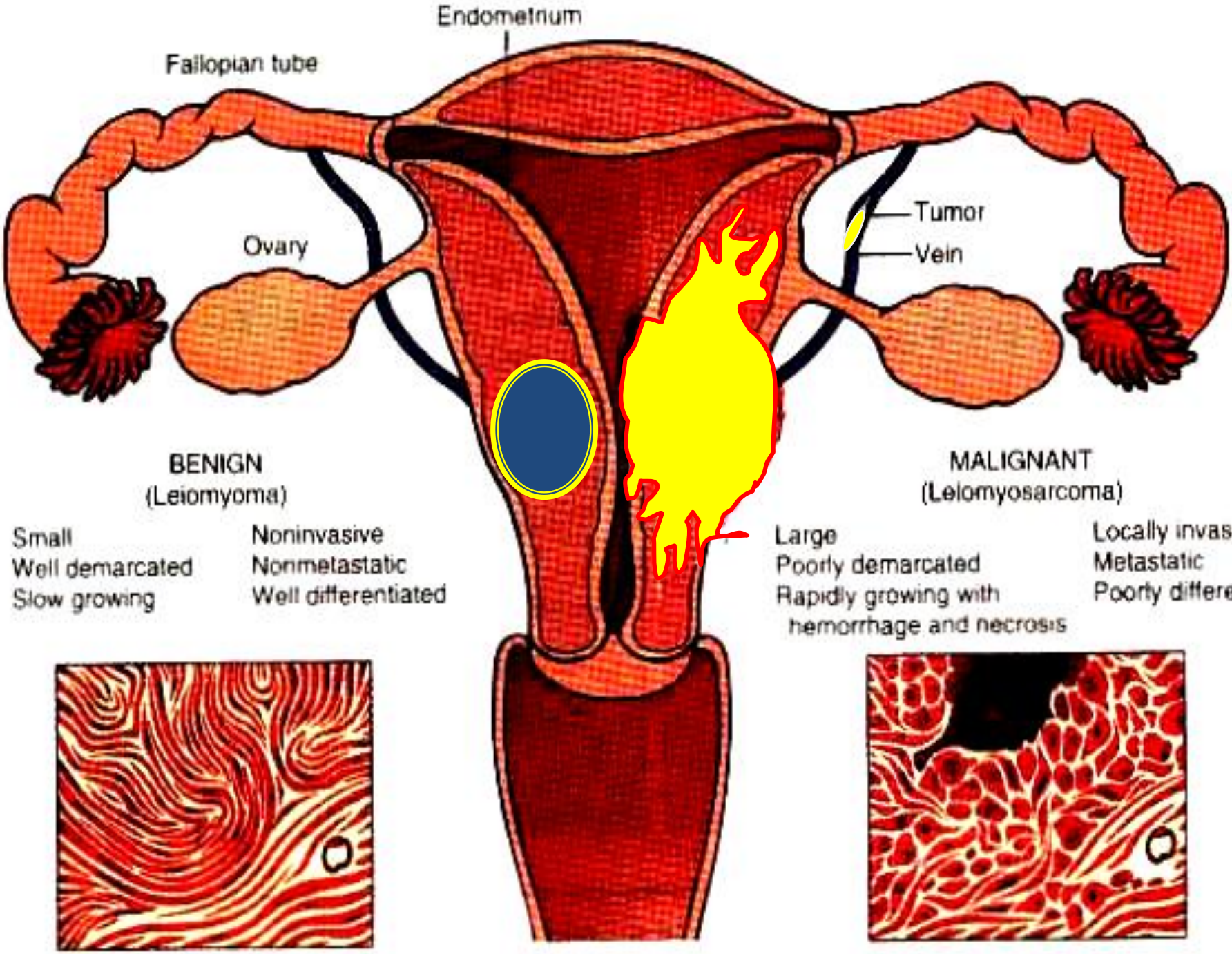
- Slow growing,
- capsulated,
- Non-invasive
- do not metastasize,
- well differentiated,
- suffix “oma” eg. Fibroma.



Malignant:

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




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.

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 (e.g., 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

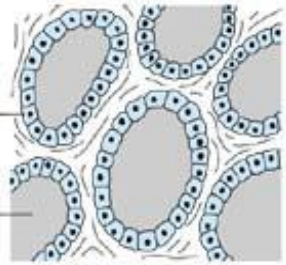
Degree of Differentiation

- 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

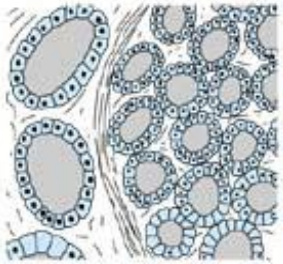
- Malignant neoplasms, on the other hand, show variable degrees of differentiation and frequently demonstrate little resemblance to normal tissue (ie, they are poorly differentiated).
- In **anaplasia,** the neoplastic cells have no morphologic resemblance whatsoever to normal tissue.

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.

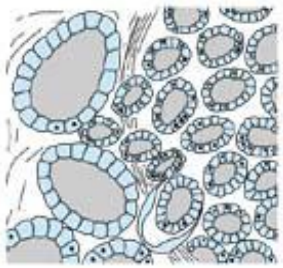


Normal thyroid



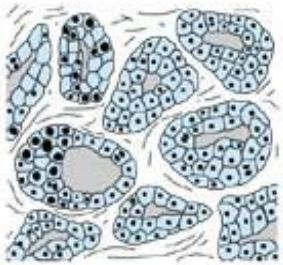
Does not metastasize

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.



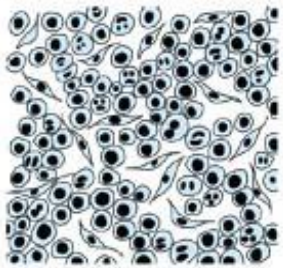
Metastatic potential +

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.

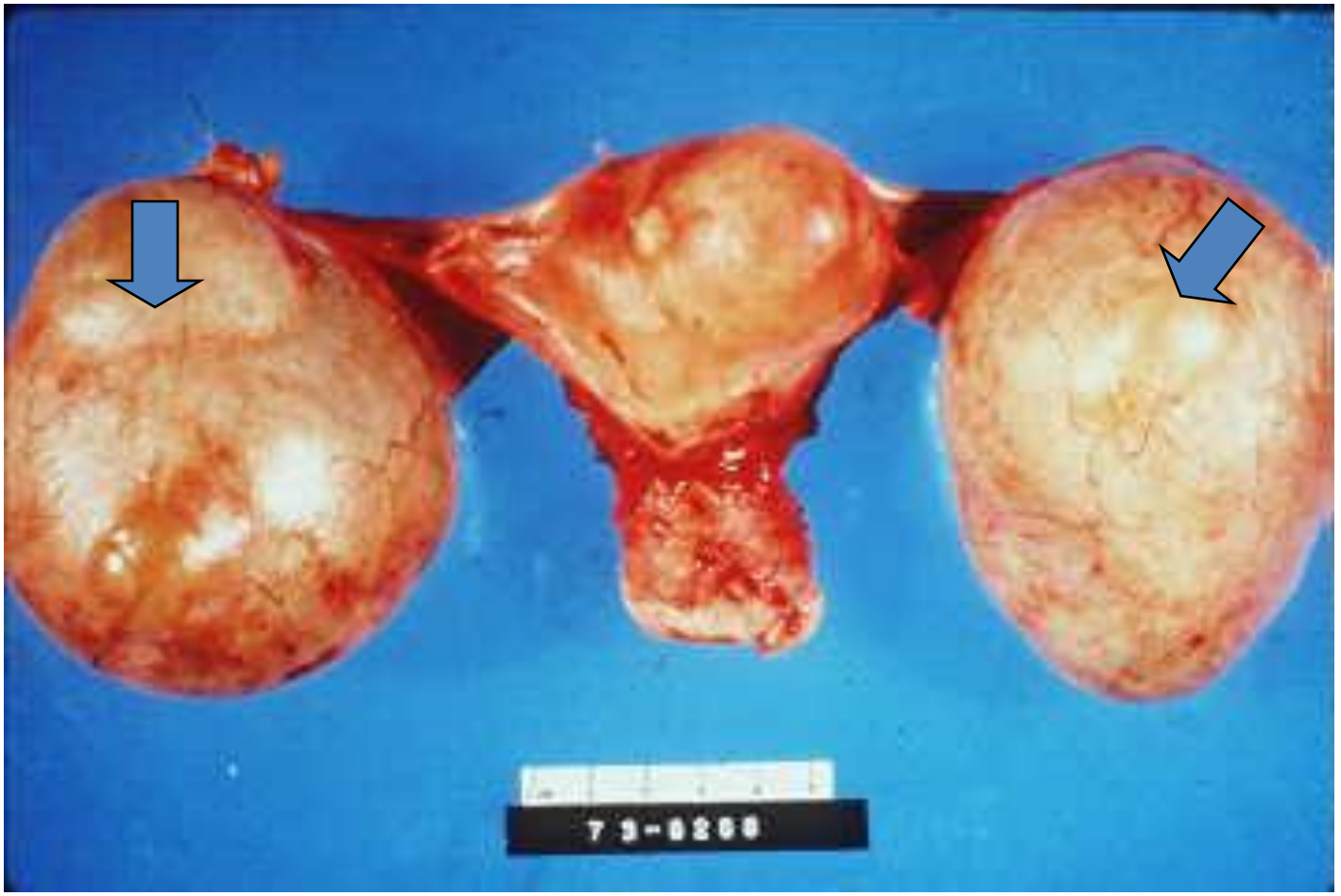
- Many exceptions to this rule exist, and some benign neoplasms—eg, granular cell tumor, dermatofibroma, and carcinoid tumors—lack a capsule and have an infiltrative margin.

Metastasis

- Absolute evidence of malignancy.

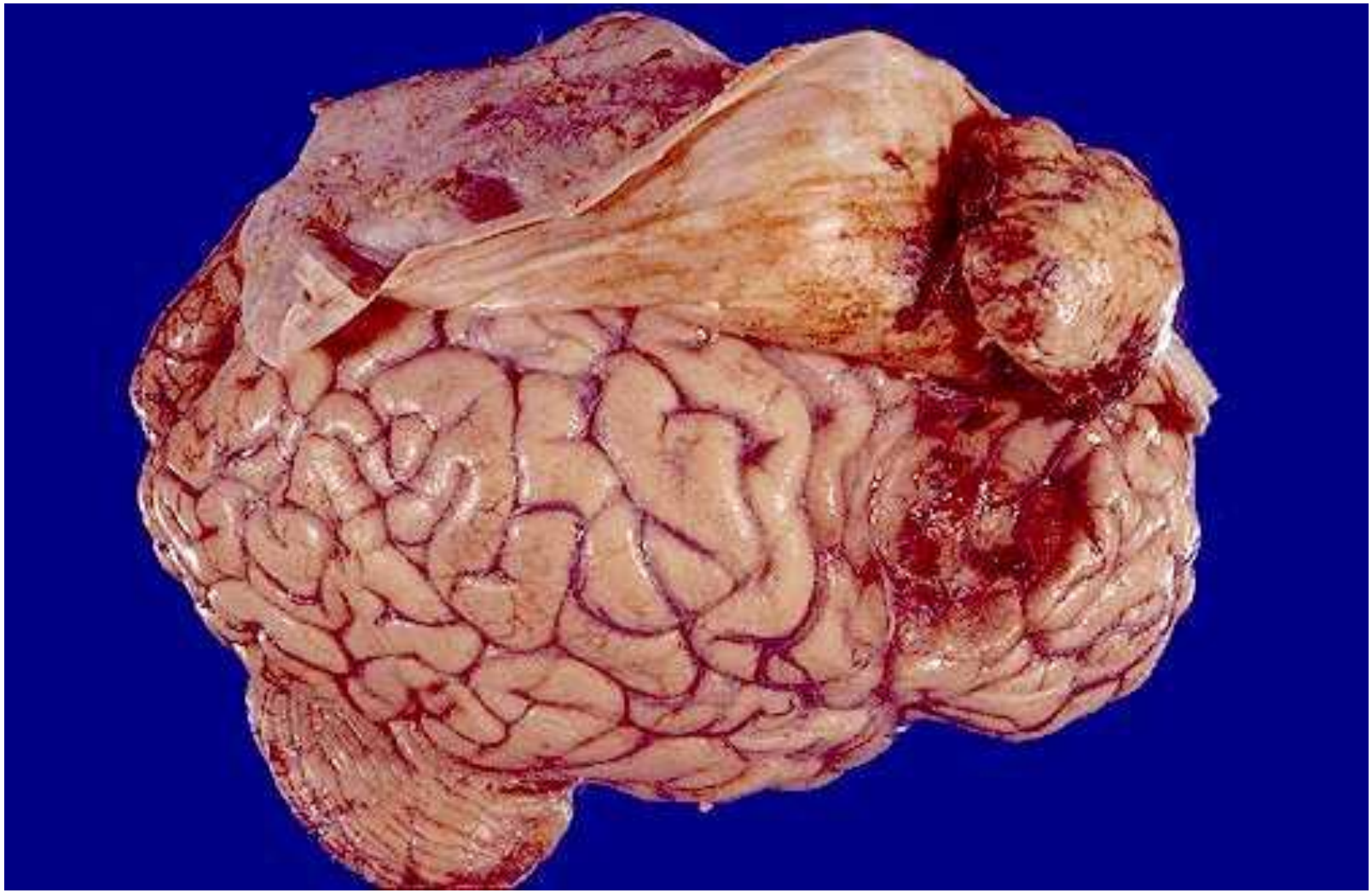
- The major reason for distinguishing benign from malignant neoplasms is to be able to predict their ability to metastasize before they do so.

Bilateral Cystadenoma Ovary:

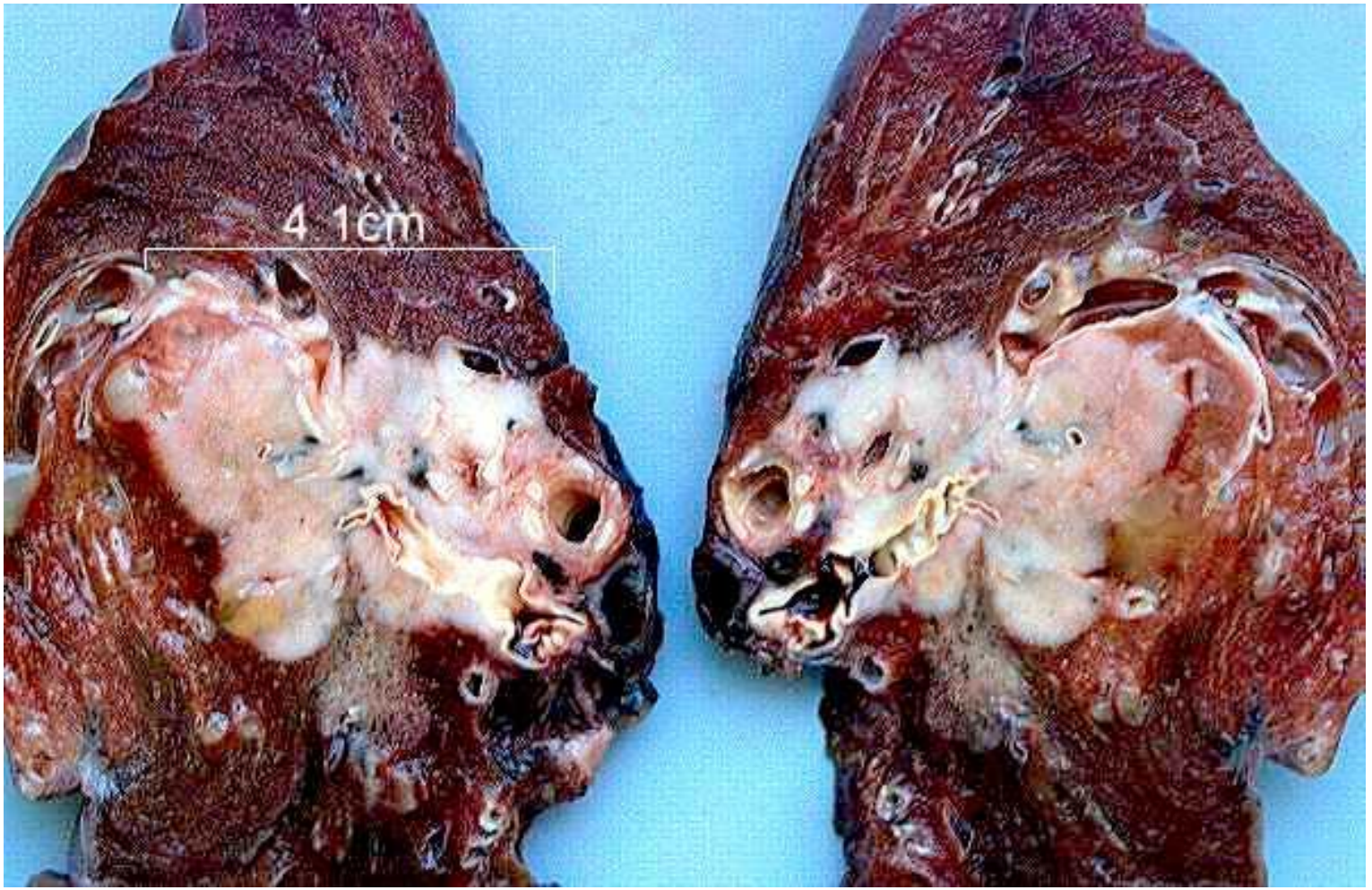


Lipoma Intestine:

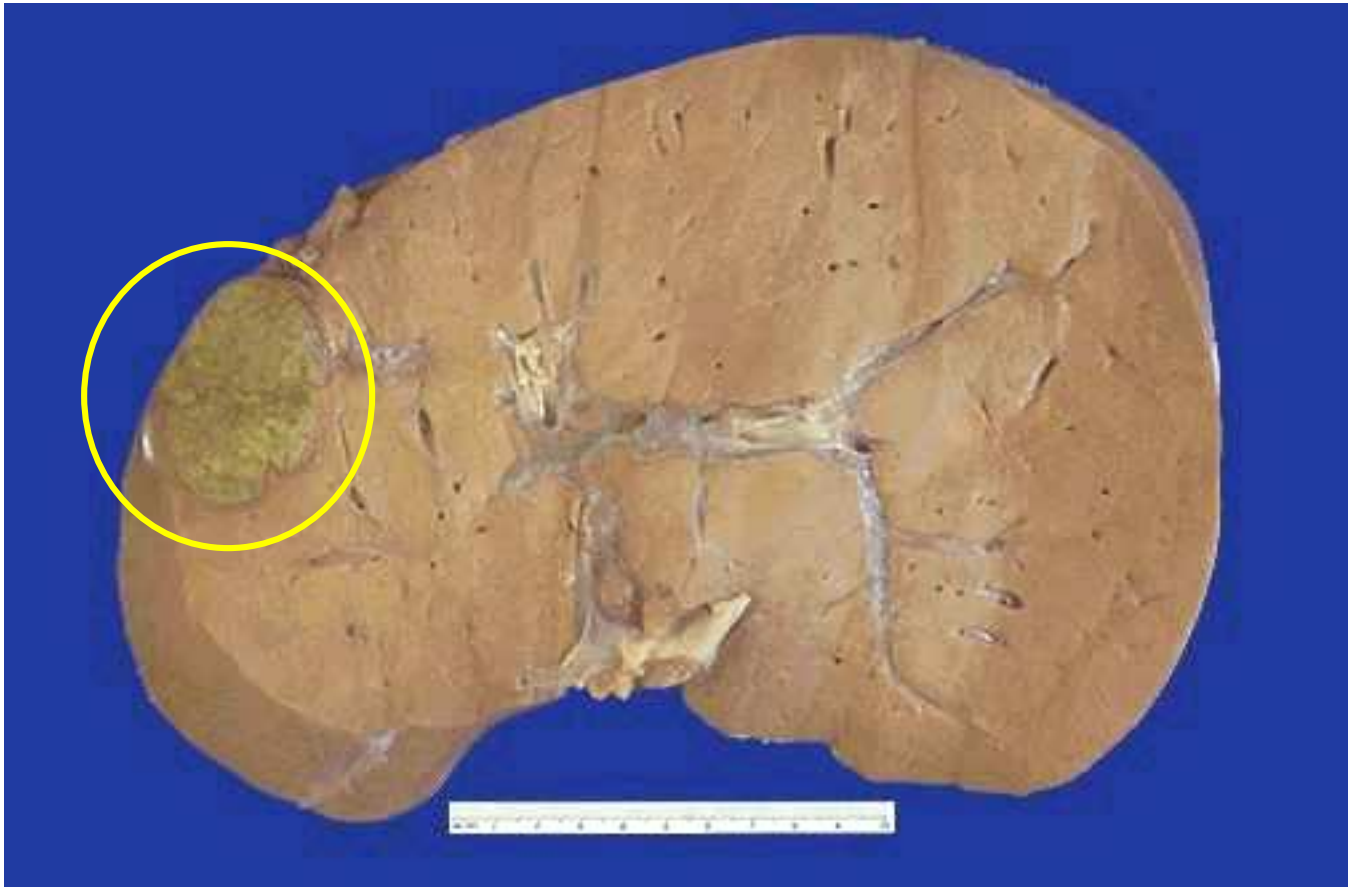
meningioma



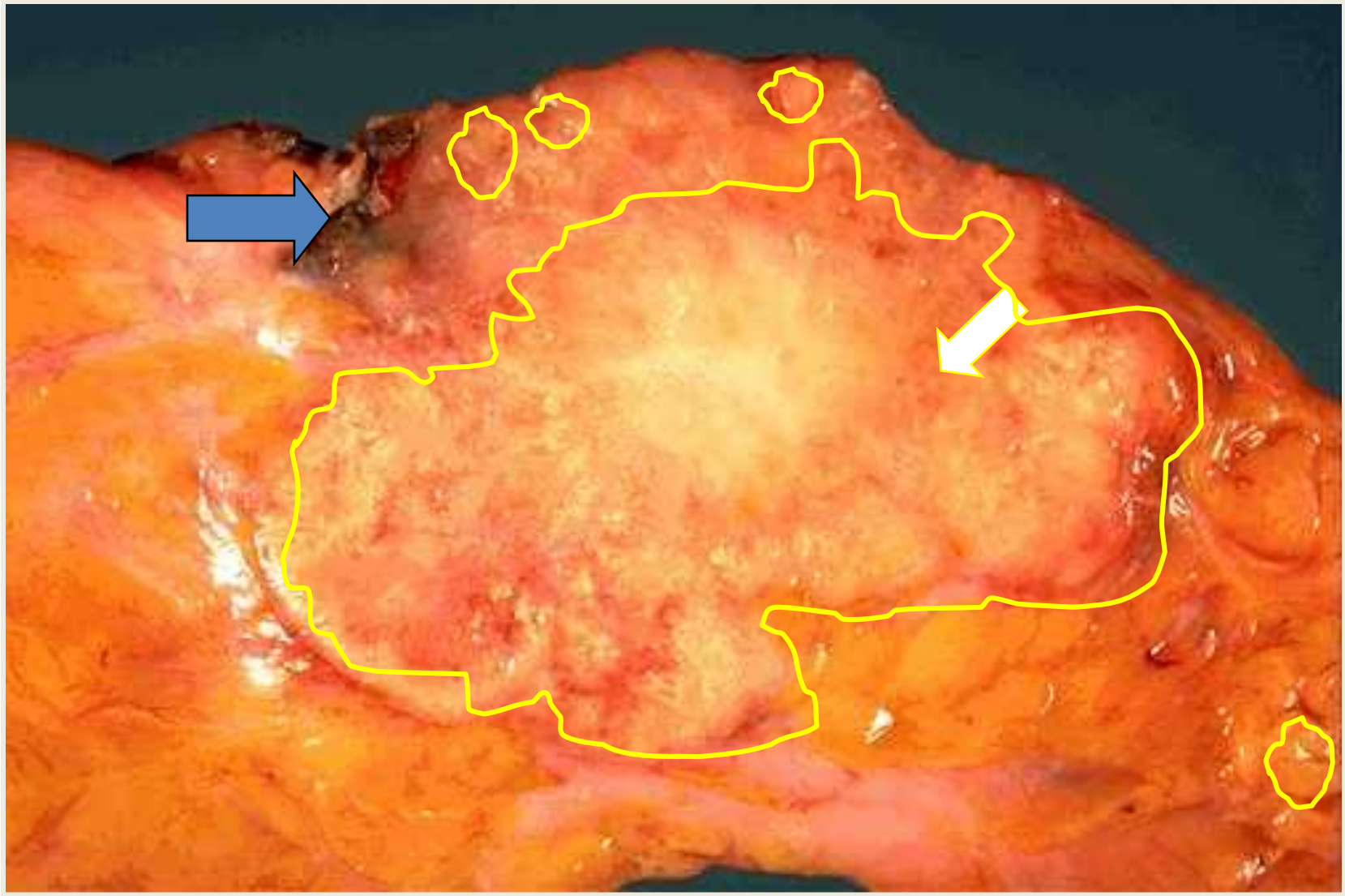
Lung carcinoma



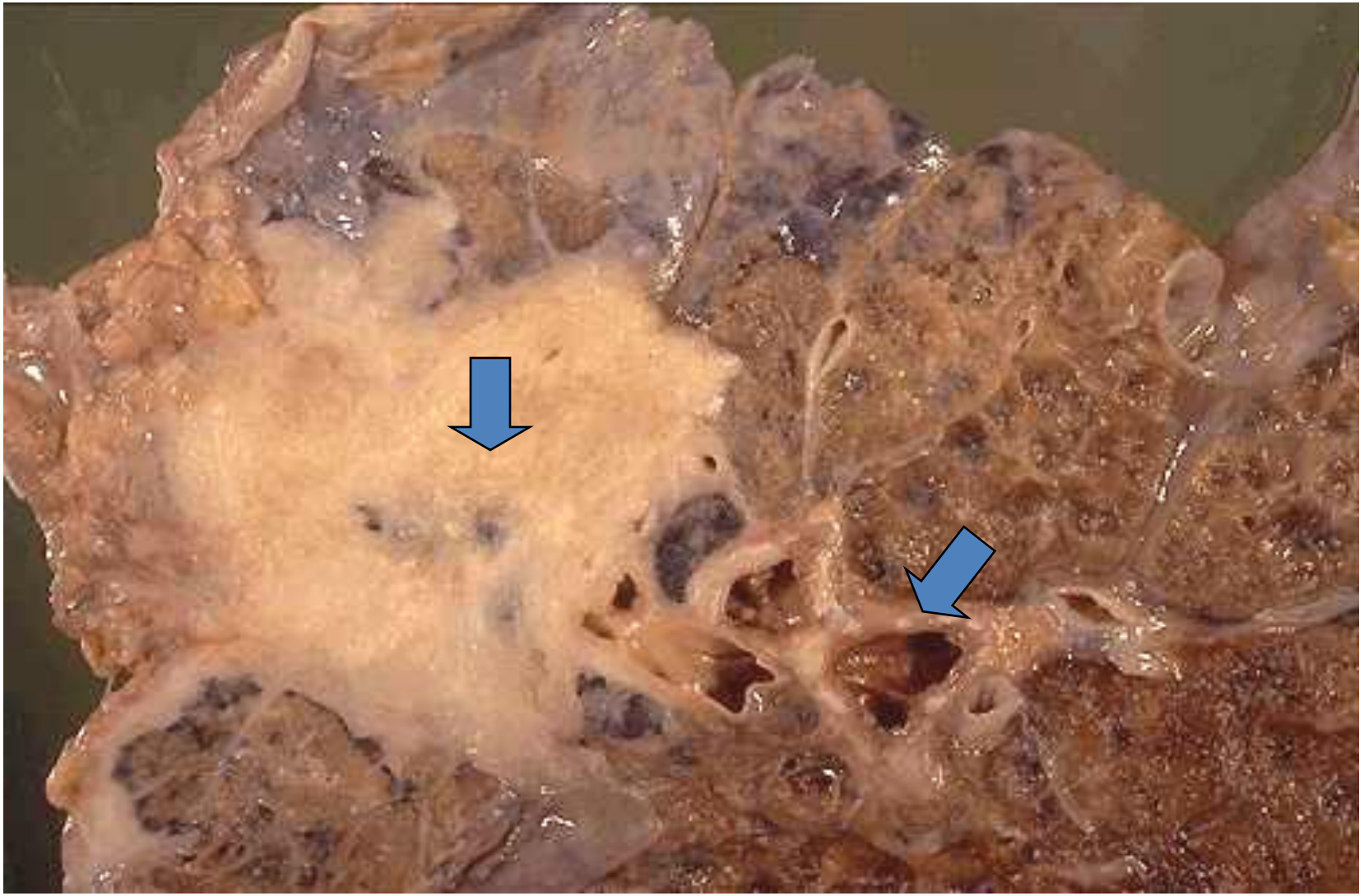
Hepatic Adenoma:



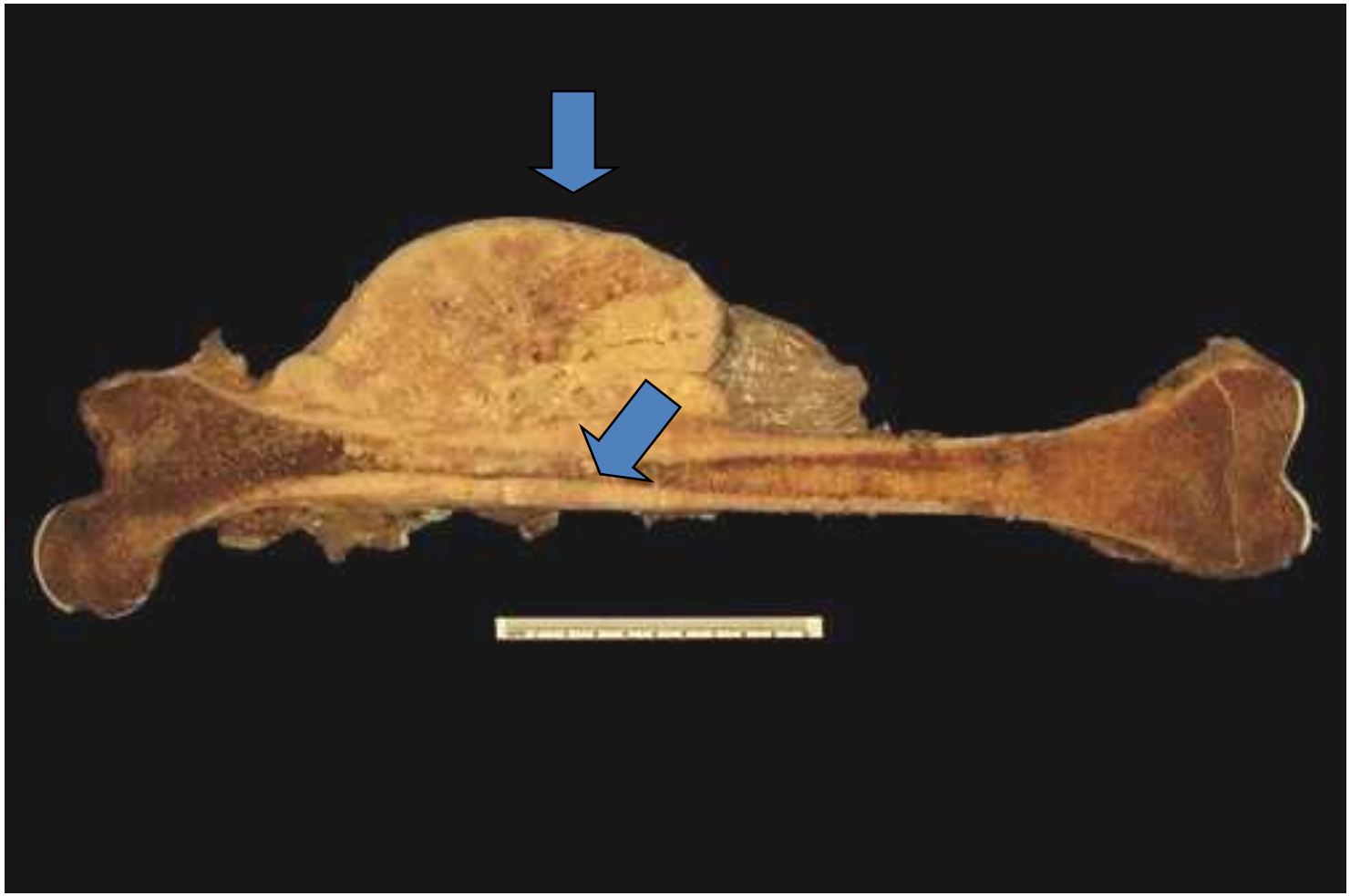
Carcinoma Breast:



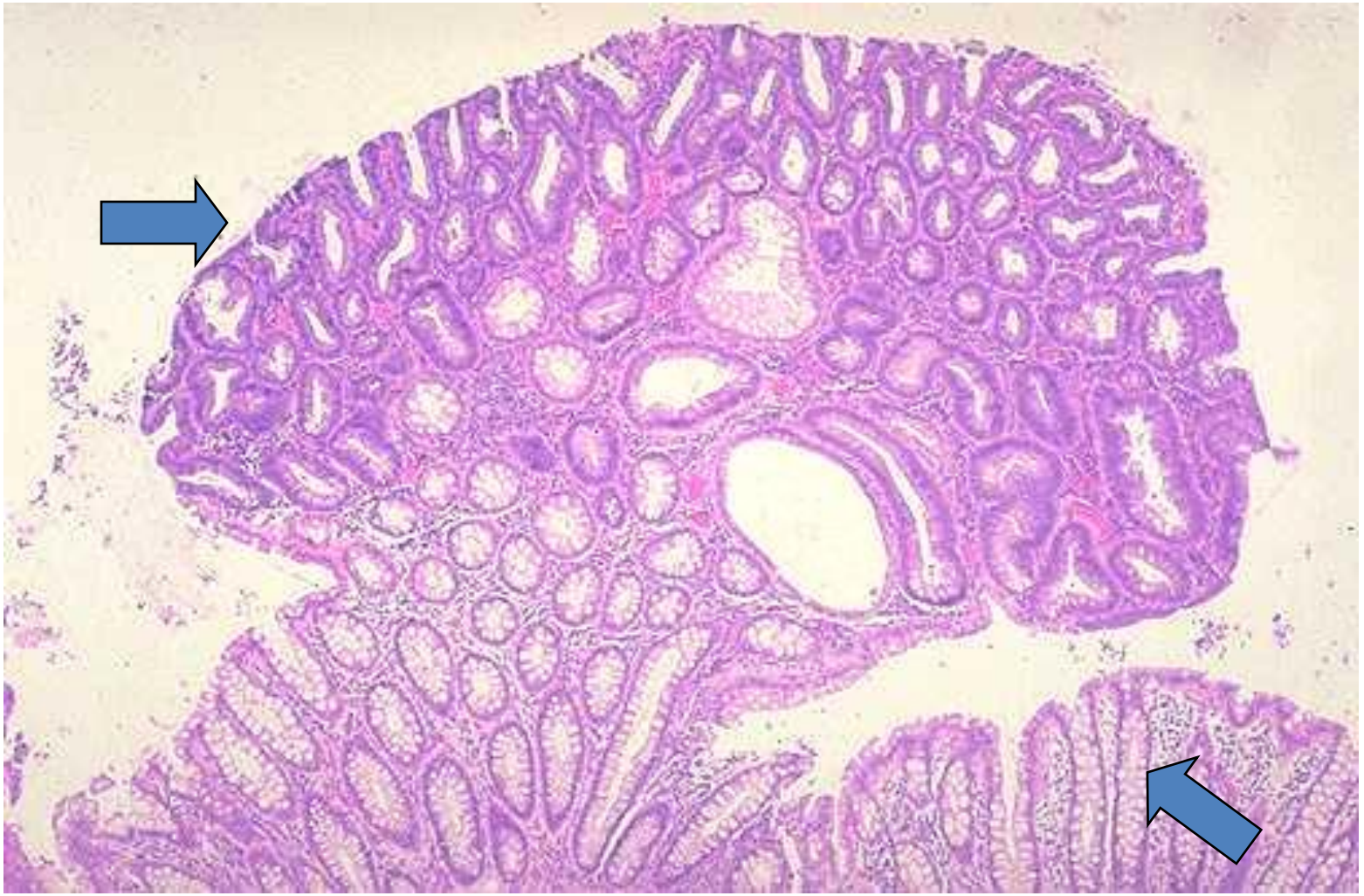
Carcinoma Lung:



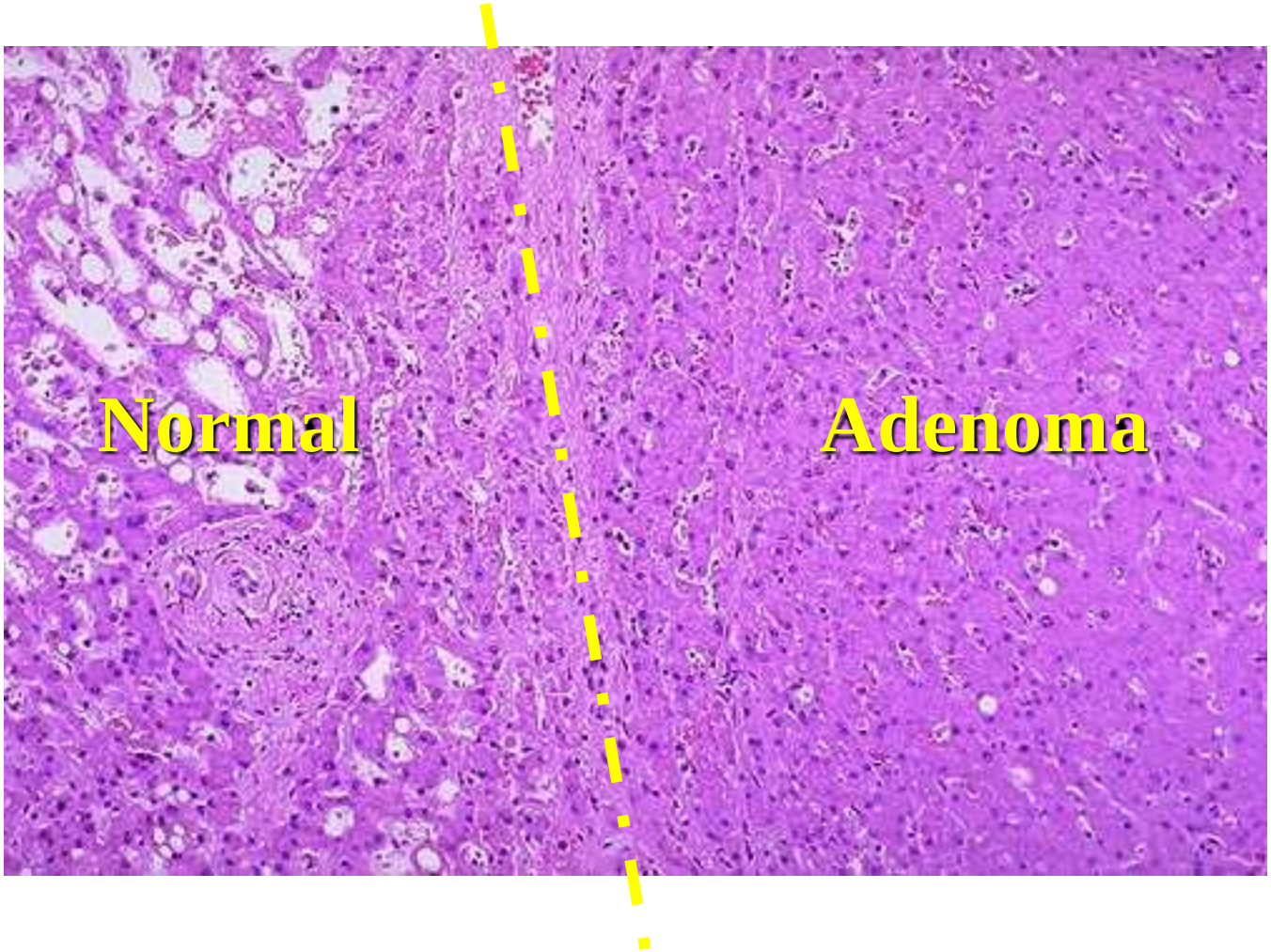
Osteo - sarcoma:



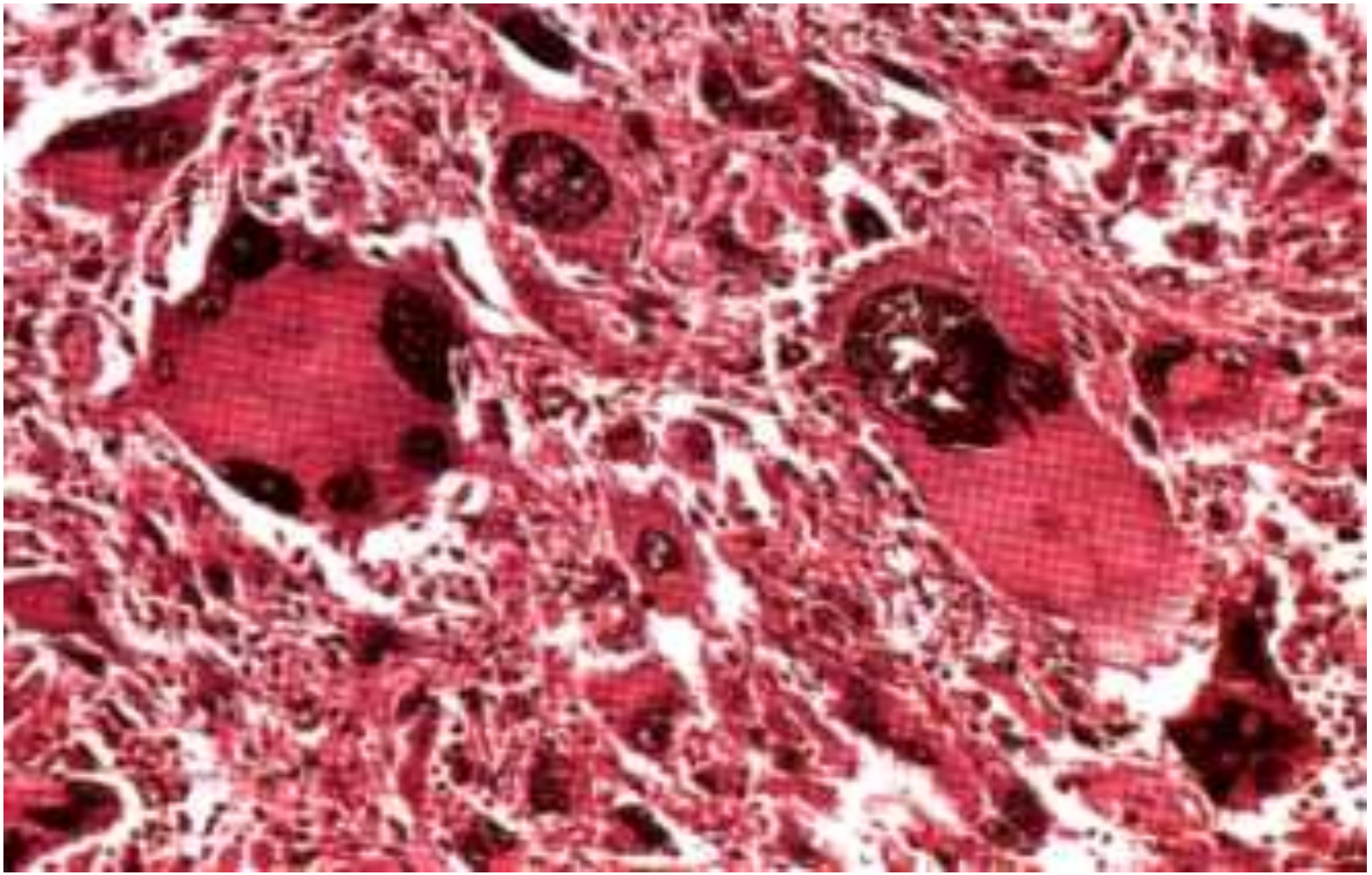
Colon Polyp:



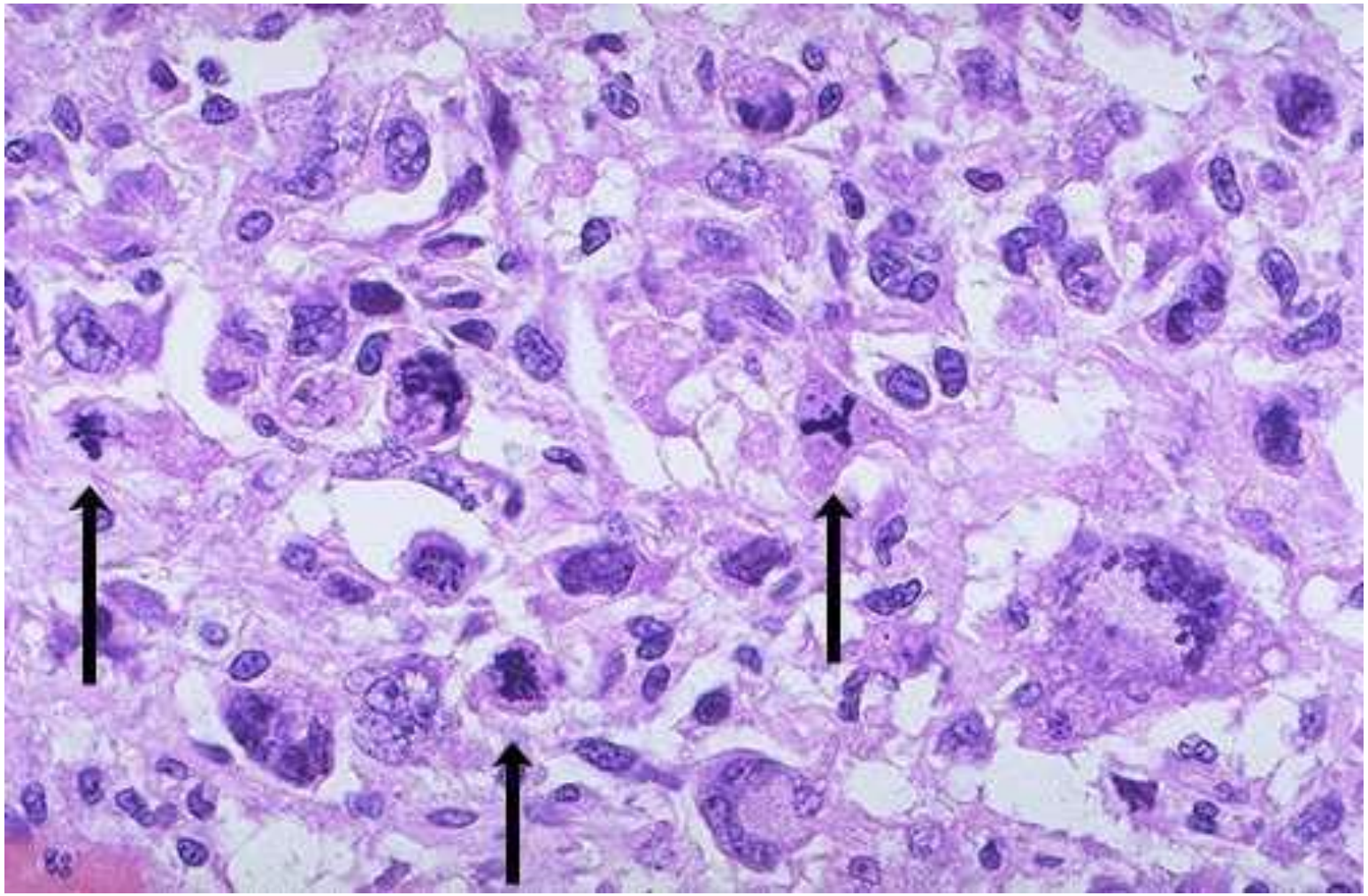
Hepatic Adenoma:



Anaplasia in Sarcoma:

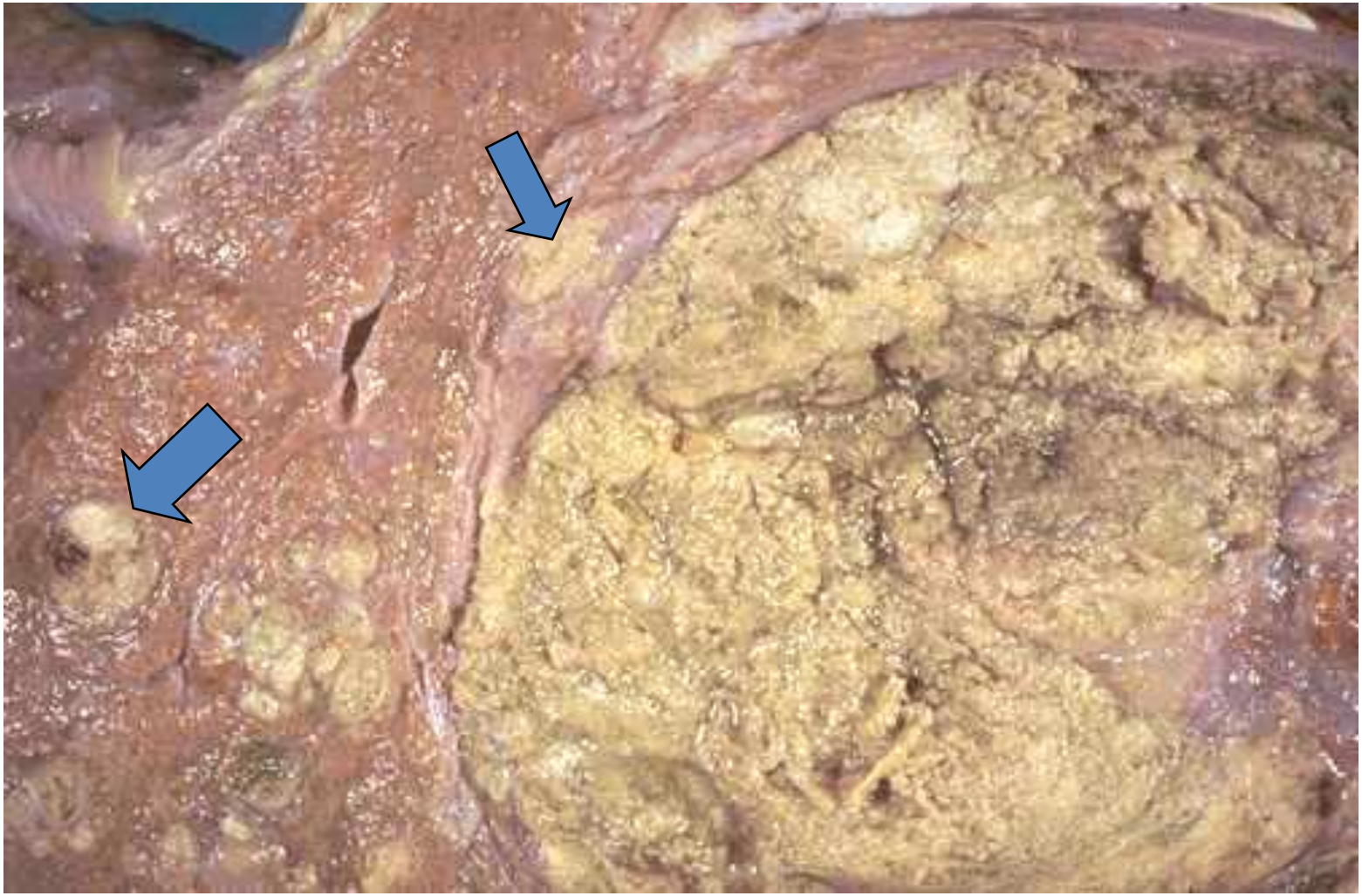


Anaplasia:

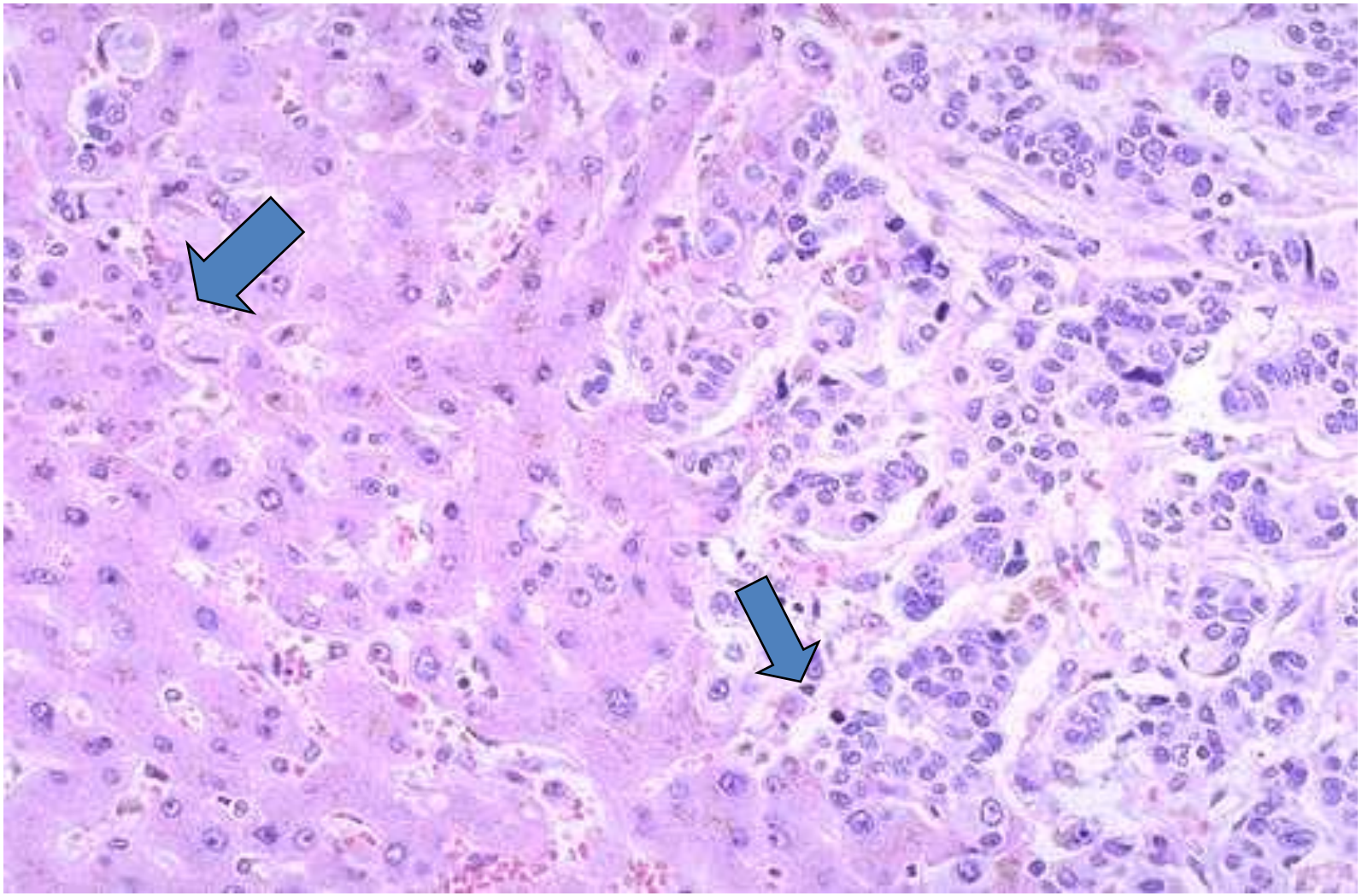


Hepatic Adenocarcinoma:

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.