NEOPLASIA I

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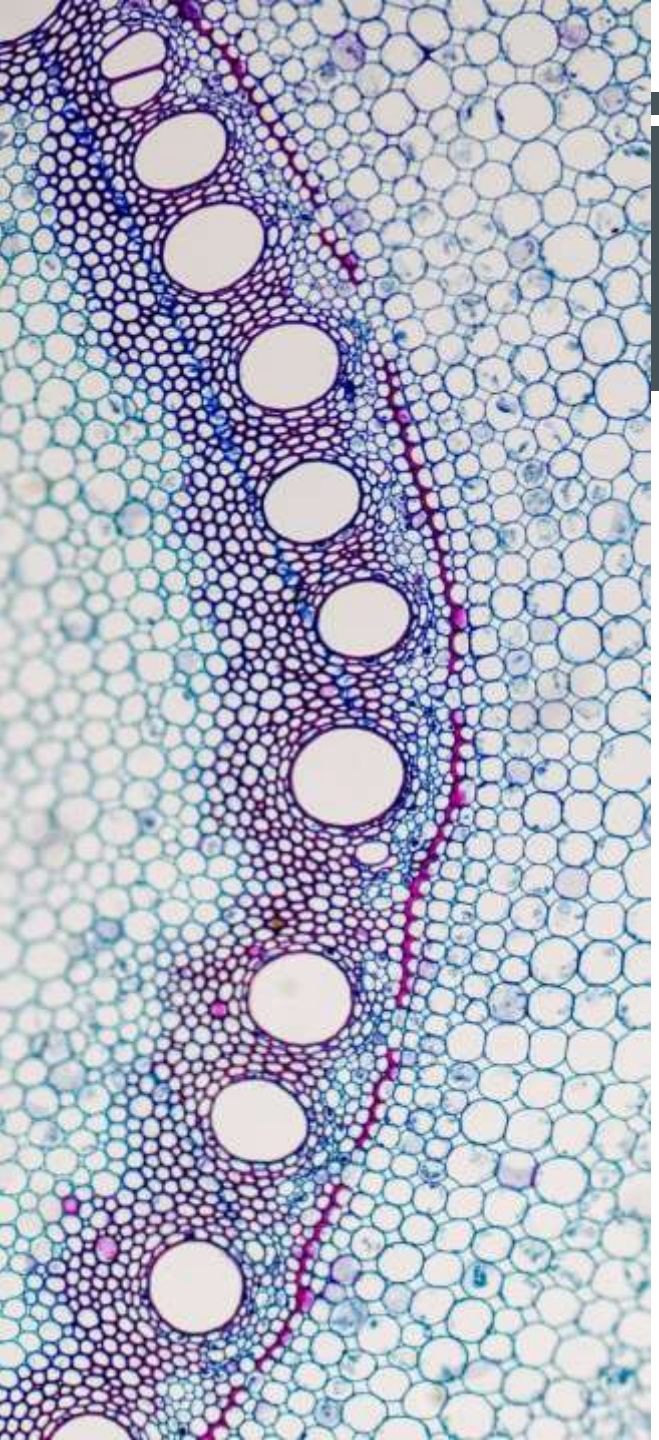
LECTURE OUTLINE

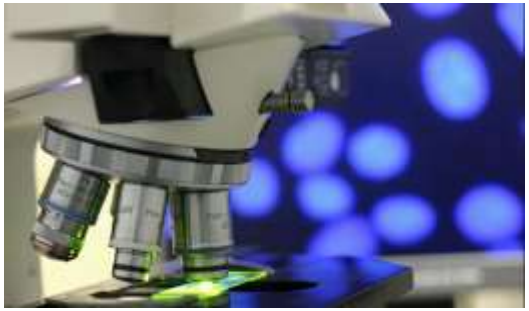
- Classification (benign, malignant and mixed tumors)
- Definition
- Nomenclature of tumors and Misnomers
- Differentiation and Anaplasia
- Metaplasia and Dysplasia
- Local invasion
- Metastasis
- Pathways of spread
- Epidemiology
- Etiology and Risk factors



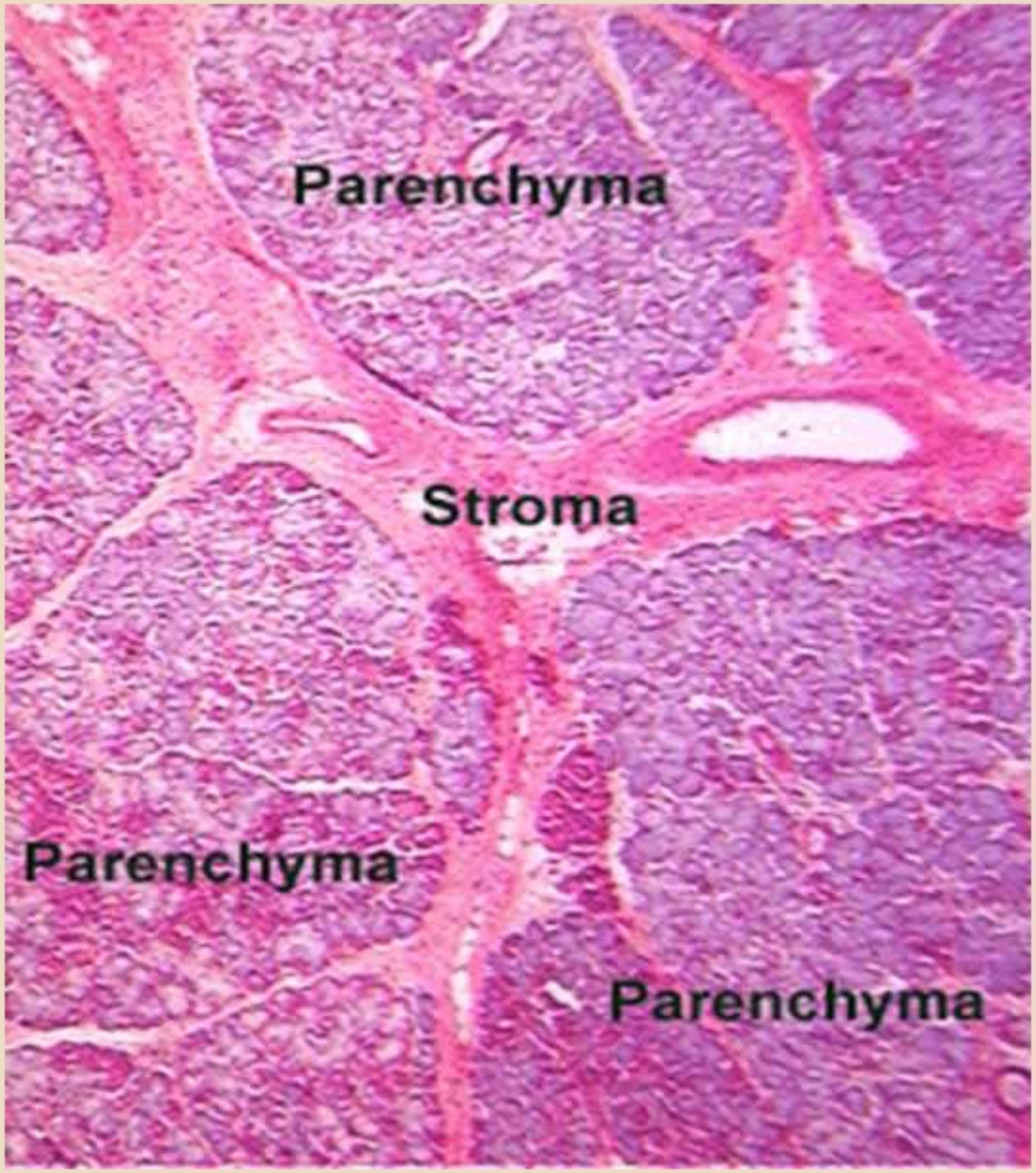
- ***Neoplasia*** means "new growth," and a new growth is called a *neoplasm*.
- ***Tumor*** originally applied to the swelling caused by inflammation
- ***Oncology*** (Greek *oncos* = tumor) is the study of tumors or neoplasms.

- Although all physicians know what they mean when they use the term *neoplasm*. British oncologist Willis came closest: "A neoplasam is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change.

COMPONENTS OF THE TUMOR



- **Neoplastic cells** that constitute the tumor *parenchyma*
- ***Reactive stroma*** made up of connective tissue, blood vessels, and variable numbers of cells of the adaptive and innate immune system.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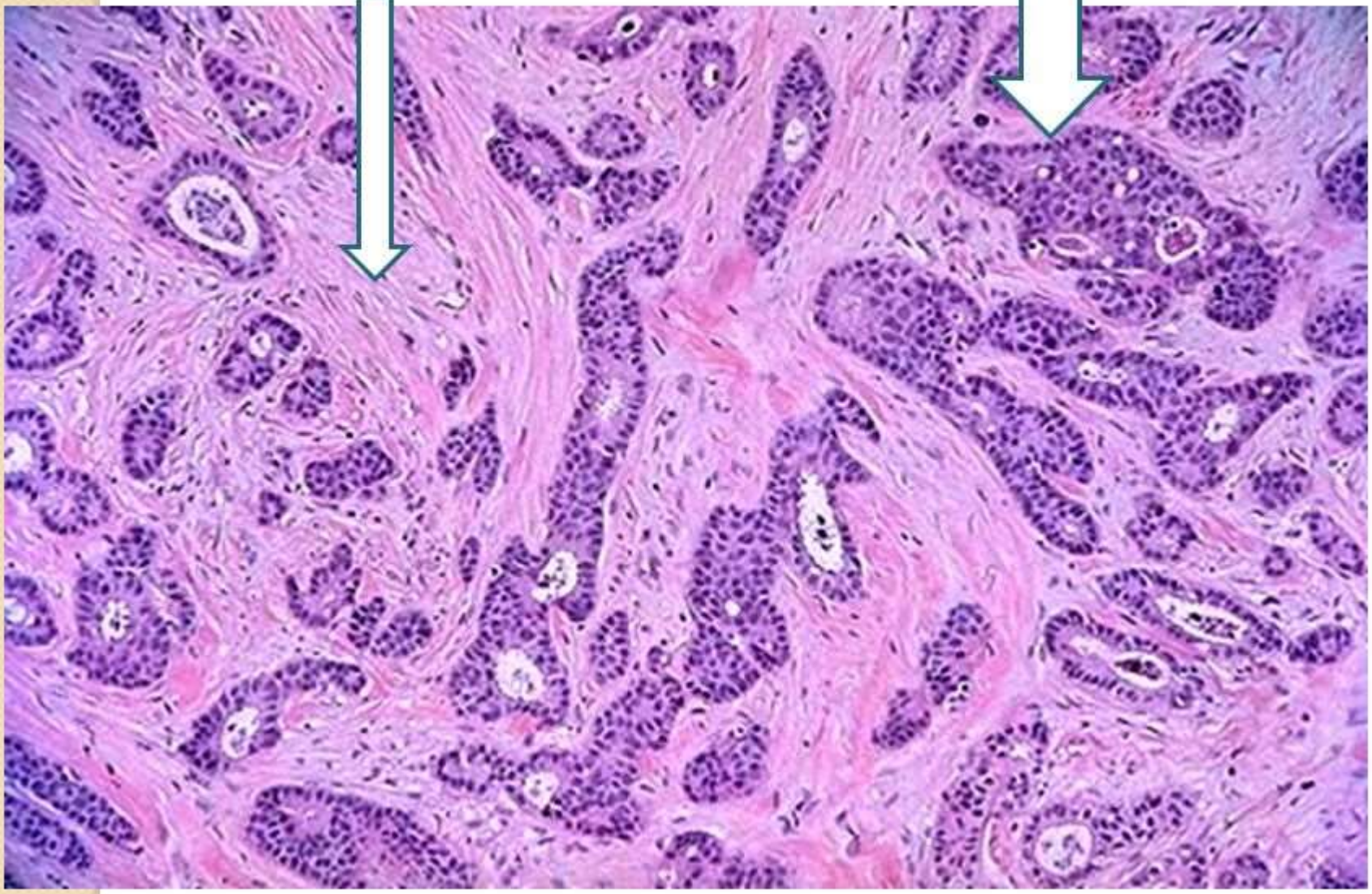
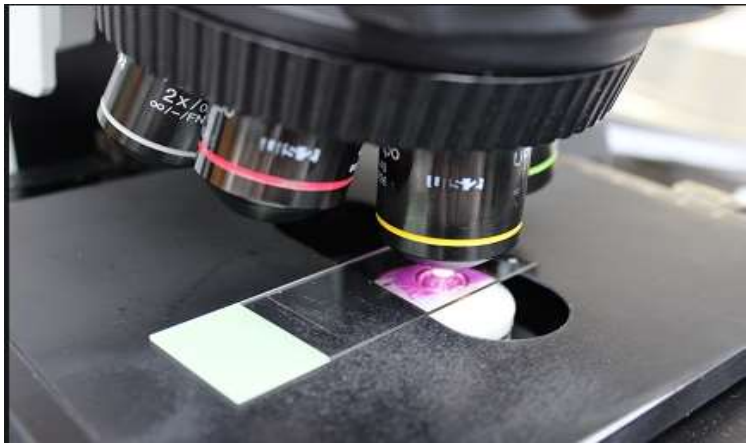
STROMA

PARENCHYMA



CLASSIFICATION OF TUMORS

- The classification of tumors and their biologic behavior are based primarily on the **parenchymal component,** but their growth and spread are critically dependent on their **stroma**.
- In some tumors, connective tissue is scant and so the neoplasm is soft and fleshy.
- In other cases, the parenchymal cells stimulate the formation of an abundant collagenous stroma, referred to as ***desmoplasia*.**
- Some demoplastic tumors—for example, some cancers of the female breast—are stony hard or *scirrhous*.



BENIGN TUMORS

- **A tumor is said to be *benign* , when its gross and microscopic appearances are considered relatively innocent, implying that it will remain localized, will not spread to other sites, and is amenable to local surgical removal;** understandably, the patient generally survives.
- However, may cause significant morbidity and are sometimes even fatal.

BENIGN TUMORS (NOMENCLATURE)

- Benign tumors are designated by attaching the suffix -oma to the name of the cell type from which the tumor originates.

- Tumors of mesenchymal cells generally follow this rule. For example, a benign tumor arising in fibrous tissue is called a fibroma, whereas a benign cartilaginous tumor is a chondroma.

- In contrast, the nomenclature of benign epithelial tumors is more complex; some are classified based on their cells of origin, others on microscopic pattern, and others on their macroscopic architecture.

BENIGN TUMORS

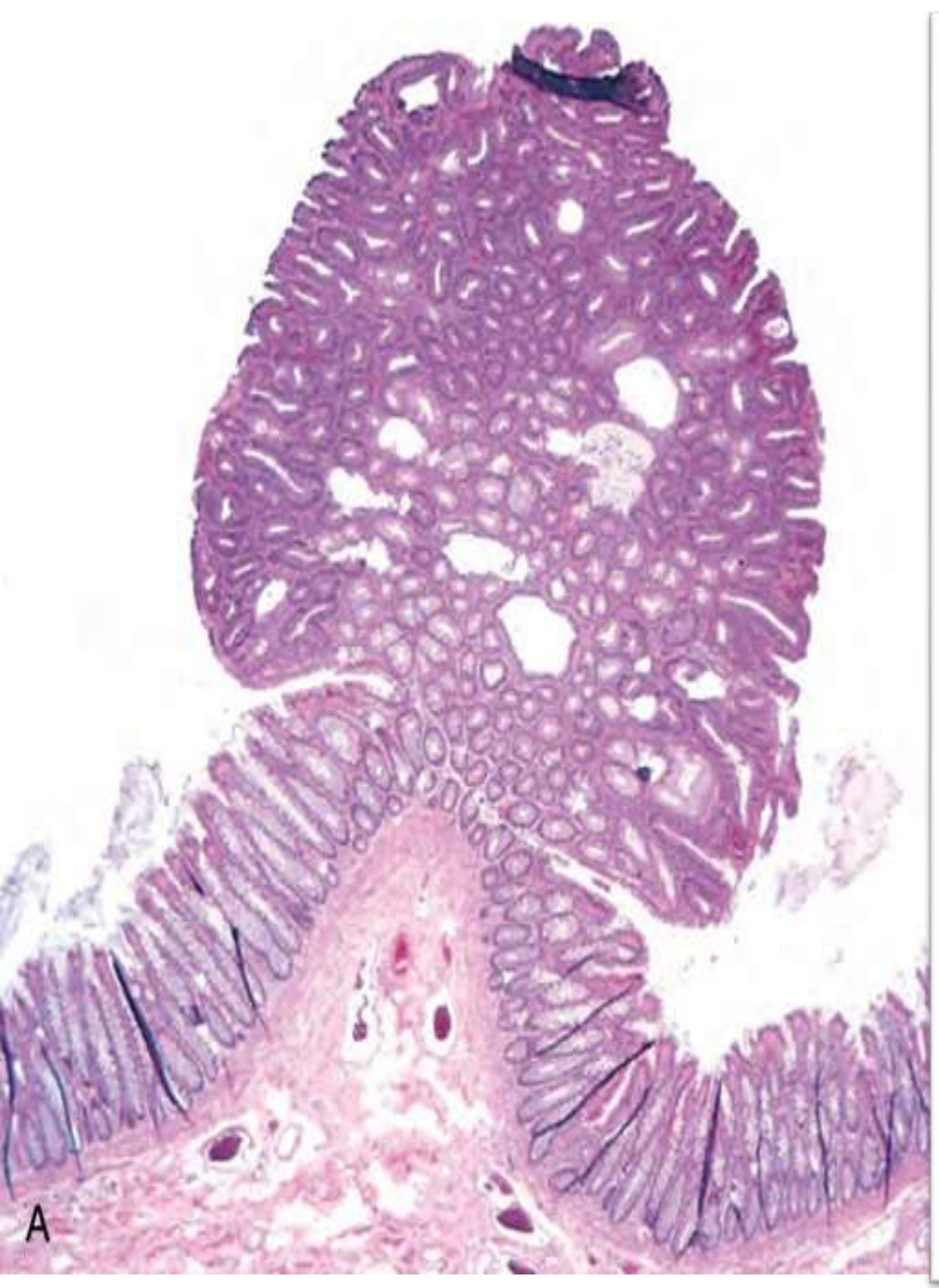
- ***Adenoma*** is applied to benign epithelial neoplasms derived from glands, although they may or may not form glandular structures.
- On this basis, a benign epithelial neoplasm that arises from renal tubular cells growing in the form of numerous tightly clustered small glands is termed an *adenoma*, as is a heterogeneous mass of adrenal cortical cells growing as a solid sheet.

BENIGN TUMORS

- Benign epithelial neoplasms producing microscopically or macroscopically visible fingerlike or warty projections from epithelial surfaces are referred to as ***papillomas***.
- Those that form large cystic masses, such as in the ovary, are referred to as ***cystadenomas***.

- Some tumors produce papillary patterns that protrude into cystic spaces and are called **papillary cystadenomas**.

HEPATIC ADENOMA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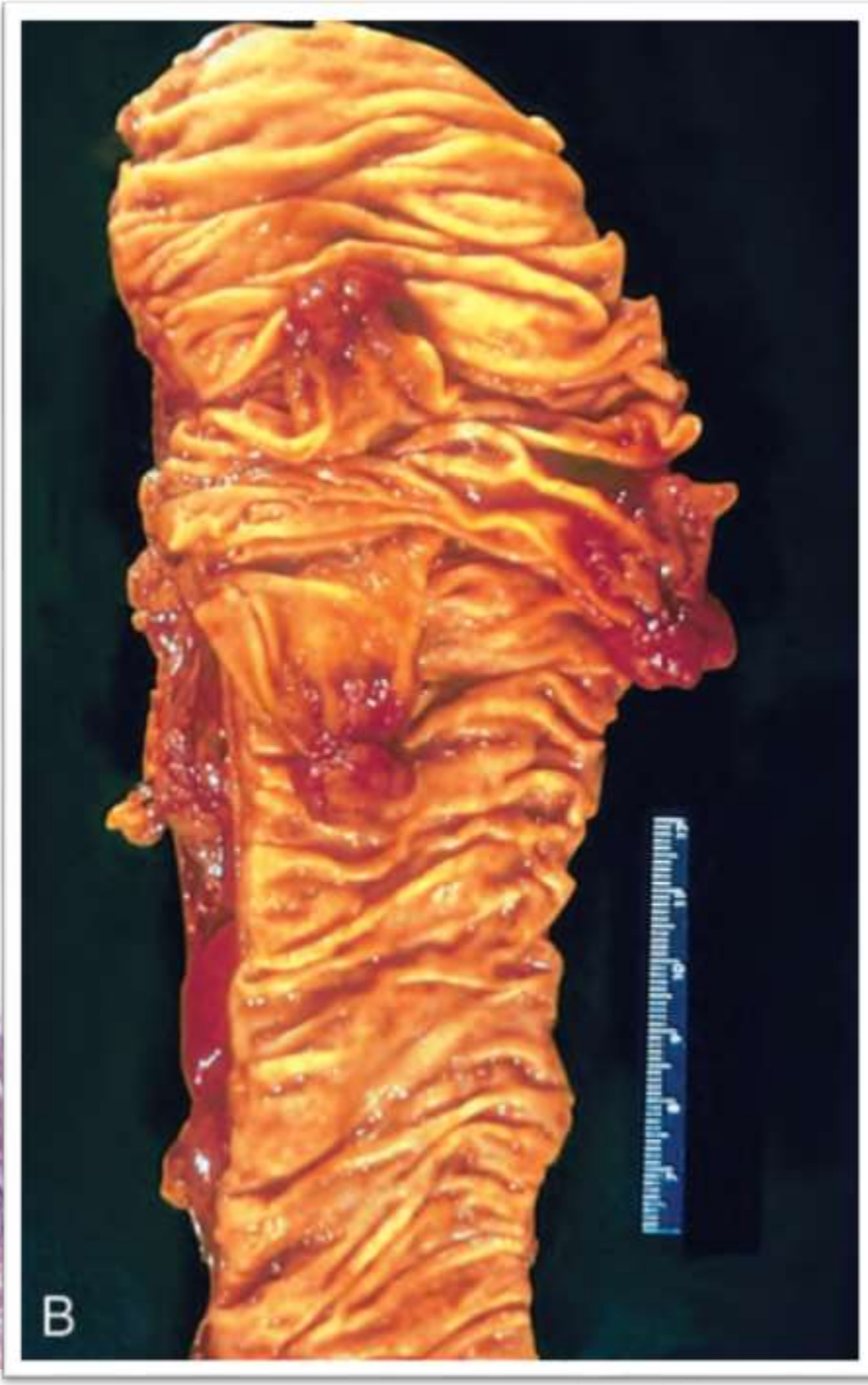
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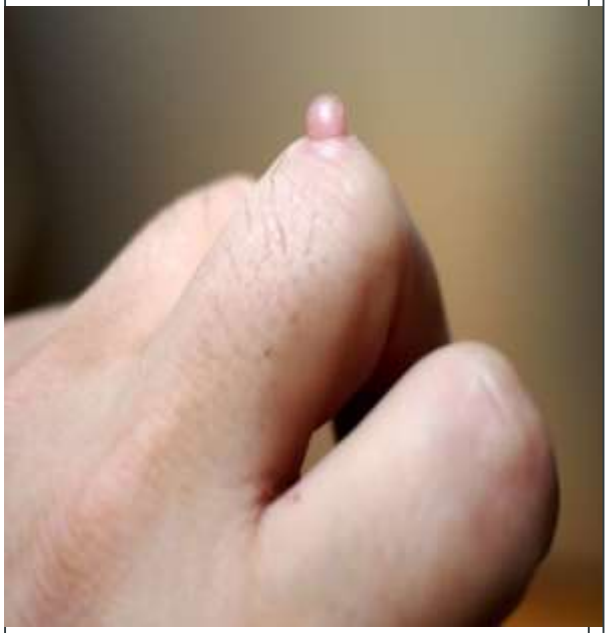

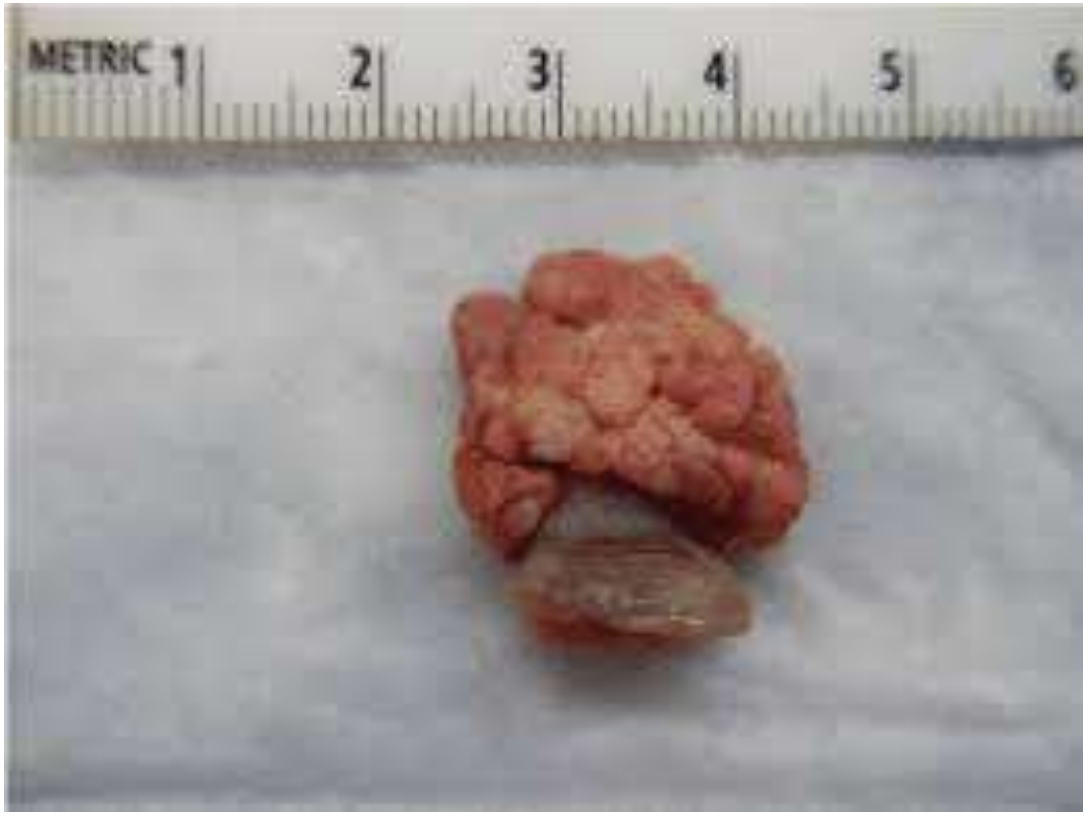
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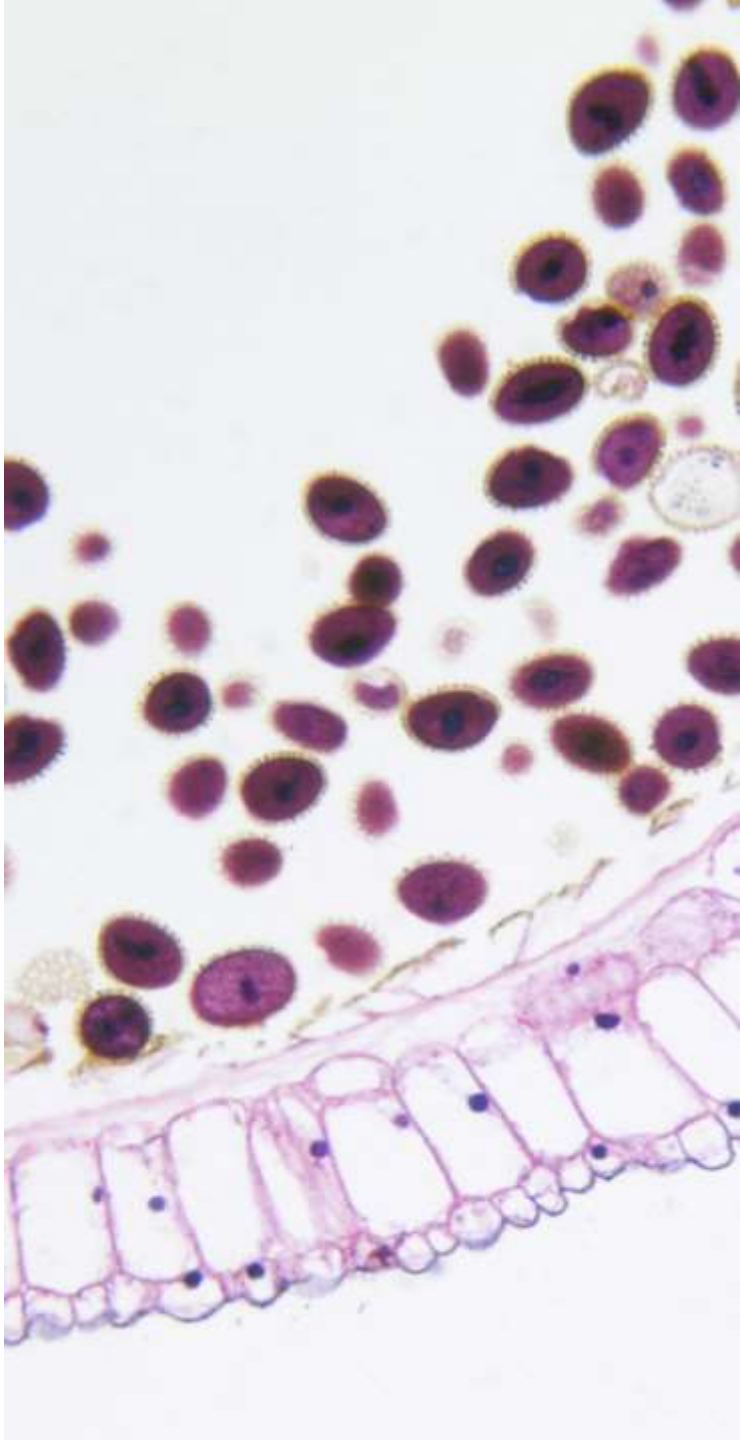
POLYPS

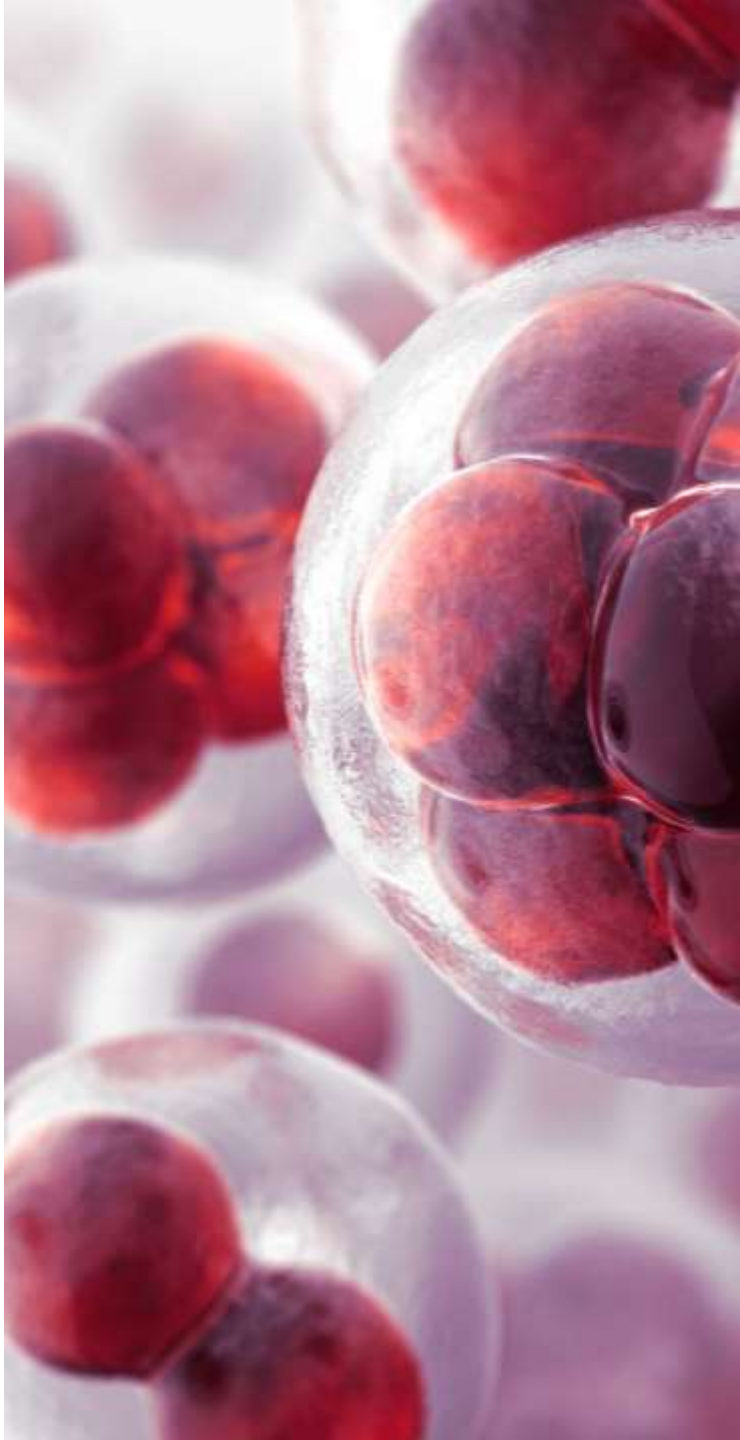
- When a neoplasm—benign or malignant— produces a macroscopically visible projection above a mucosal surface and projects, for example, into the gastric or colonic lumen, it is termed a *polyp*.
- If the polyp has glandular tissue, it is called an adenomatous polyp



MALIGNANT TUMORS

- Malignant tumors are collectively referred to as cancers

- Malignant tumors can invade and destroy adjacent structures and spread to distant sites (metastasize) to cause death.



MALIGNANT TUMORS

Not all cancers pursue so deadly a course.

Some are discovered early enough to be excised surgically or are treated successfully with chemotherapy or radiation

Malignant always raises a red flag.

MALIGNANT TUMORS (NOMENCLATURE)

Malignant tumors arising in solid mesenchymal tissues are usually called ***sarcomas*** (Greek *sar* = fleshy; e.g., fibrosarcoma, chondrosarcoma, leiomyosarcoma, and rhabdomyosarcoma), whereas those arising from blood-forming cells are designated *leukemias* (literally, white blood) or *lymphomas* (tumors of lymphocytes or their precursors).

Malignant neoplasms of epithelial cell origin, derived from any of the three germ layers, are called *carcinomas*. Thus, cancers arising in the ectodermally derived epidermis, the mesodermally derived renal tubules, and the endodermally derived lining of the gastrointestinal tract are all termed carcinomas.

MALIGNANT TUMORS

- Carcinomas may be further qualified. *Squamous cell carcinoma* denotes a cancer in which the tumor cells resemble stratified squamous epithelium, and *adenocarcinoma* denotes a lesion in which the neoplastic epithelial cells grow in a glandular pattern.

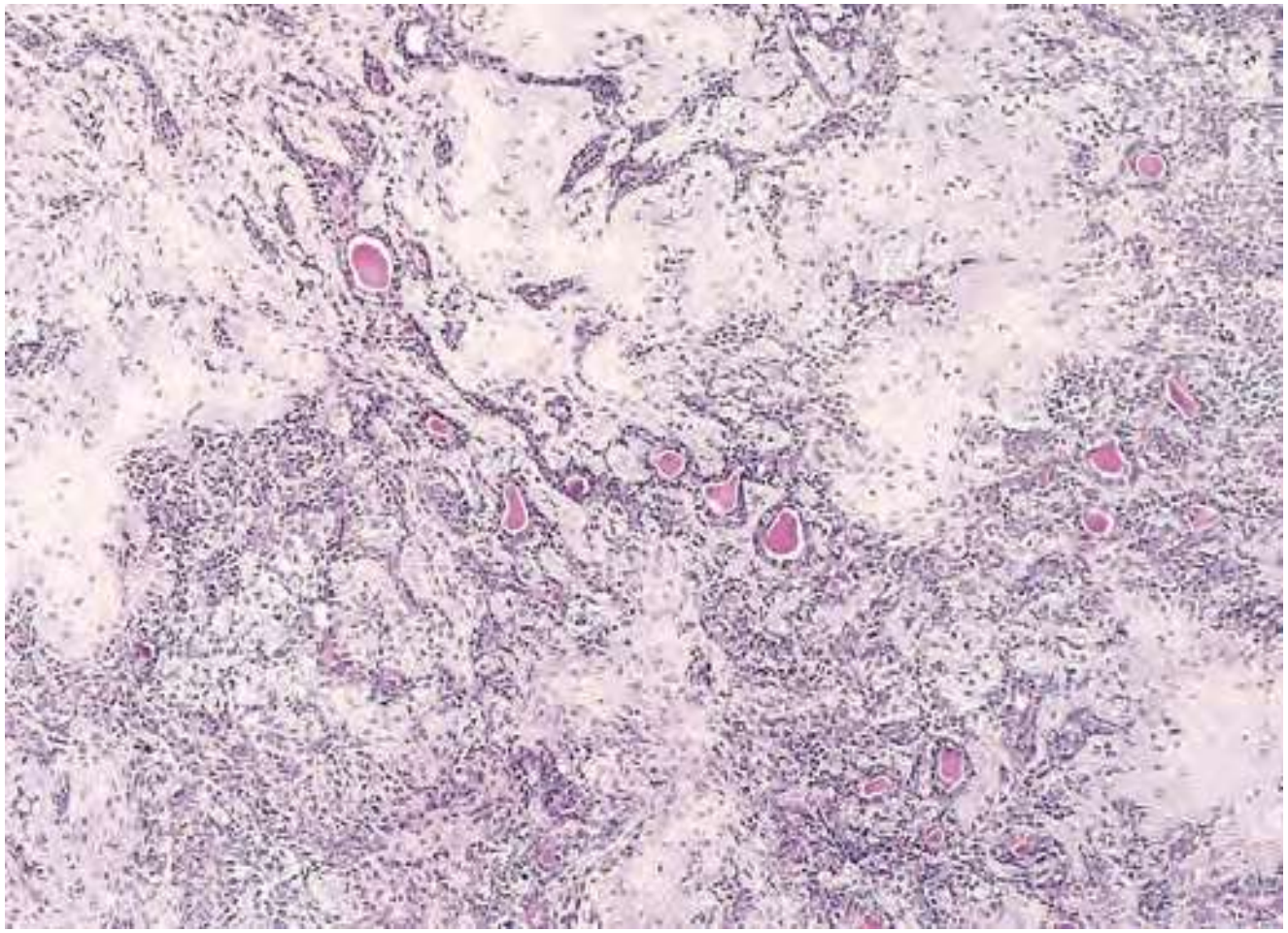
- Sometimes the tissue or organ of origin can be identified and is added as a descriptor, as in renal cell adenocarcinoma or bronchogenic squamous cell carcinoma.

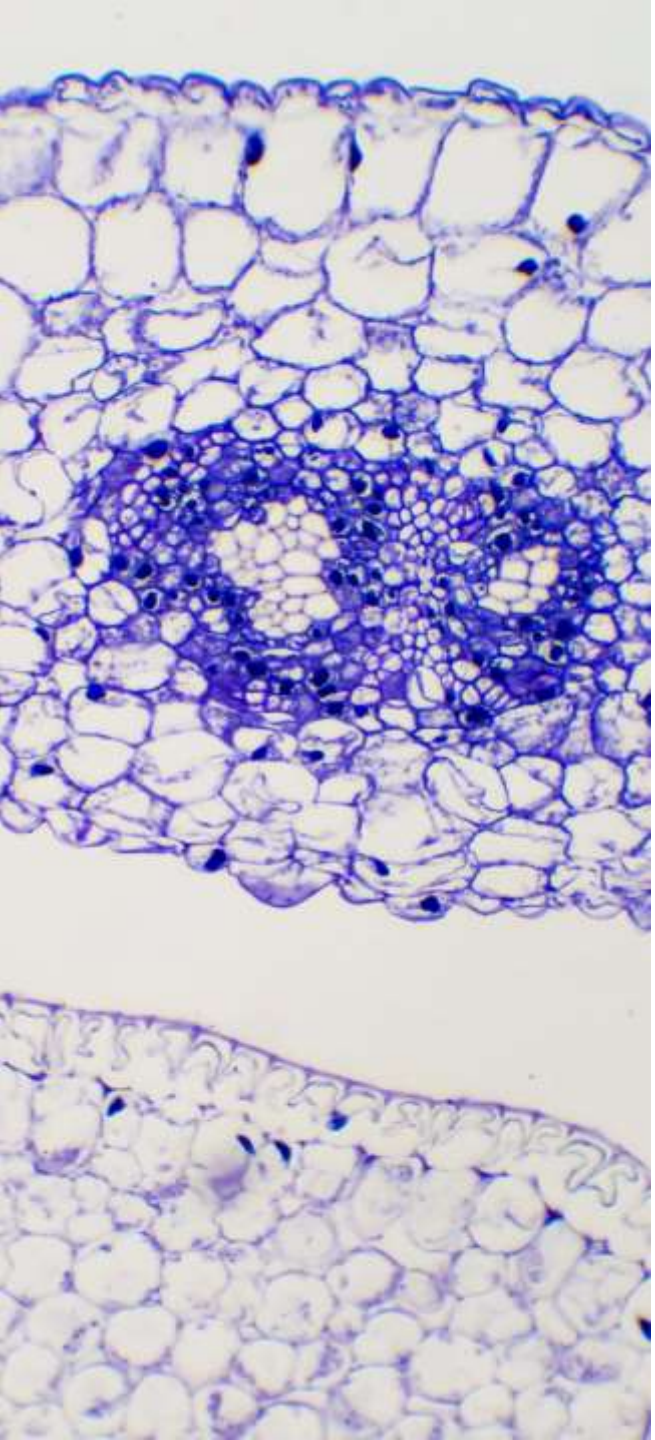
- Not infrequently, a cancer is composed of cells of unknown tissue origin (undifferentiated malignant tumor)

MIXED TUMORS

- In most benign and malignant neoplasms, all of the parenchymal cells closely resemble one another. Infrequently, however, divergent differentiation of a single neoplastic clone creates a mixed tumor, such as the mixed tumor of salivary gland.

- These tumors contain epithelial components scattered within a myxoid stroma that may contain islands of cartilage or bone .All of these elements arise from a single clone capable of producing both epithelial and myoepithelial cells; thus, the preferred designation of this neoplasm is pleomorphic adenoma.





- The great majority of neoplasms, even mixed tumors, are composed of cells from a single germ layer. An exception is a tumor called a *teratoma*, which contains recognizable mature or immature cells or tissues belonging to more than one germ cell layer (and sometimes all three).

- Teratoma originates from germ cells that are normally present in the ovary and testis and sometimes also found in abnormal midline embryonic rests. Such cells can differentiate into any of the cell types found in the adult body and so, may give rise to neoplasms that contain, in **a helter-skelter** fashion, bone, epithelium, muscle, fat, nerve, and other tissues.

- Common pattern is seen in the *ovarian cystic teratoma (dermoid cyst),* which create a cystic tumor lined by skin replete with hair, sebaceous glands, and tooth structures.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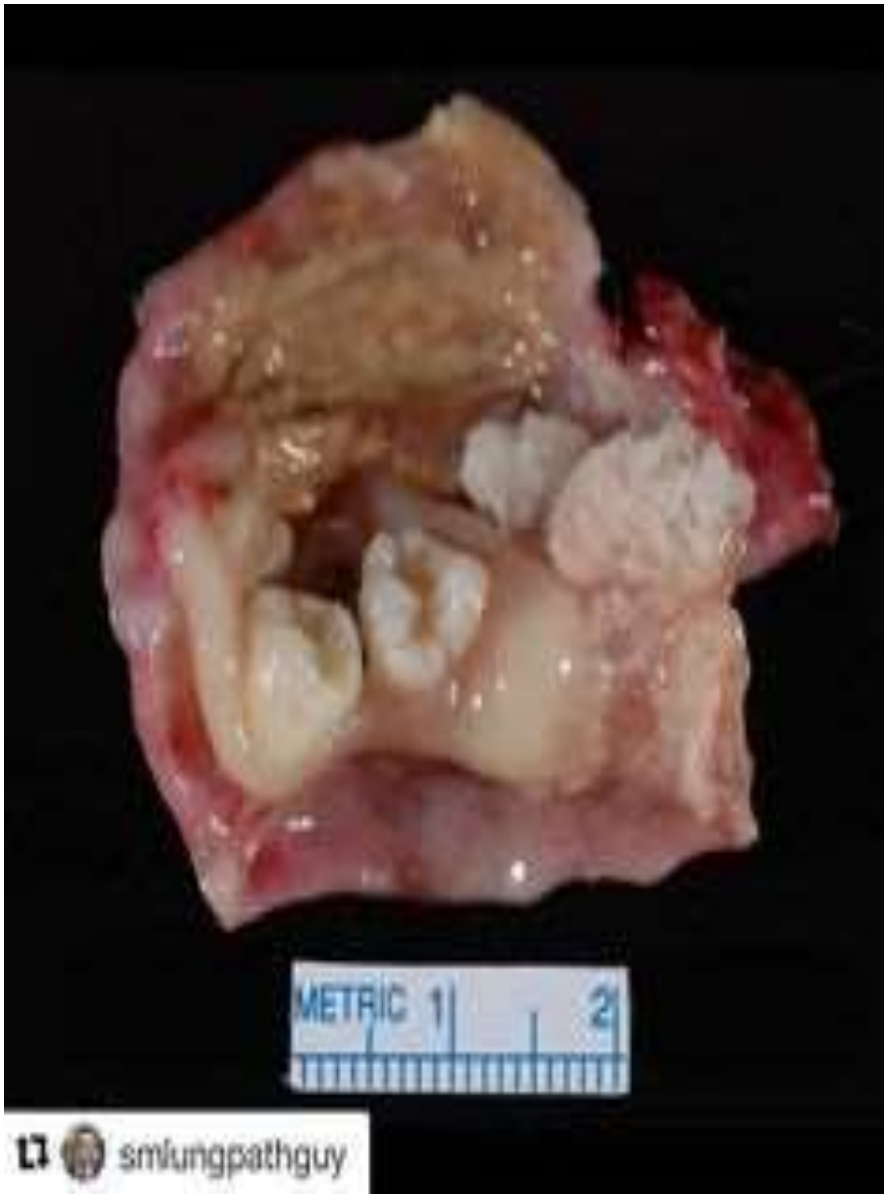
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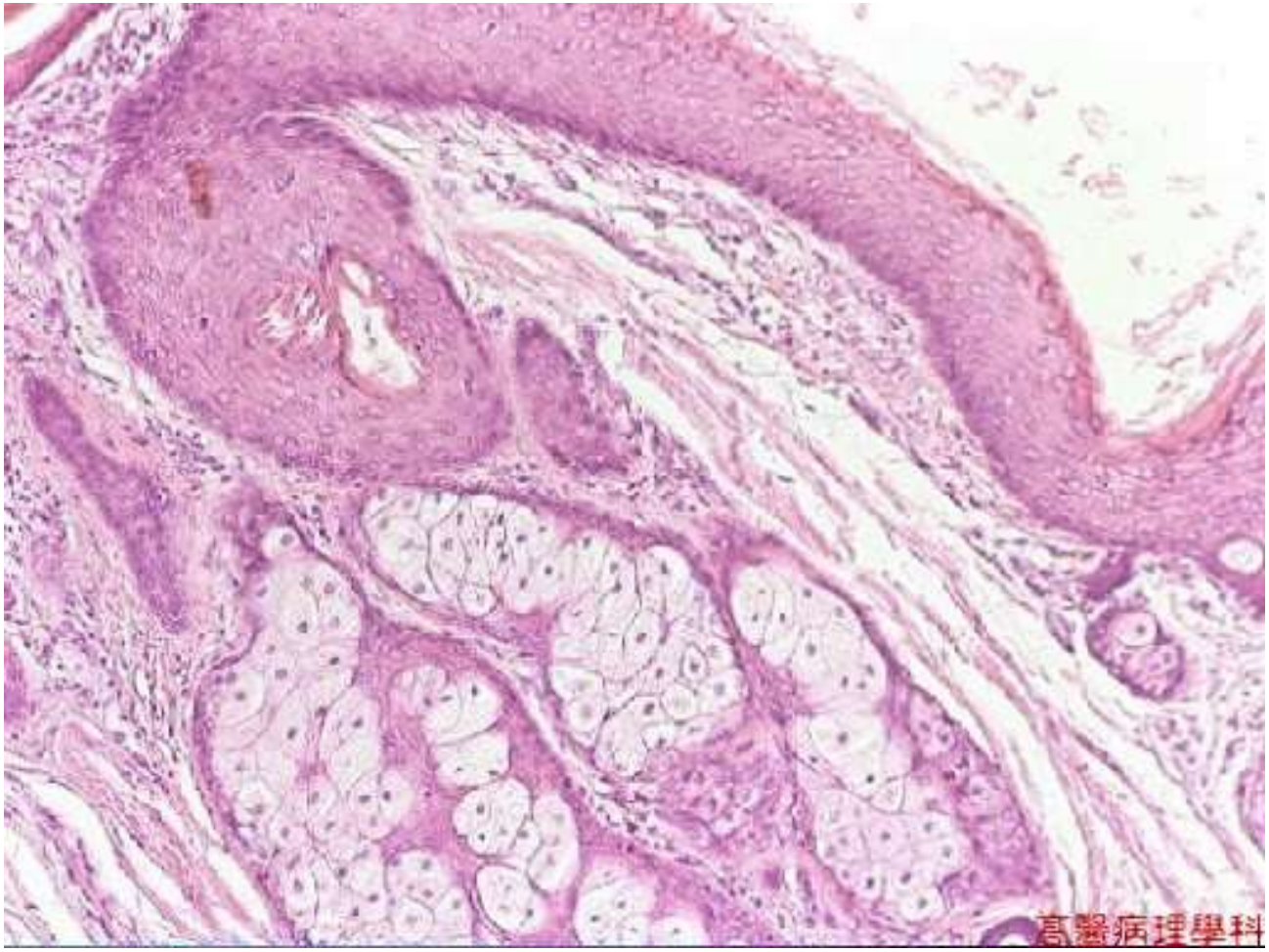
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MISNOMERS

There are some inappropriate usages. For instance, benign-sounding designations such as lymphoma, melanoma, mesothelioma, and seminoma are used for certain malignant neoplasms.

HAMARTOMA

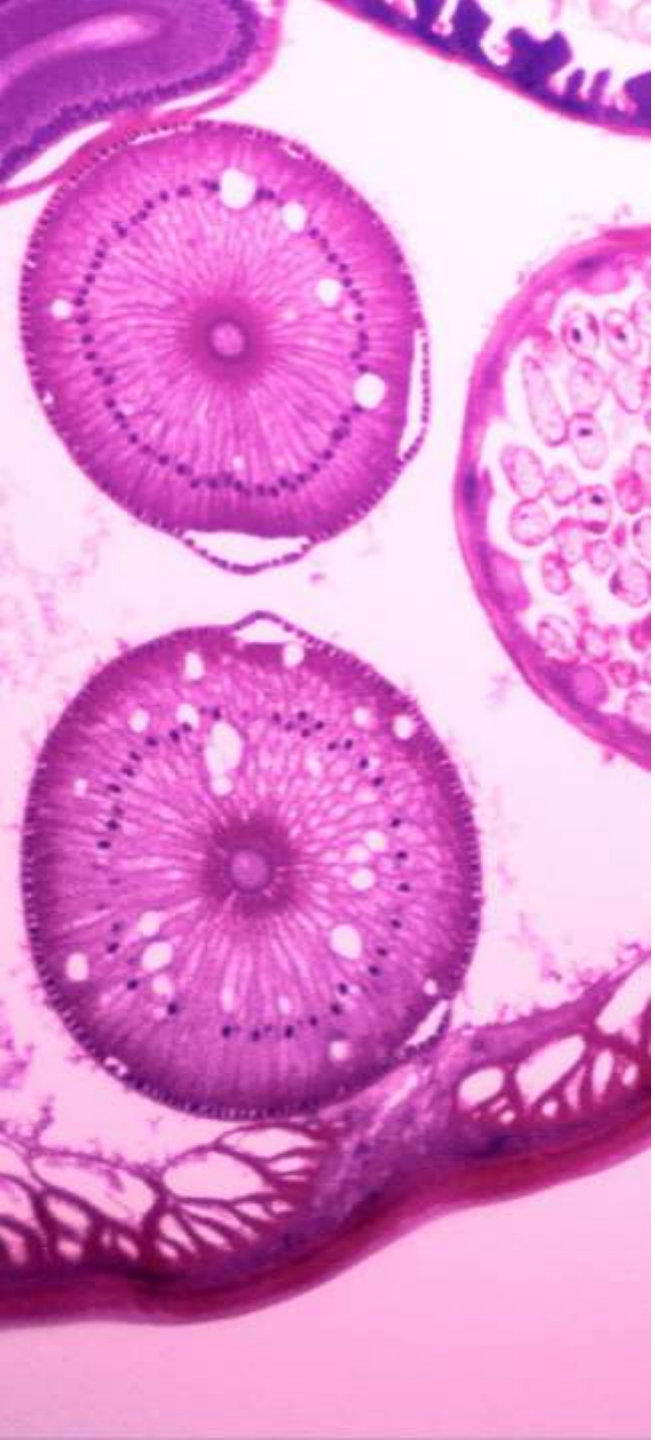
- **Hamartomas** are disorganized but benign masses composed of cells indigenous to the involved site. Once thought to be a developmental malformation unworthy of the -oma designation, many in fact have clonal chromosomal aberrations that are acquired through somatic mutations and on this basis are now considered neoplasm.

CHORISTOMA

- ***Choristoma*** is a heterotopic rest of cells. For example, a small nodule of well-developed and normally organized pancreatic tissue may be found in the submucosa of the stomach, duodenum, or small intestine.

Table 7-1 Nomenclature of Tumors

Tissue of Origin	Benign	Malignant
Composed of one parenchymal cell type		
Tumors of Mesenchymal Origin		
Connective tissue and derivatives	Fibroma Lipoma Chondroma Osteoma	Fibrosarcoma Liposarcoma Chondrosarcoma Osteogenic sarcoma
Vessels and surface coverings		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Mesothelium	Benign fibrous tumor	Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
Blood Cells and Related Cells		
Hematopoietic cells		Leukemias
Lymphoid tissue		Lymphomas
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
Tumors of Epithelial Origin		
Stratified squamous	Squamous cell papilloma	Squamous cell carcinoma
Basal cells of skin or adnexa		Basal cell carcinoma
Tumors of Epithelial Origin (cont'd)		
Epithelial lining of glands or ducts	Adenoma Papilloma Cystadenoma	Adenocarcinoma Papillary carcinomas Cystadenocarcinoma
Respiratory passages	Bronchial adenoma	Bronchogenic carcinoma
Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
Liver cells	Hepatic adenoma	Hepatocellular carcinoma
Urinary tract epithelium (transitional)	Transitional cell papilloma	Transitional cell carcinoma
Placental epithelium	Hydatidiform mole	Choriocarcinoma
Testicular epithelium (germ cells)		Seminoma Embryonal carcinoma
Tumors of Melanocytes	Nevus	Malignant melanoma
More than one neoplastic cell type—mixed tumors, usually derived from one germ cell layer		
Salivary glands	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin
Renal anlage		Wilms tumor
More than one neoplastic cell type derived from more than one germ cell layer—teratogenous		
Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma



Malignant tumors also tend to grow more rapidly than benign tumors, but there are so many exceptions that growth rate is not a very useful discriminator between benignity and malignancy.

In fact, even cancers exhibit remarkably varied growth rates, from slow-growing tumors associated with survival for years, often without treatment, to rapidly growing tumors that may be lethal within months or weeks .

DIFFERENTIATION AND ANAPLASIA

- **Differentiation refers to the extent to which neoplastic parenchymal cells resemble the corresponding normal parenchymal cells, both morphologically and functionally; lack of differentiation is called *anaplasia*.**

- In general, benign tumors are well differentiated

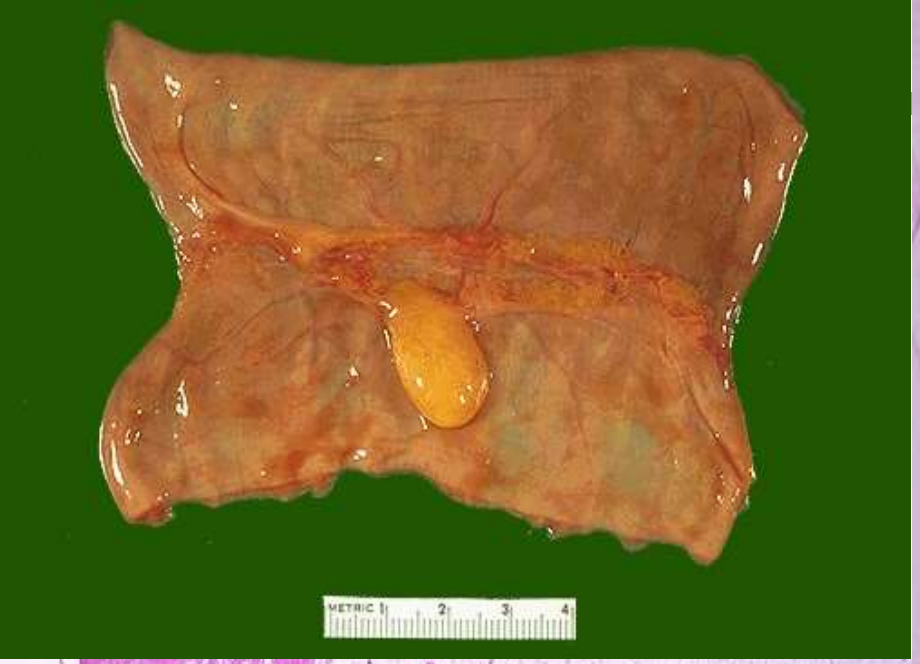
DIFFERENTIATION AND ANAPLASIA

- The neoplastic cell in a tumor of benign adipocytes—a lipoma—so closely resembles normal adipocytes that it may be impossible to recognize the tumor by microscopic examination of individual cells. Only the growth of these cells into a discrete mass discloses the neoplastic nature of the lesion .

- In well-differentiated benign tumors, mitoses are usually rare and are of normal configuration.

Table 7-2 Comparisons Between Benign and Malignant Tumors

Characteristics	Benign	Malignant
Differentiation/ anaplasia	Well differentiated; structure sometimes typical of tissue of origin	Some lack of differentiation (anaplasia); structure often atypical
Rate of growth	Usually progressive and slow; may come to a standstill or regress; mitotic figures rare and normal	Erratic, may be slow to rapid; mitotic figures may be numerous and abnormal
Local invasion	Usually cohesive, expansile, well-demarcated masses that do not invade or infiltrate surrounding normal tissues	Locally invasive, infiltrating surrounding tissue; sometimes may be misleadingly cohesive and expansile
Metastasis	Absent	Frequent; more likely with large undifferentiated primary tumors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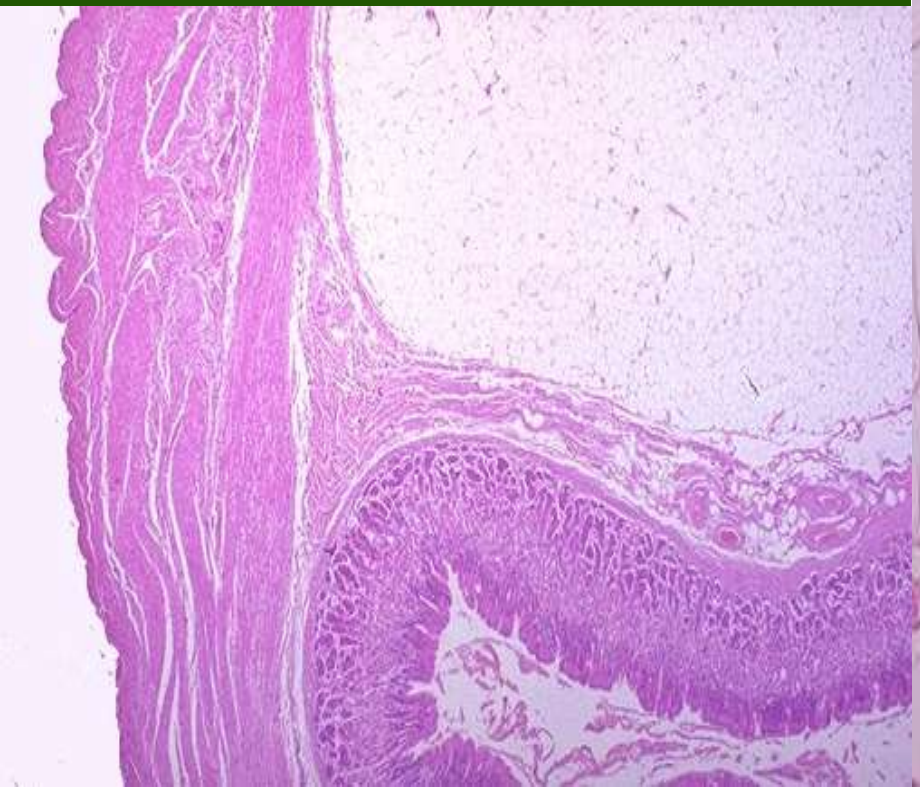

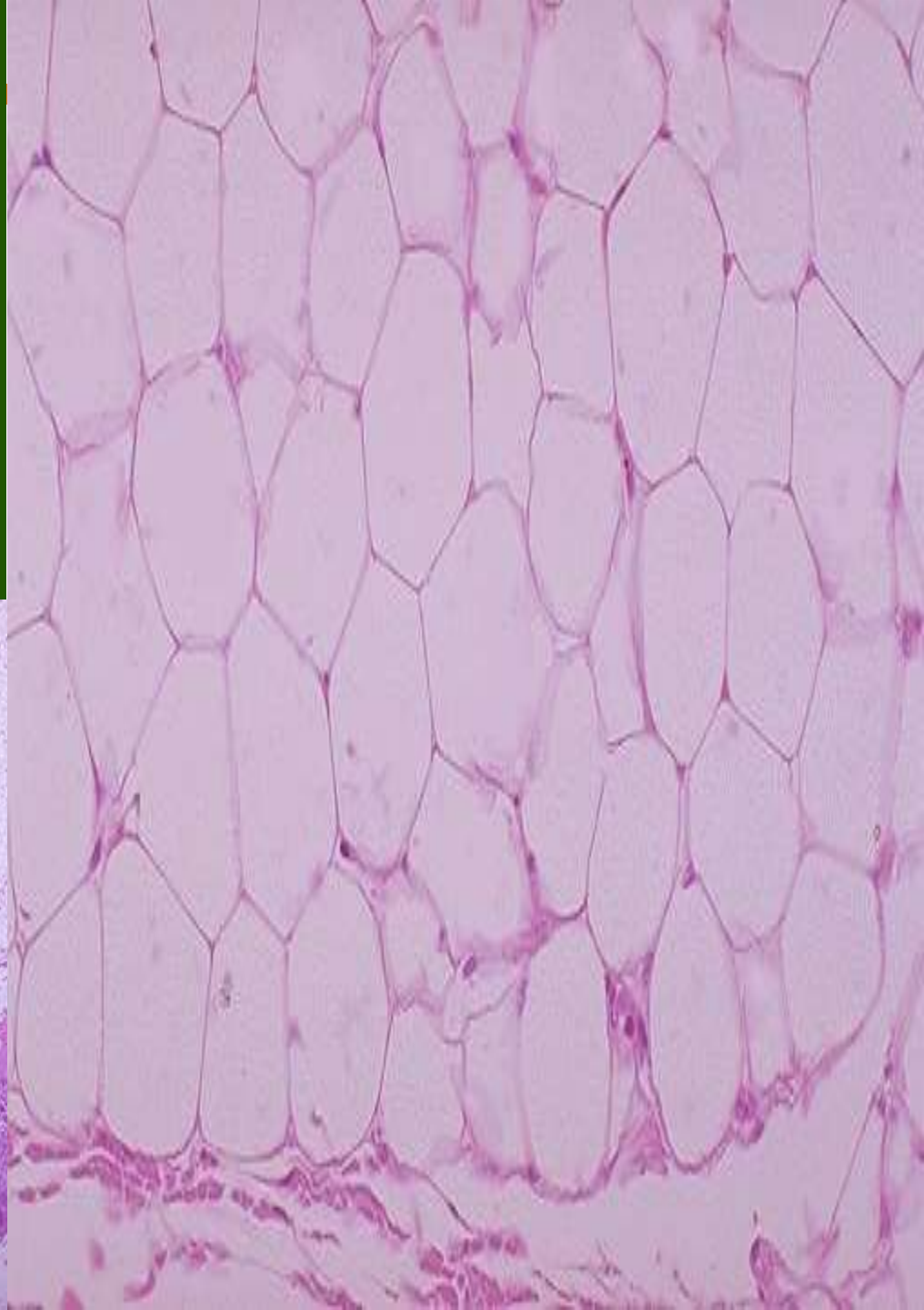

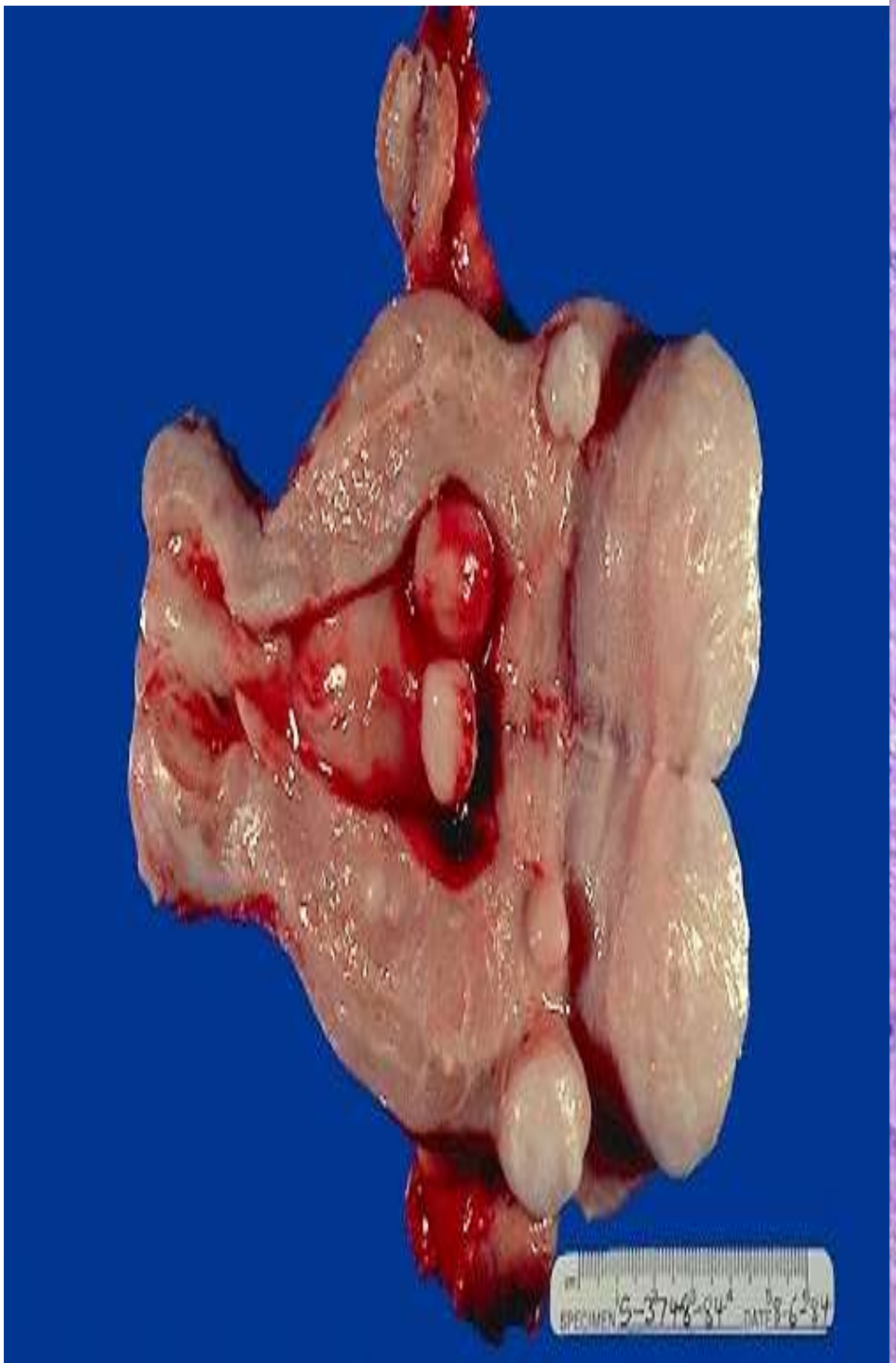
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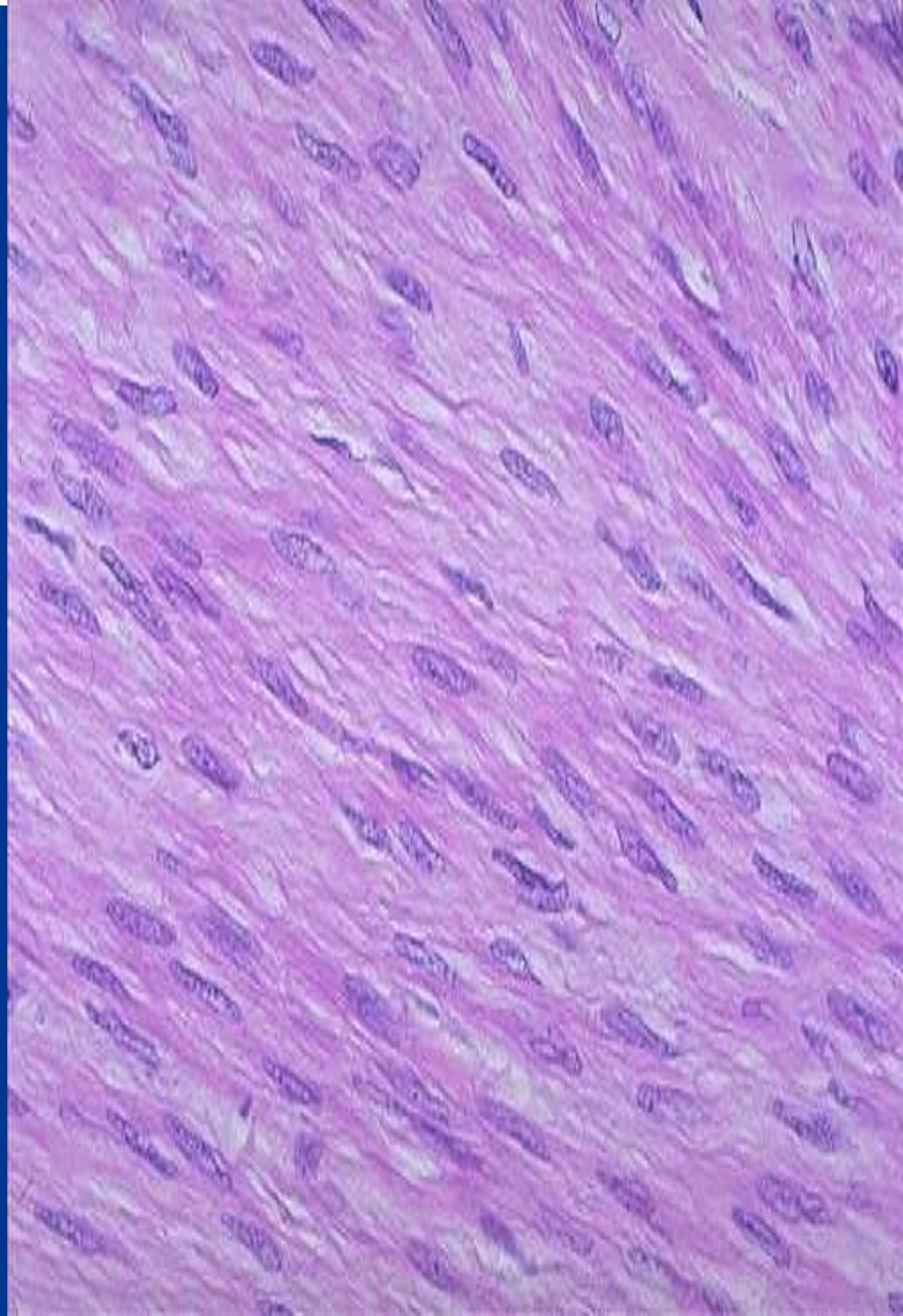

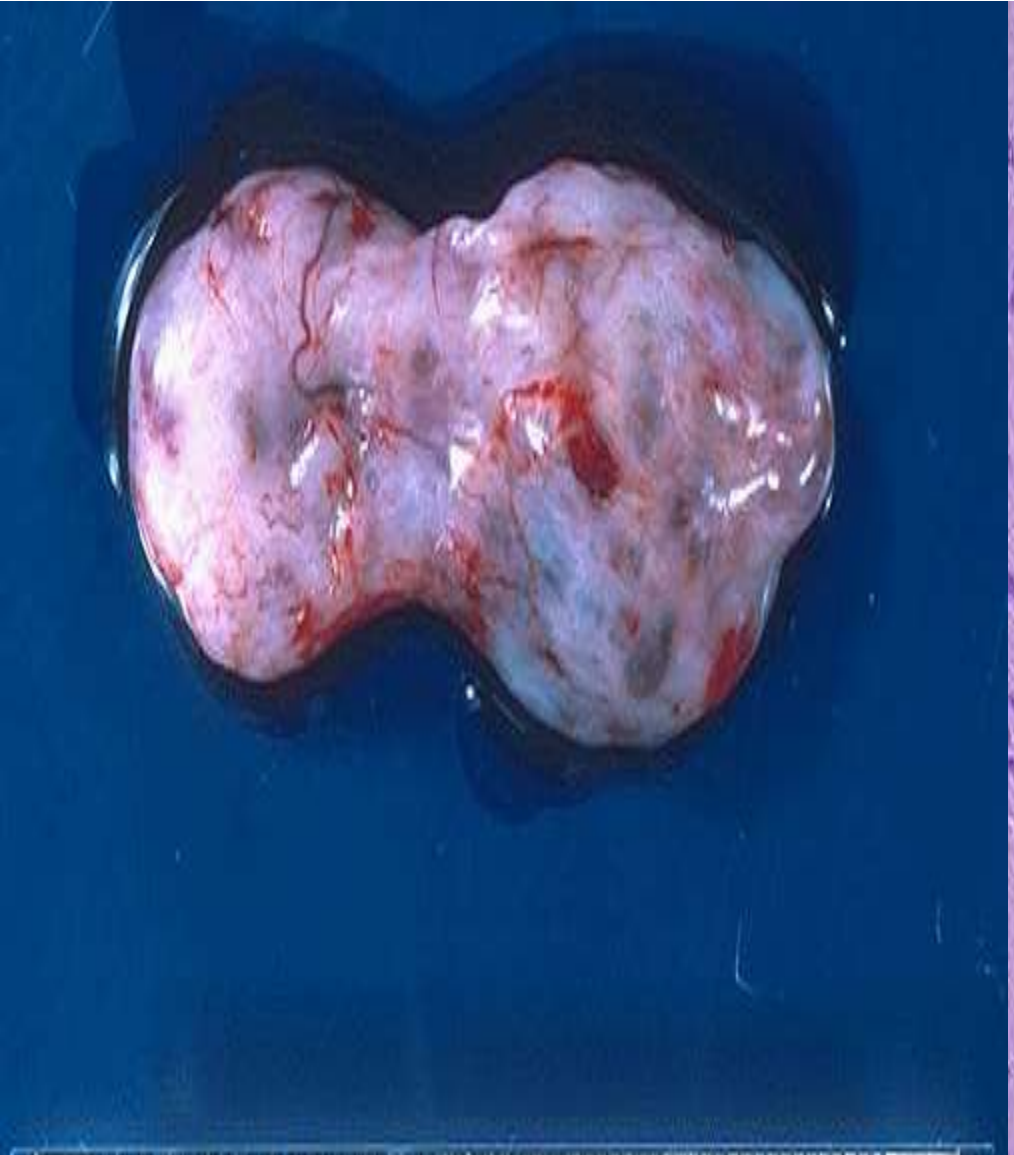
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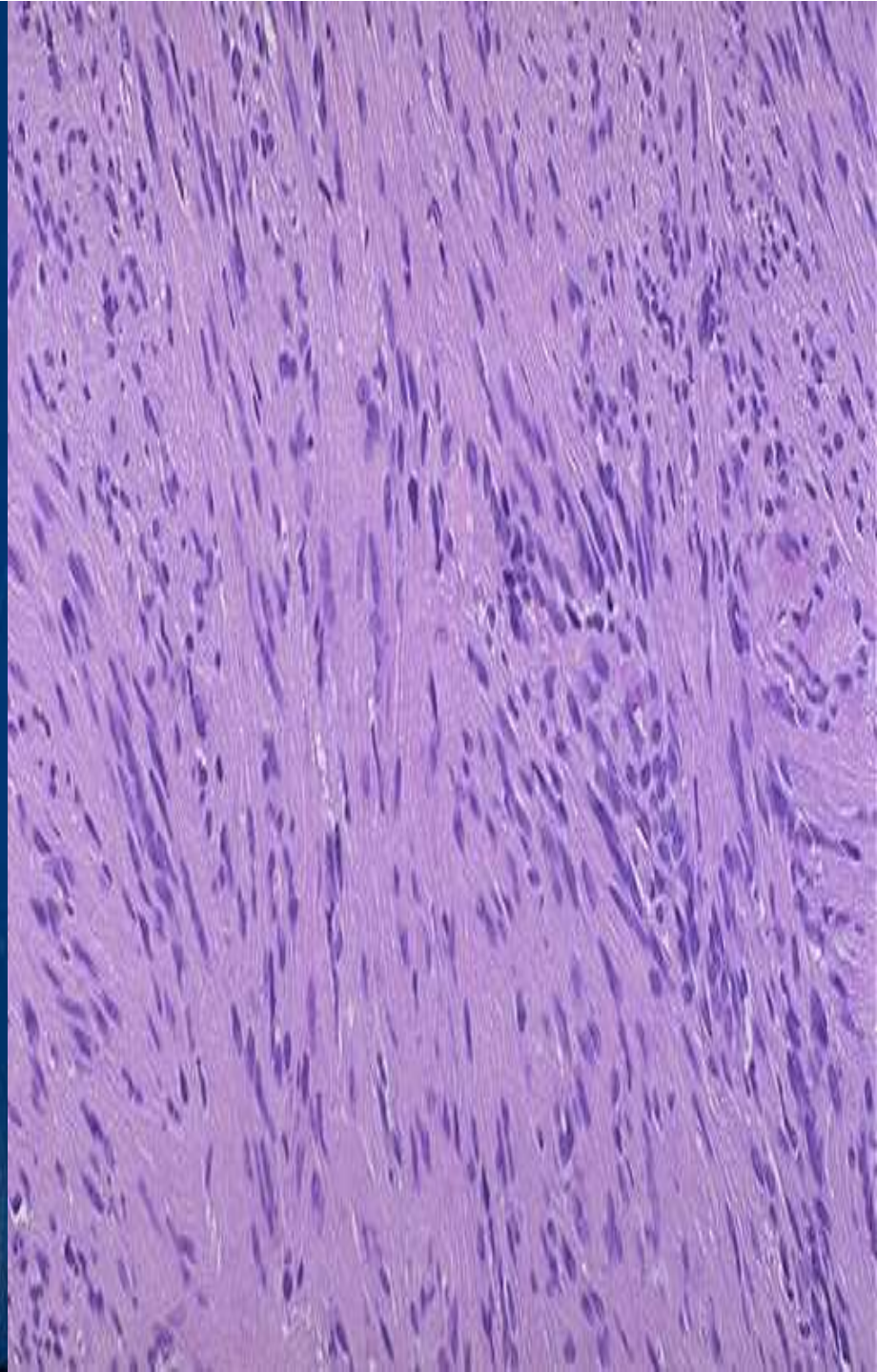
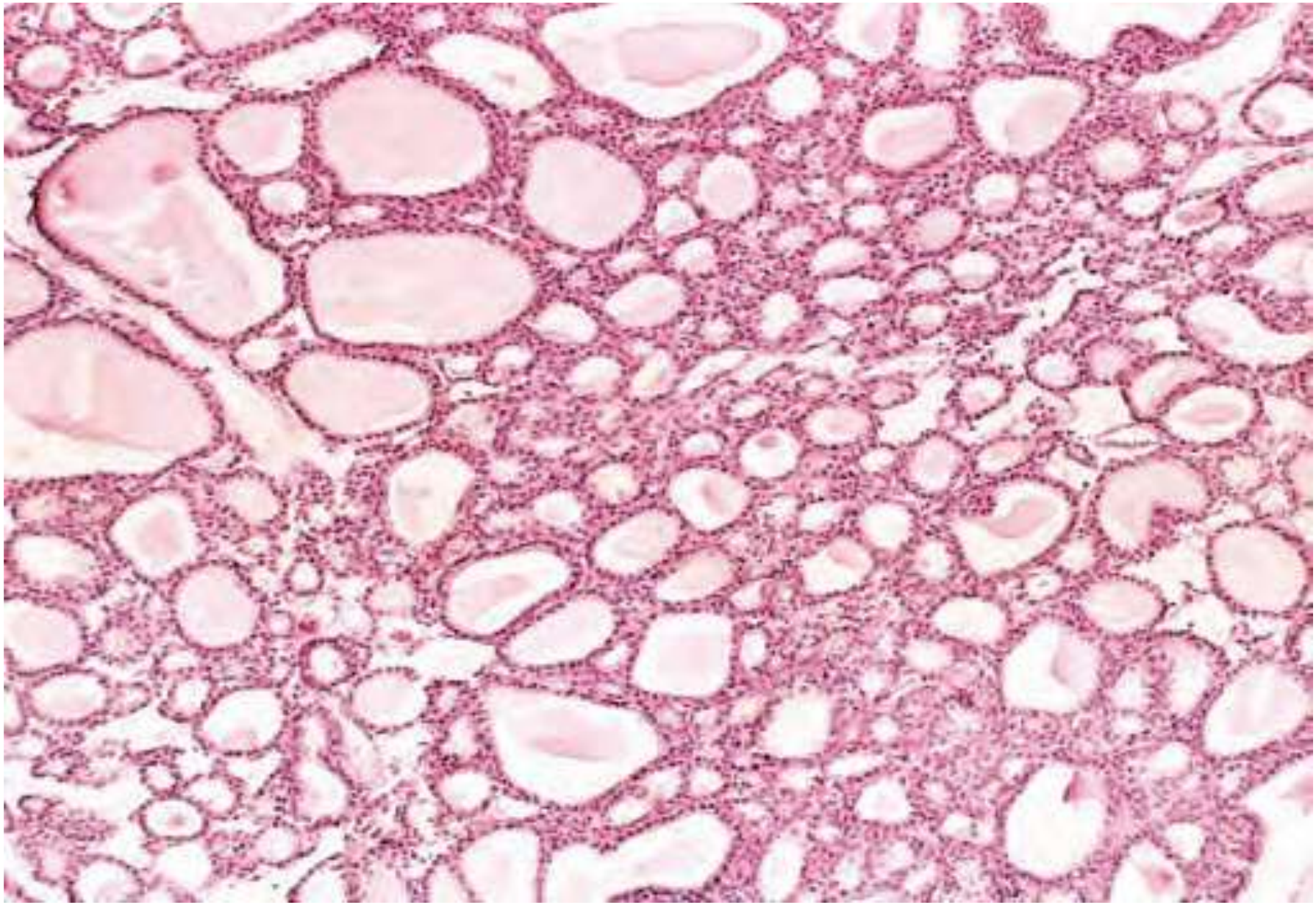
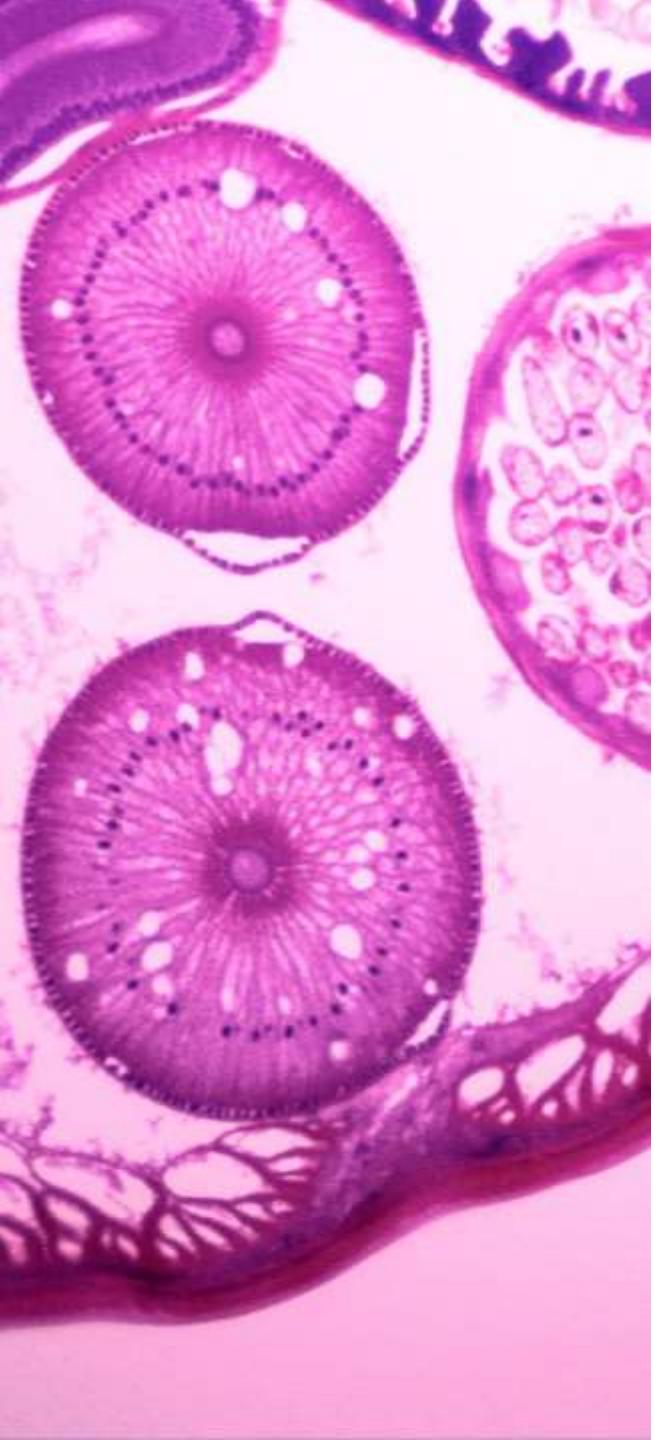


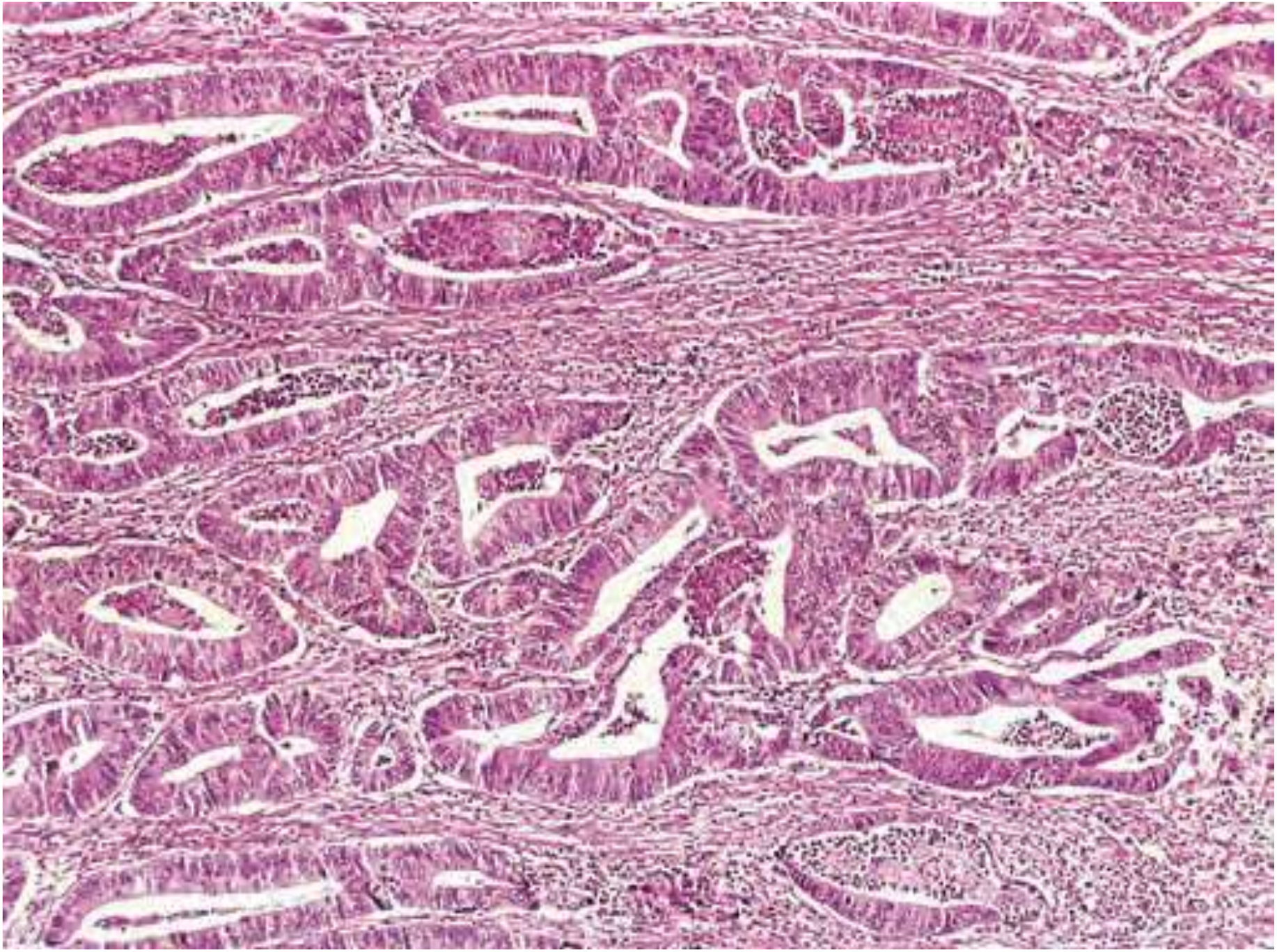


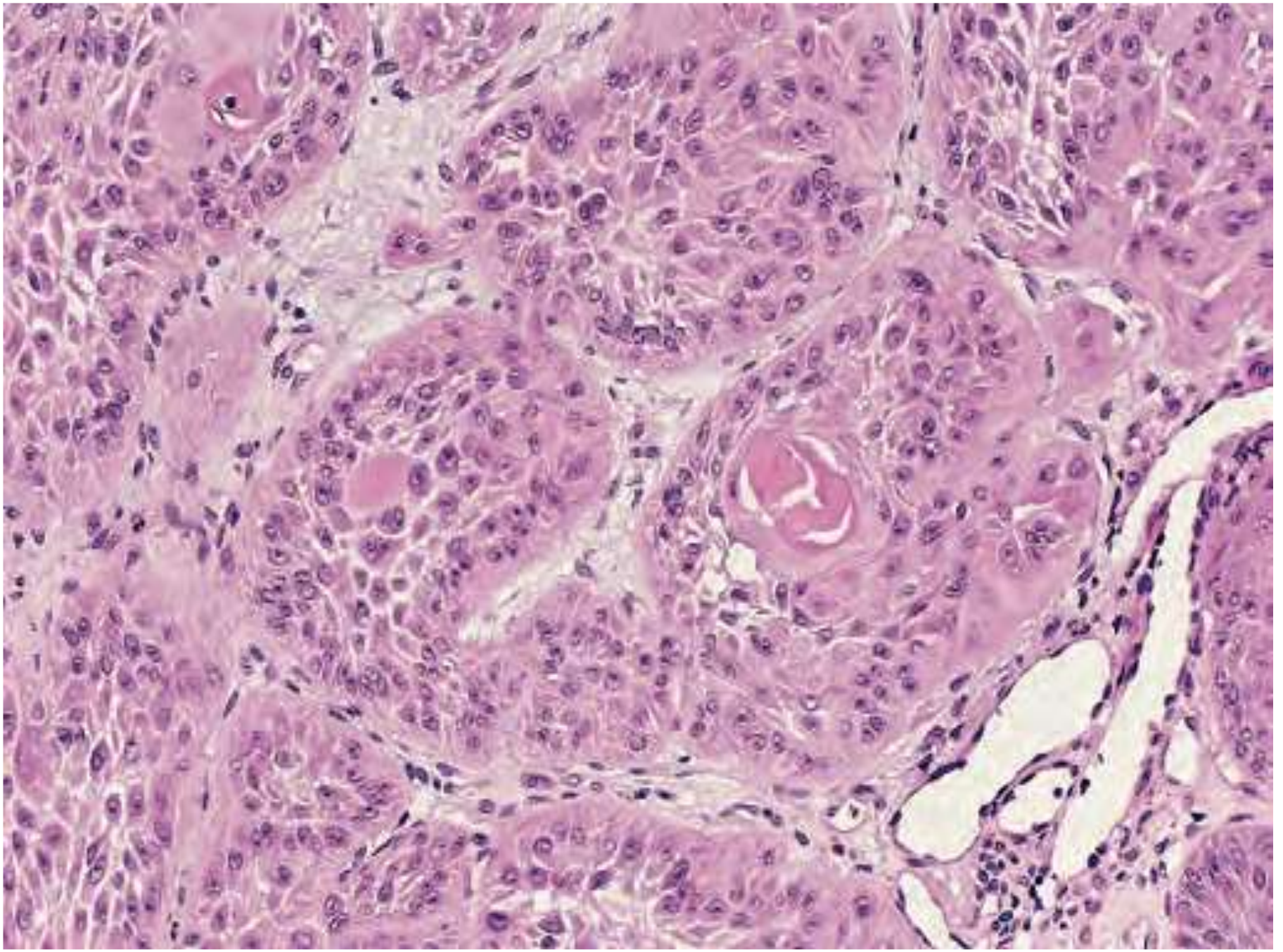


DIFFERENTIATION AND ANAPLASIA

- **malignant neoplasms exhibit a wide range of parenchymal cell differentiation, most exhibit morphologic alterations that betray their malignant nature**.

- There are exceptions , certain well-differentiated adenocarcinomas of the thyroid, for example, form normal-appearing follicles, and some squamous cell carcinomas contain cells that appear identical to normal squamous epithelial cells. Thus, the morphologic distinction between well differentiated malignant tumors and benign tumors may be difficult .

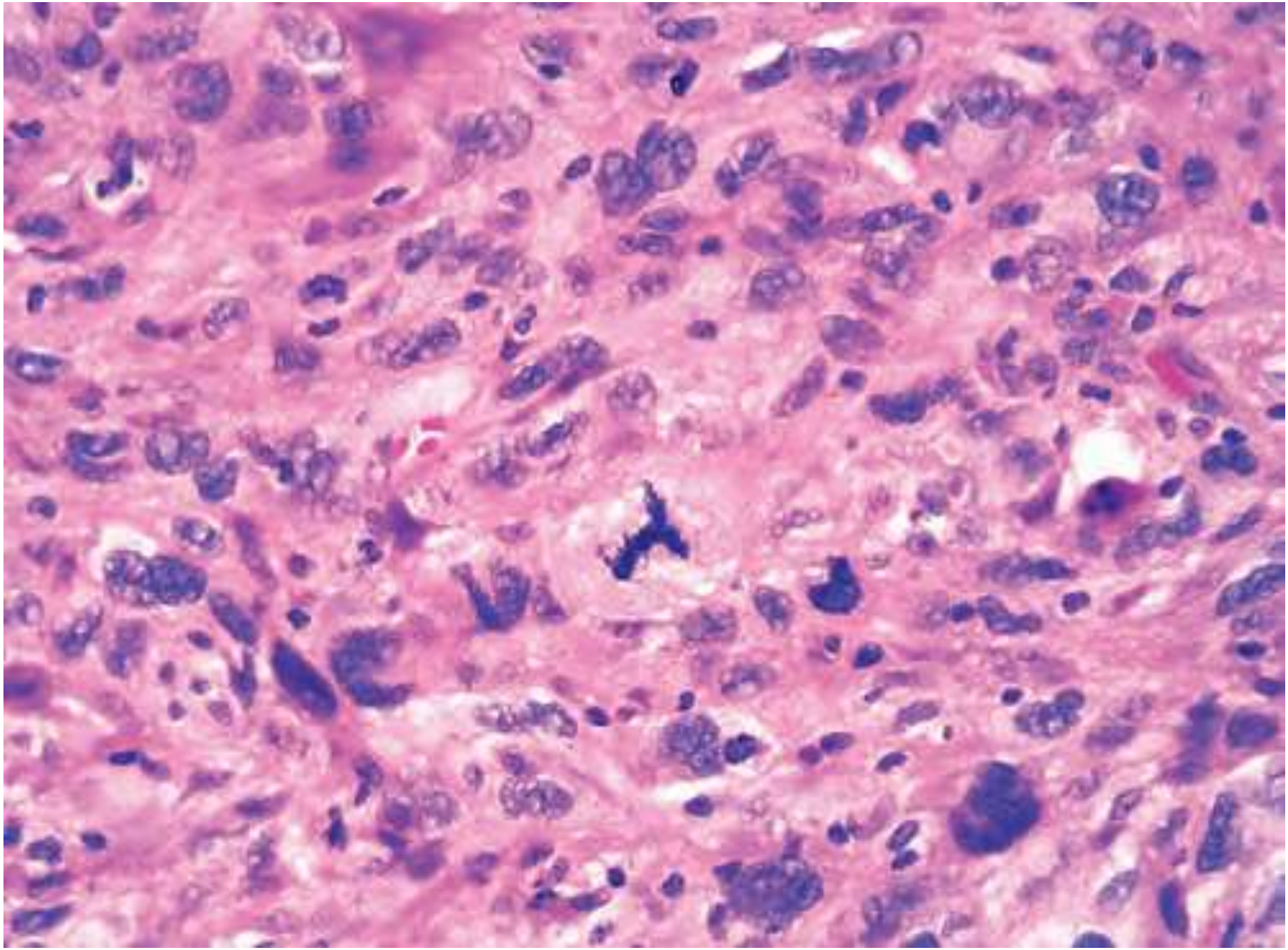




DIFFERENTIATION AND ANAPLASIA

- At the other end of the spectrum lie tumors exhibiting little or no evidence of differentiation .

- In between the two extremes lie tumors that are loosely referred to as moderately well differentiated.



DIFFERENTIATION AND ANAPLASIA

- Malignant neoplasms that are composed of poorly differentiated cells are said to be *anaplastic*.

- **Lack of differentiation, or anaplasia, is considered a hallmark of malignancy.** The term *anaplasia* means "to form backward," implying a reversal of differentiation to a more primitive level.

ANAPLASIA

Anaplasia, is often associated with many other morphologic changes :

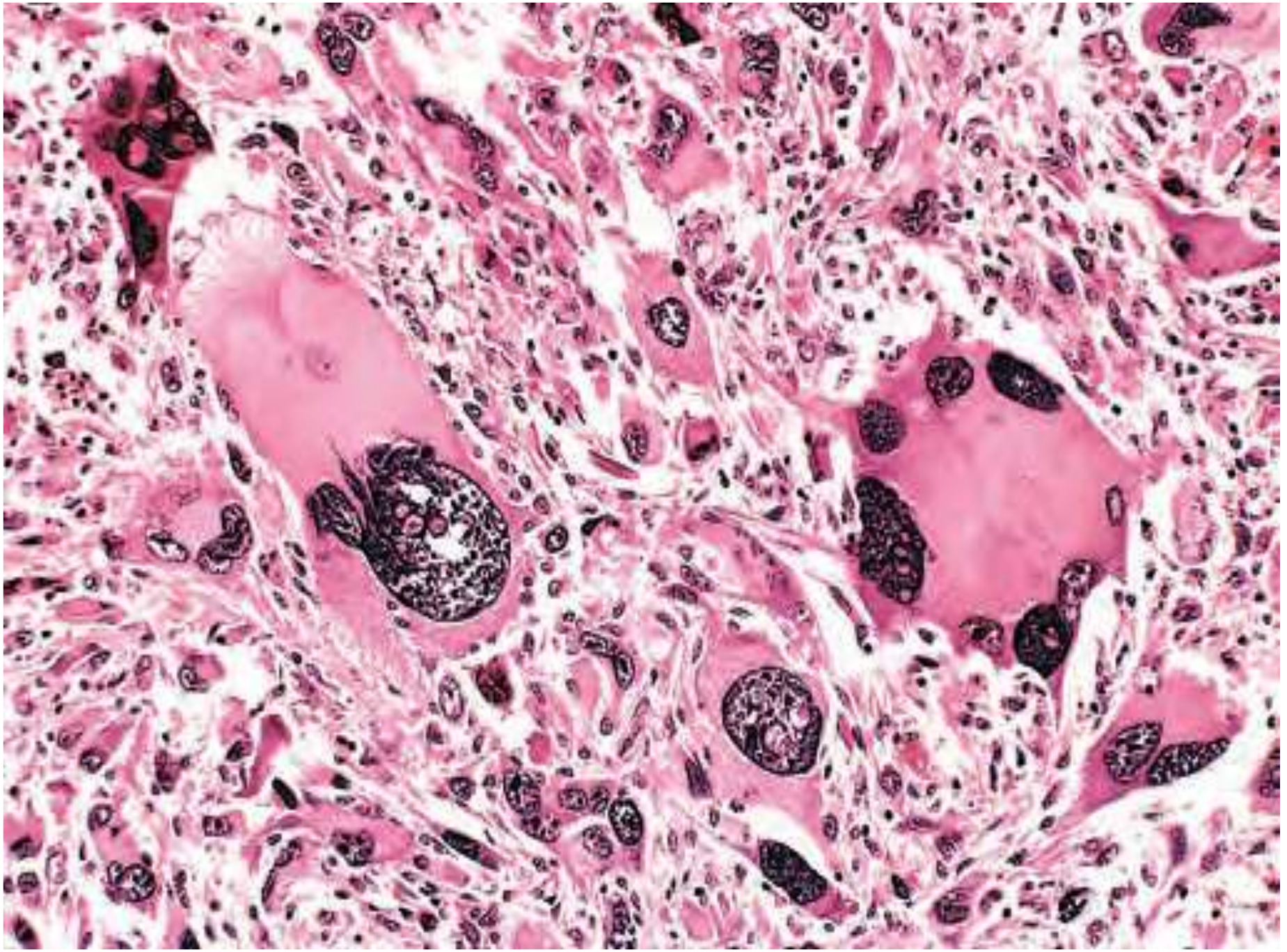
1- **Pleomorphism:** variation in size and shape . Thus, cells within the same tumor are not uniform, but range from small cells with an undifferentiated appearance, to *tumor giant cells* many times larger than their neighbors.

- Some tumor giant cells possess only a single huge polymorphic nucleus, while others may have two or more large hyperchromatic nuclei.
- These giant cells are not to be confused with inflammatory Langhans or foreign body giant cells, which are derived from macrophages contain many small, normal-appearing nuclei.

ANAPLASIA, IS OFTEN ASSOCIATED WITH MANY OTHER MORPHOLOGIC CHANGES :

II- Abnormal nuclear morphology:

- The nuclei are disproportionately large for the cell, with a nuclear-to cytoplasm ratio that may approach 1 : 1 instead of the normal 1 : 4 or 1 : 6.
- The nuclear shape is variable and often irregular, and the chromatin is often coarsely clumped and distributed along the nuclear membrane, or more darkly stained than normal *(hyperchromatic)*.
- Abnormally large nucleoli are also commonly seen.



ANAPLASIA, IS OFTEN ASSOCIATED WITH MANY OTHER MORPHOLOGIC CHANGES :

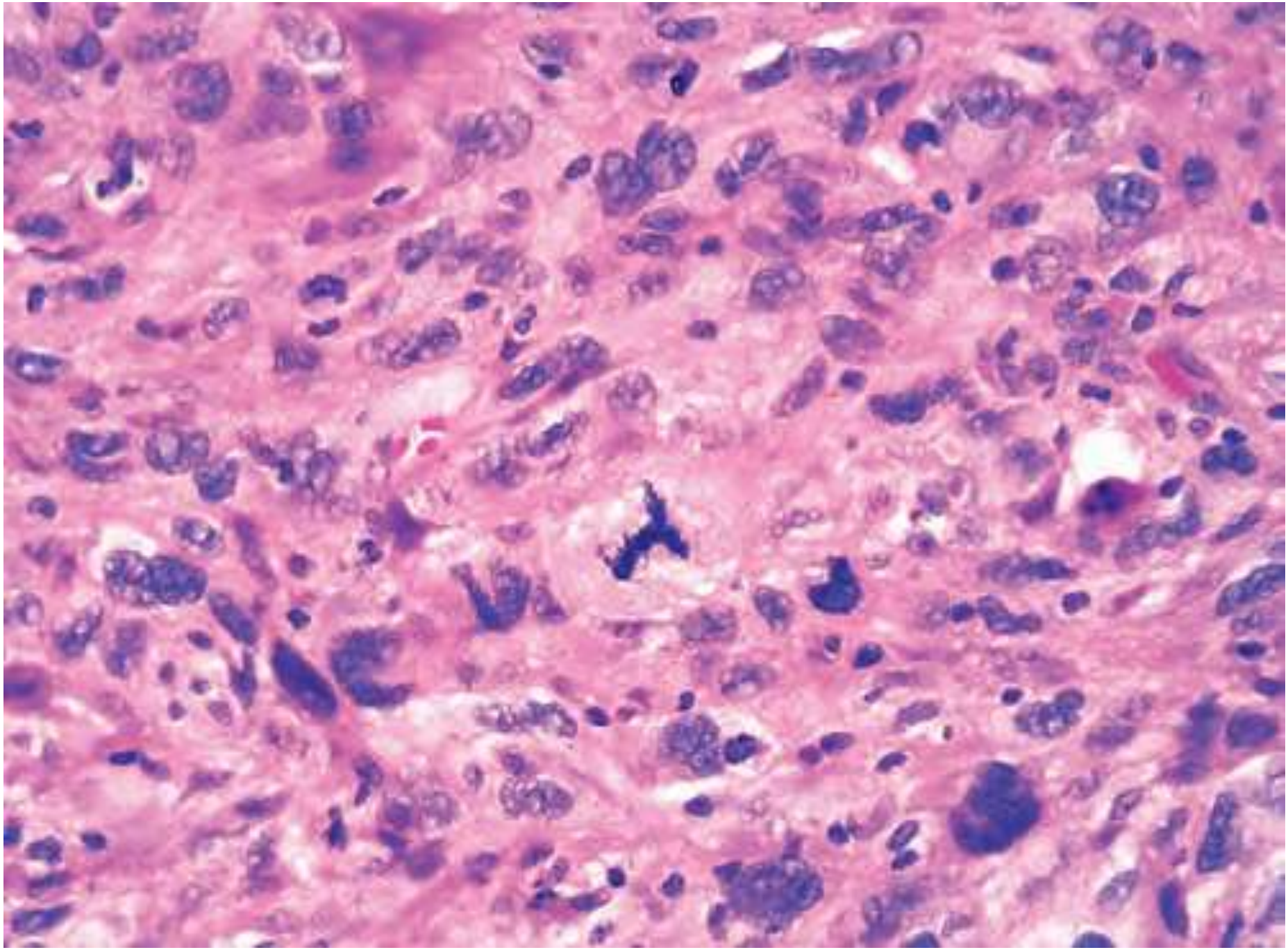
III- Mitoses:

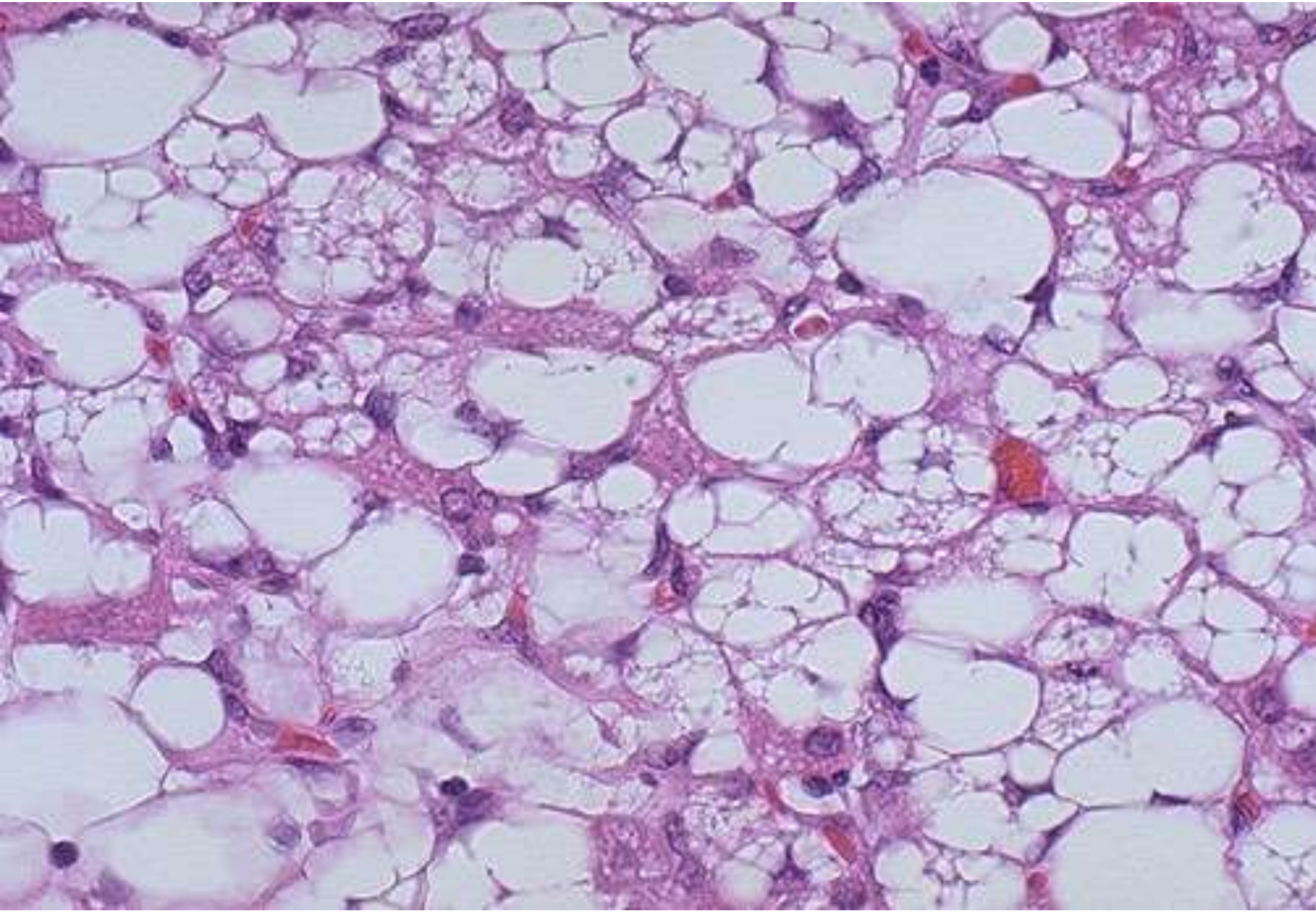
- The presence of mitoses, however, does not necessarily indicate that a tumor is malignant.
- Mitoses are indicative of rapid cell growth. Hence, cells in mitosis are often seen in normal tissues exhibiting rapid turnover, such as the epithelial lining of the gut and nonneoplastic proliferations such as hyperplasias.
- More important morphologic feature of malignancy are *atypical, bizarre mitotic figures,* sometimes with tripolar, quadripolar, or multipolar spindle.

ANAPLASIA, IS OFTEN ASSOCIATED WITH MANY OTHER MORPHOLOGIC CHANGES :

IV-Loss of polarity:

- In addition to the cytologic abnormalities, the orientation of anaplastic cells is markedly disturbed. Sheets or large masses of tumor cells grow in an disorganized fashion.





Anaplasia, is often associated with many other morphologic changes :

- **Other changes**. Growing tumor cells obviously require a blood supply, but often the vascular stroma is insufficient, and as a result in many rapidly growing malignant tumors develop large central areas of ischemic necrosis.

DIFFERENTIATION AND ANAPLASIA

- As one might surmise, the better the differentiation of the transformed cell, the more completely it retains the functional capabilities of its normal counterpart.
- Thus, benign neoplasms and well-differentiated carcinomas of endocrine glands frequently secrete hormones characteristic of their origin. Increased levels of these hormones in the blood are used clinically to detect and follow such tumors.
- Well-differentiated squamous cell carcinomas of the epidermis synthesize keratin, and well-differentiated hepatocellular carcinomas elaborate bile.

DIFFERENTIATION AND ANAPLASIA

- In some instances, new and unanticipated functions emerge. Thus, some tumors express fetal proteins that are not produced by comparable cells in the adult, while others express proteins that are normally only found in other types of adult cells. For example, bronchogenic carcinomas may produce corticotropin, parathyroid-like hormone, insulin, glucagon, and other hormones, giving rise to paraneoplastic syndromes.

- Despite such exceptions, rapidly growing anaplastic tumors are less likely to have specialized functional activity.

METAPLASIA AND DYSPLASIA

- *Metaplasia* is defined as the replacement of one type of cell with another type.

- Metaplasia is nearly always found in association with tissue damage, repair, and regeneration.

- Often the replacing cell type is better suited to some alteration in the local environment. For example, gastroesophageal reflux damages the squamous epithelium of the esophagus, leading to its replacement by glandular (gastric or intestinal) epithelium more suited to an acidic environment.

METAPLASIA AND DYSPLASIA

- ***Dysplasia*** means "disordered growth." It is characterized by a constellation of changes that include a loss in the uniformity of the individual cells as well as a loss in their architectural orientation.

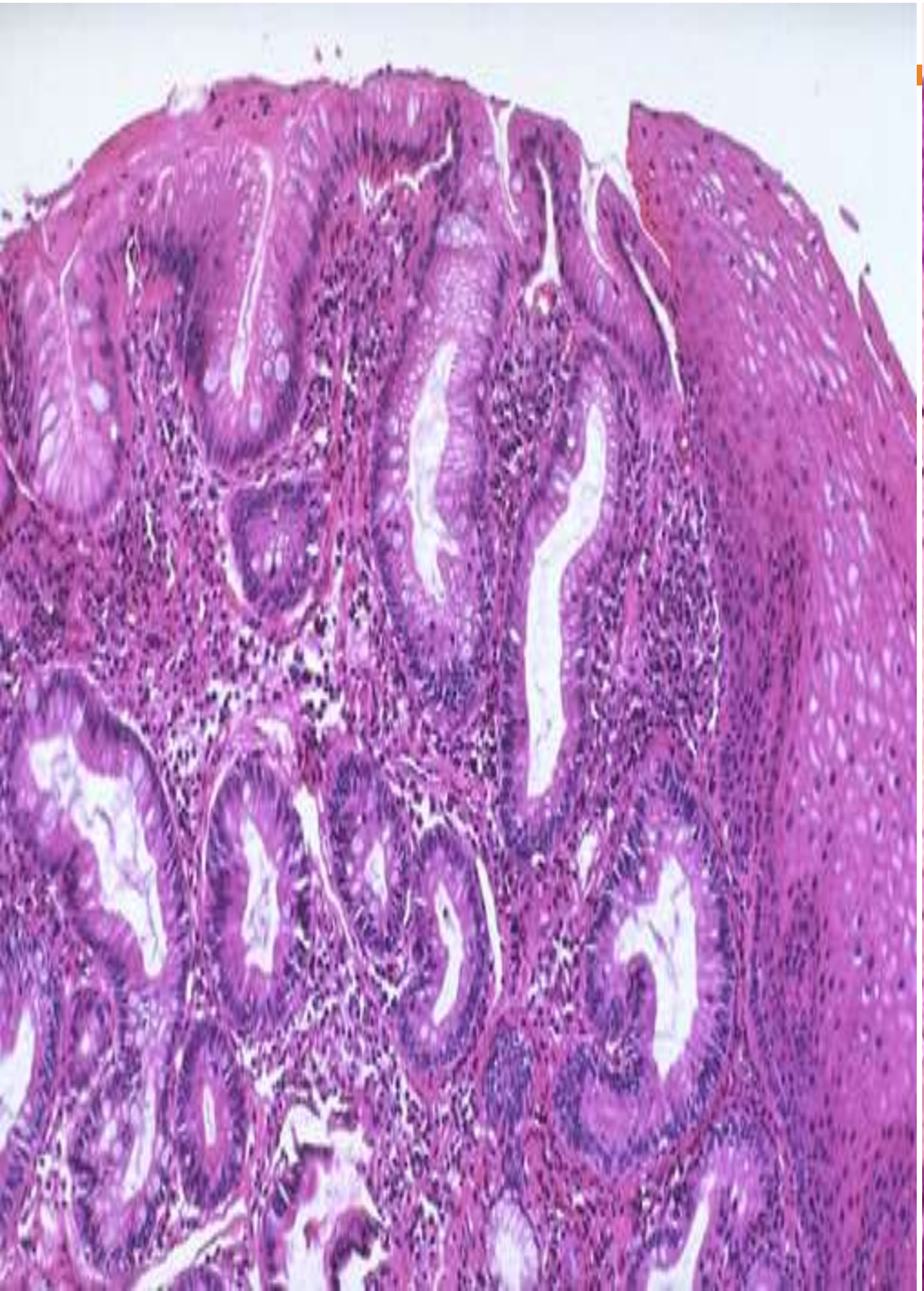
- For example, in dysplastic squamous epithelium the normal progressive maturation of tall cells in the basal layer to flattened squames on the surface may fail in part or entirely, leading to replacement of the epithelium by basal-appearing cells with hyperchromatic nuclei.

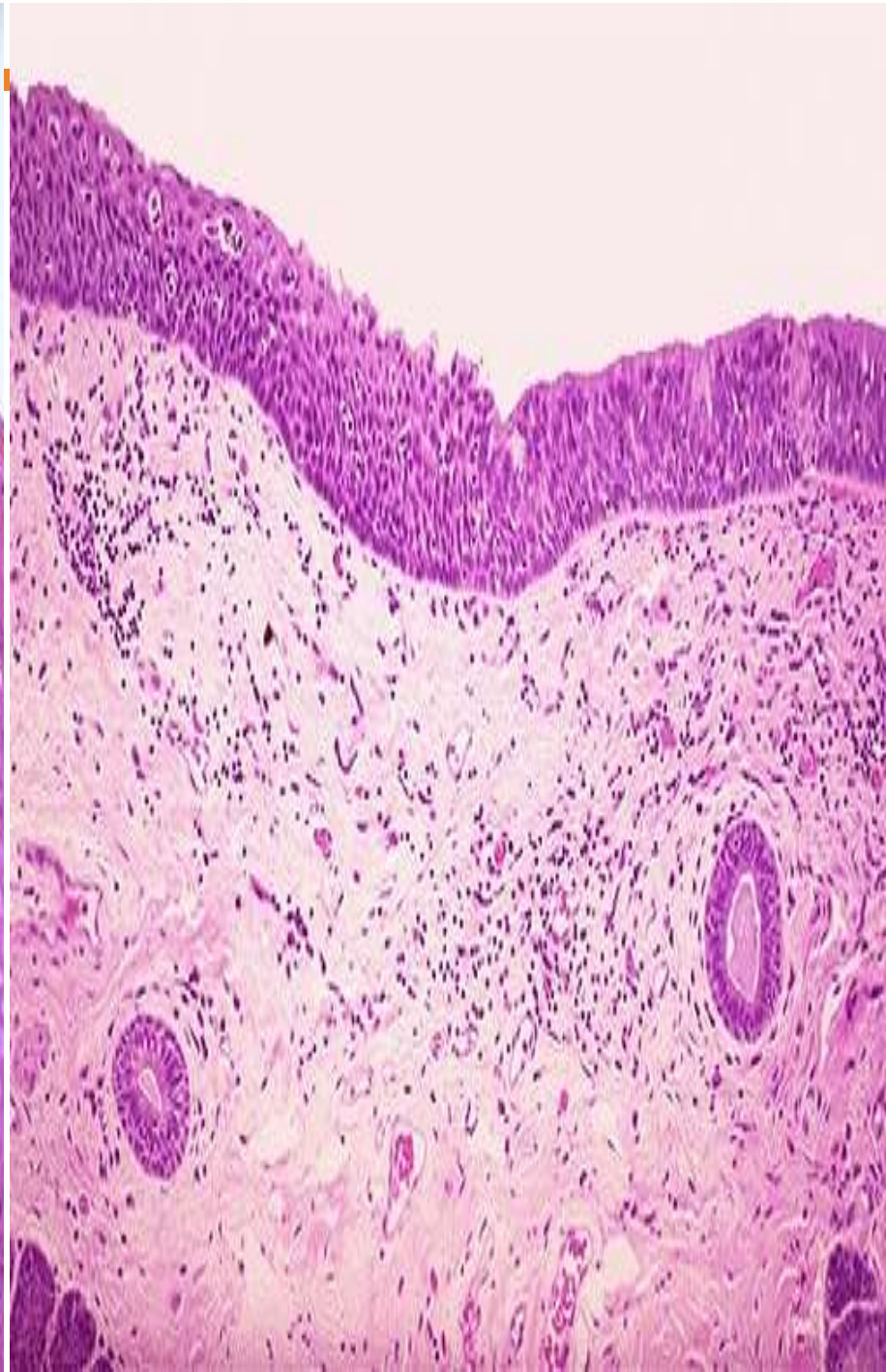
- In addition, mitotic figures are more abundant than in the normal tissue and rather than being confined to the basal layer may instead be seen at all levels, including surface cells.

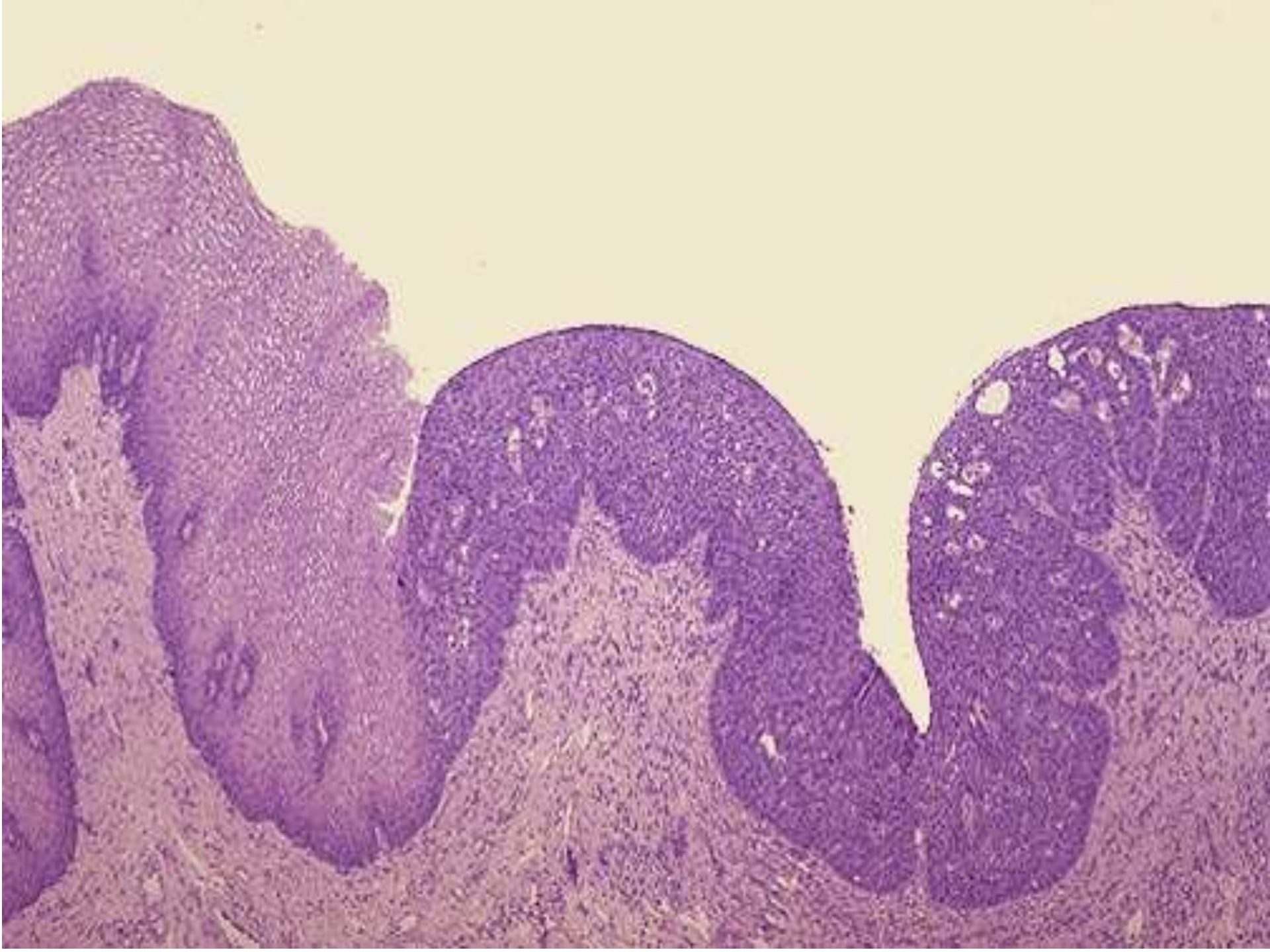
METAPLASIA AND DYSPLASIA

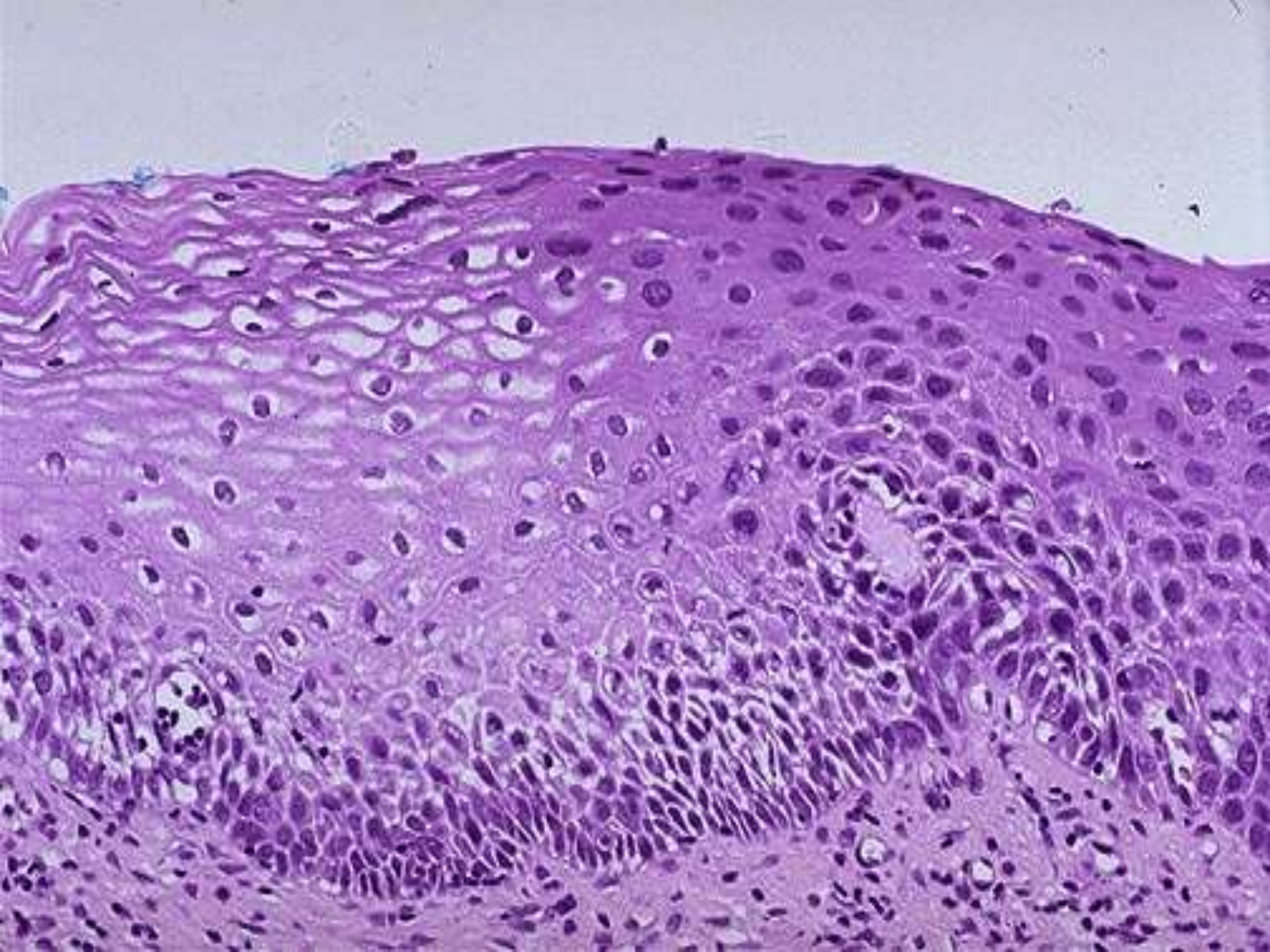
- When dysplastic changes are marked and involve the full thickness of the epithelium, but the lesion does not penetrate the basement membrane, it is considered a preinvasive neoplasm and is referred to as **carcinoma in situ**.

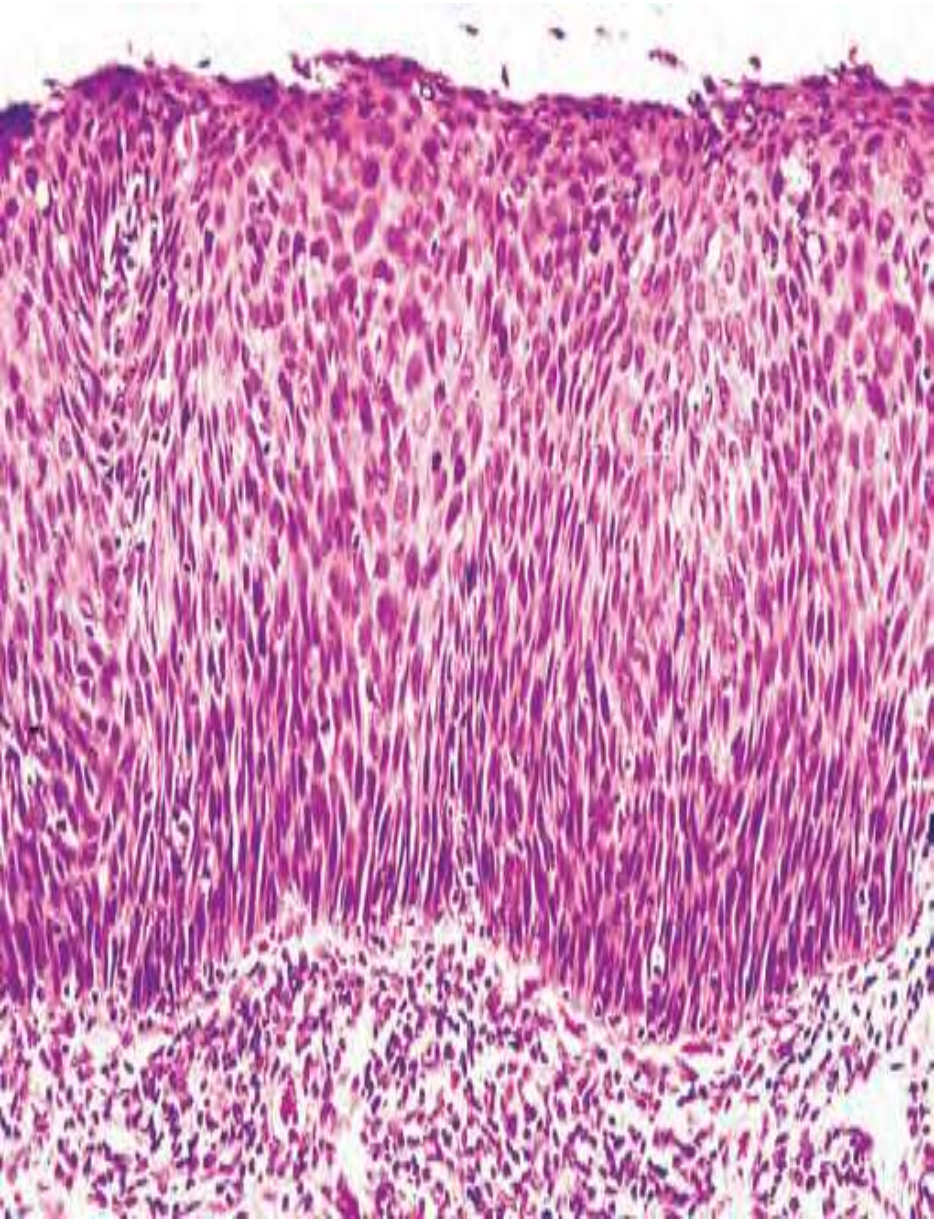
- Once the tumor cells breach the basement membrane, the tumor is said to be invasive.

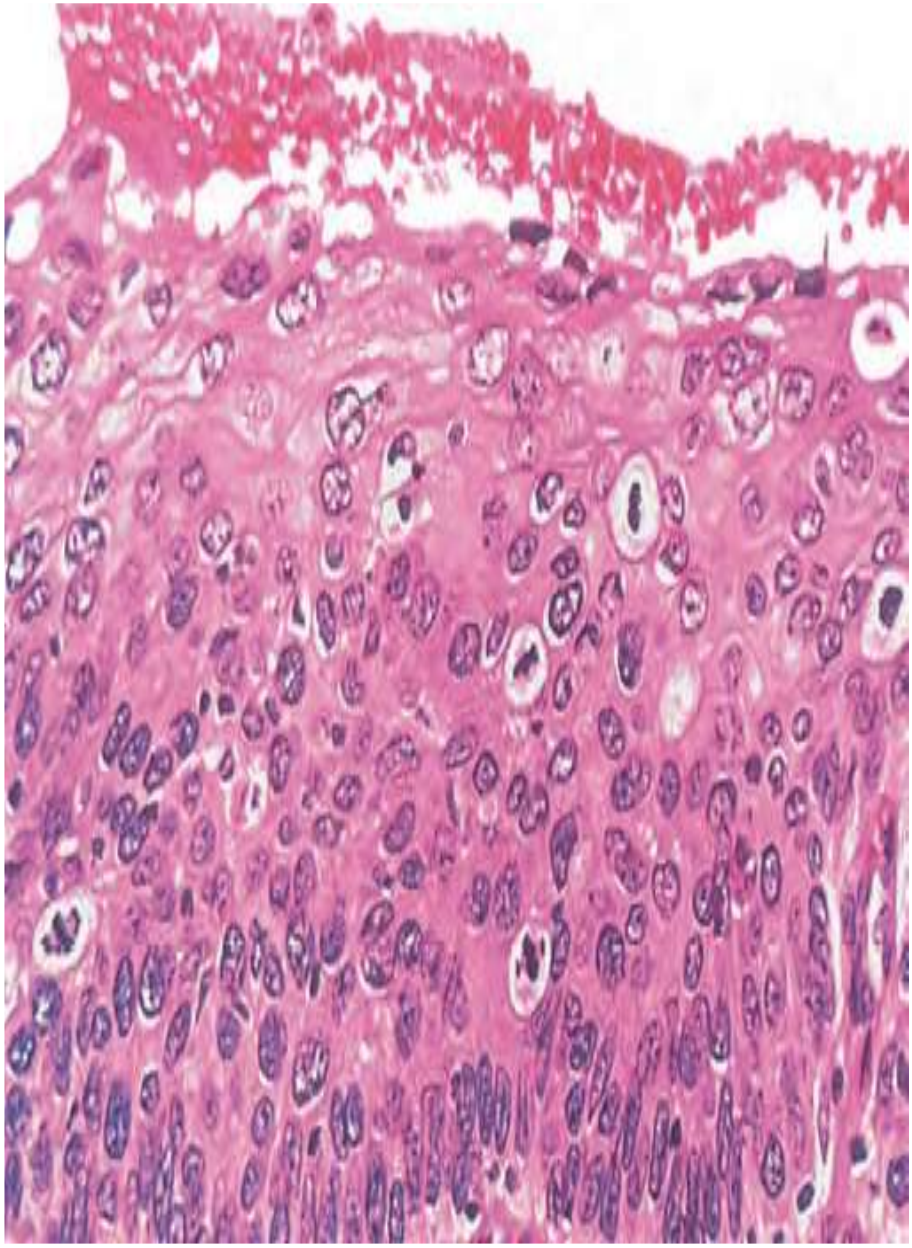






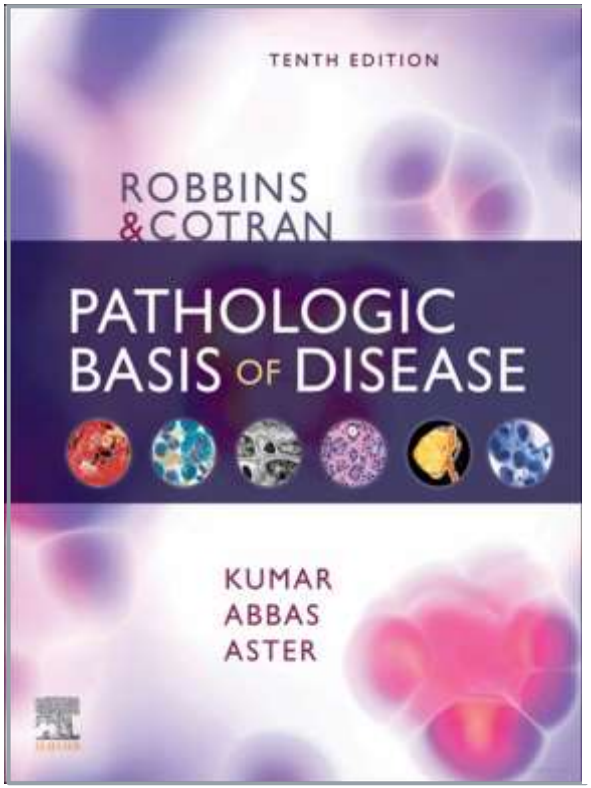






METAPLASIA AND DYSPLASIA

- **Dysplasia may be a precursor to malignant transformation, it does not always progress to cancer.**
- Carcinoma in situ may persist for years before it becomes invasive.
- Dysplasia often occurs in metaplastic epithelium, but **not all** metaplastic epithelium is dysplastic.


TENTH EDITION
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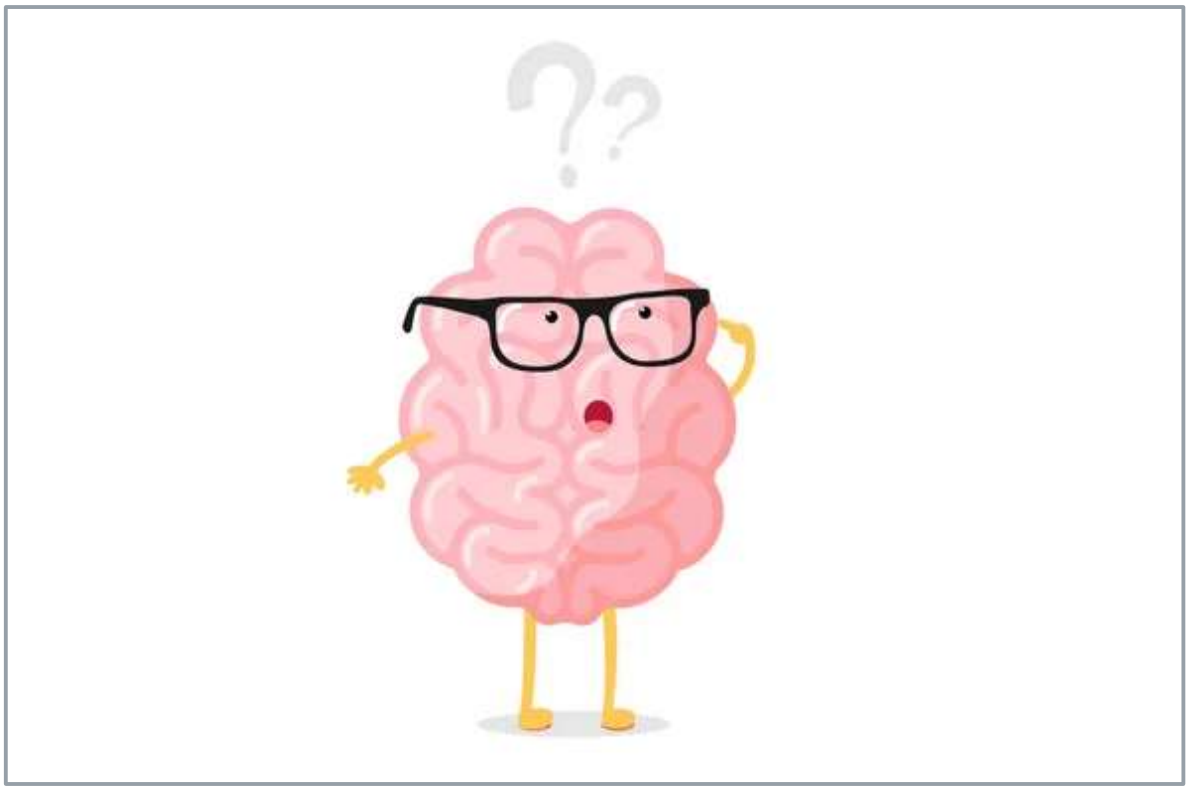
PATHOLOGIC
BASIS OF DISEASE
KUMAR
ABBAS
ASTER



THANK YOU