



NOVA

Charting New Horizons in Education

Intr **Neoplasia II** ism

16
Pathology



VA Growth



- 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 neoplasms resemble their parenchymal cells of origin, both morphologically and functionally.
- Lack of differentiation is called **anaplasia**.
- In general, benign neoplasms are composed of well-differentiated cells that closely resemble their normal counterparts.
- ✓ For example, a lipoma is made up of mature fat cells that are laden with cytoplasmic lipid vacuoles.
- ✓ A chondroma is made up of mature cartilage cells that synthesize their usual cartilaginous matrix.

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.

DIFFERENTIATION AND ANAPLASIA

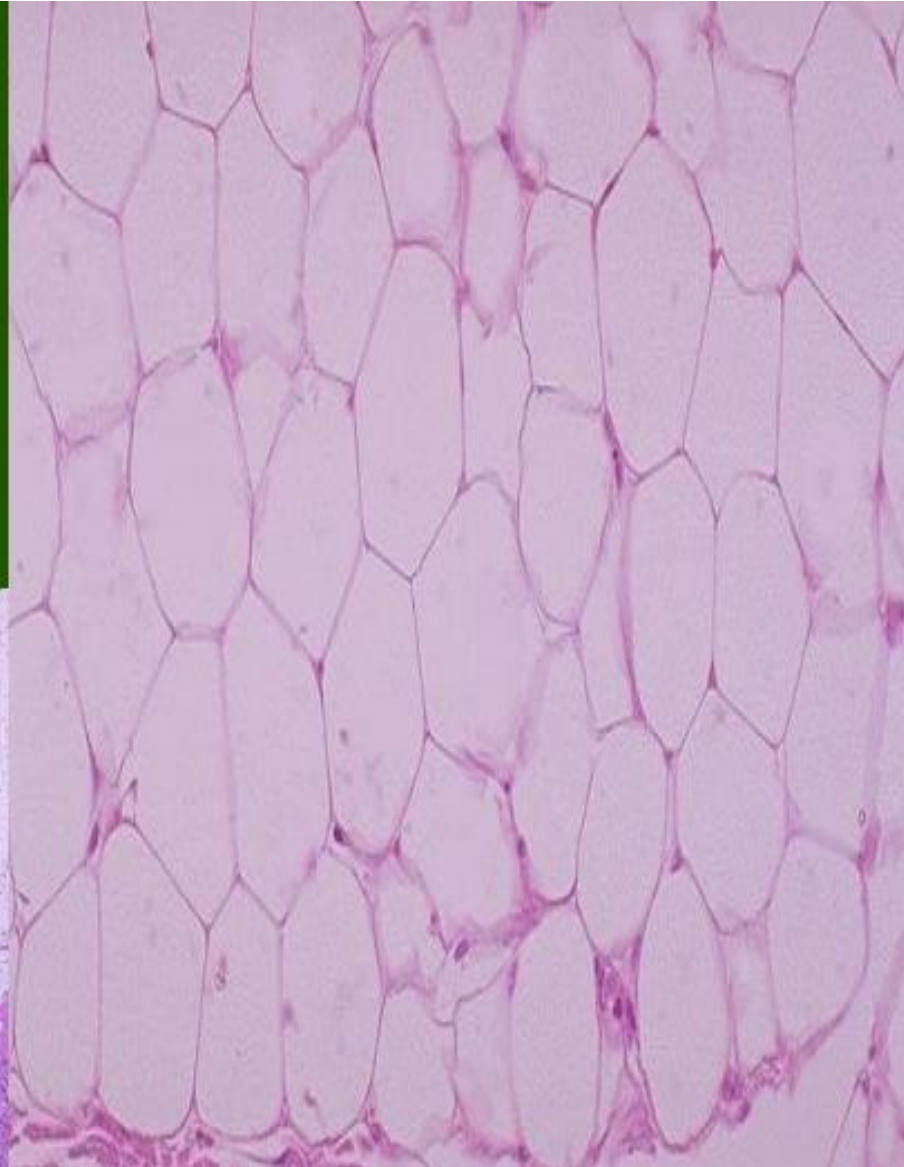
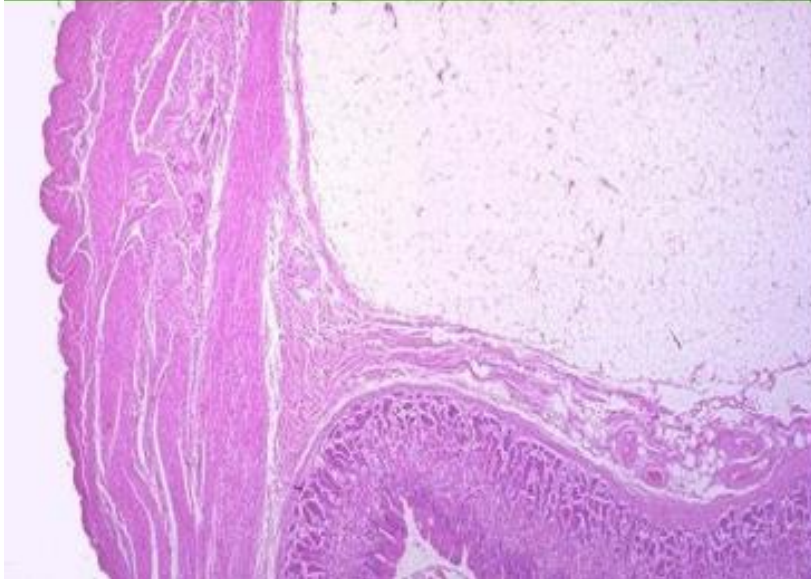


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Table 7.2 Comparisons Between Benign and Malignant Tumors

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

Intestinal lipoma



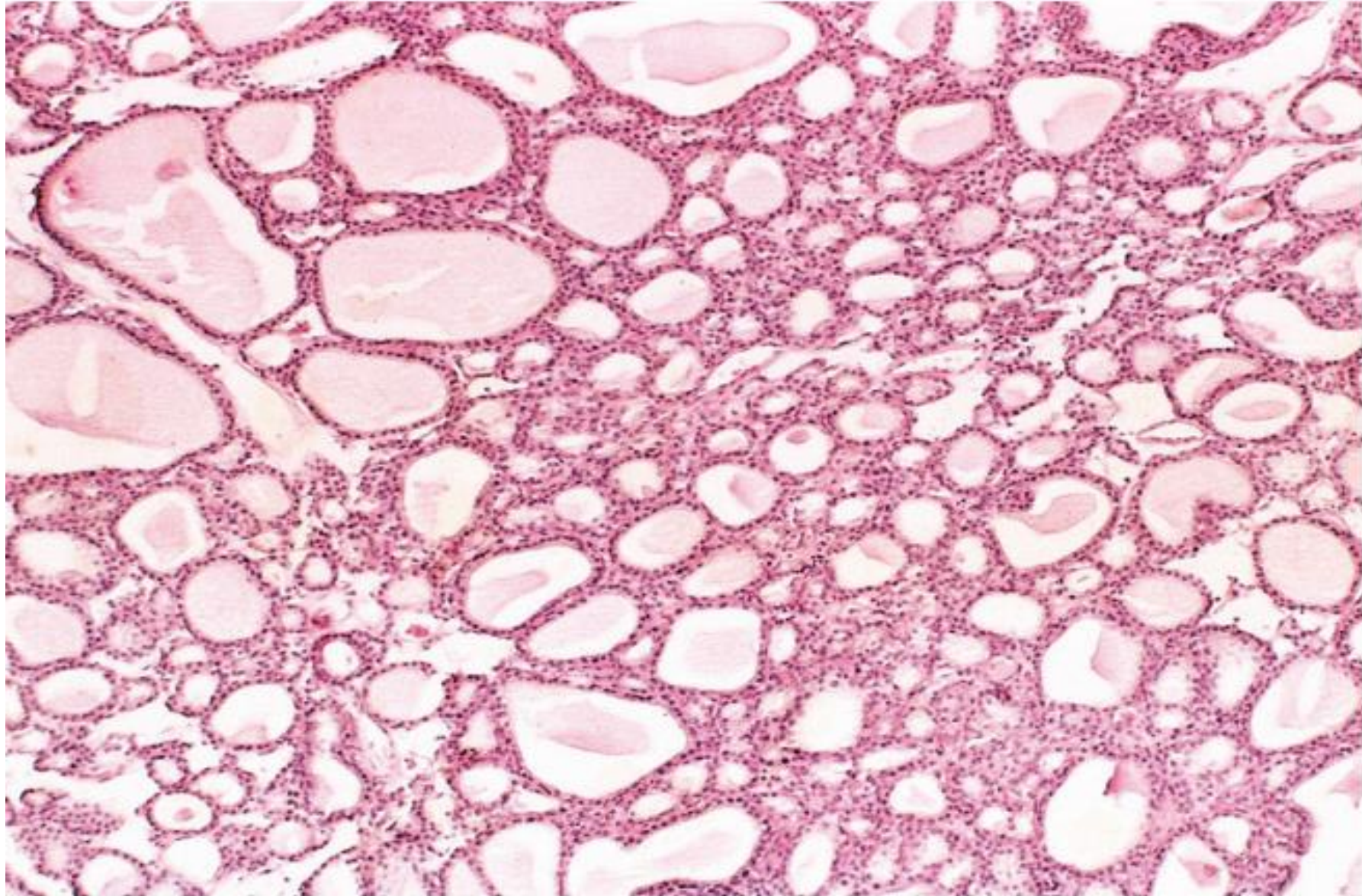
Uterine Leiomyoma (fibroid)



Fibroma



va Benign tumor (adenoma) of the thyroid.



DIFFERENTIATION AND ANAPLASIA

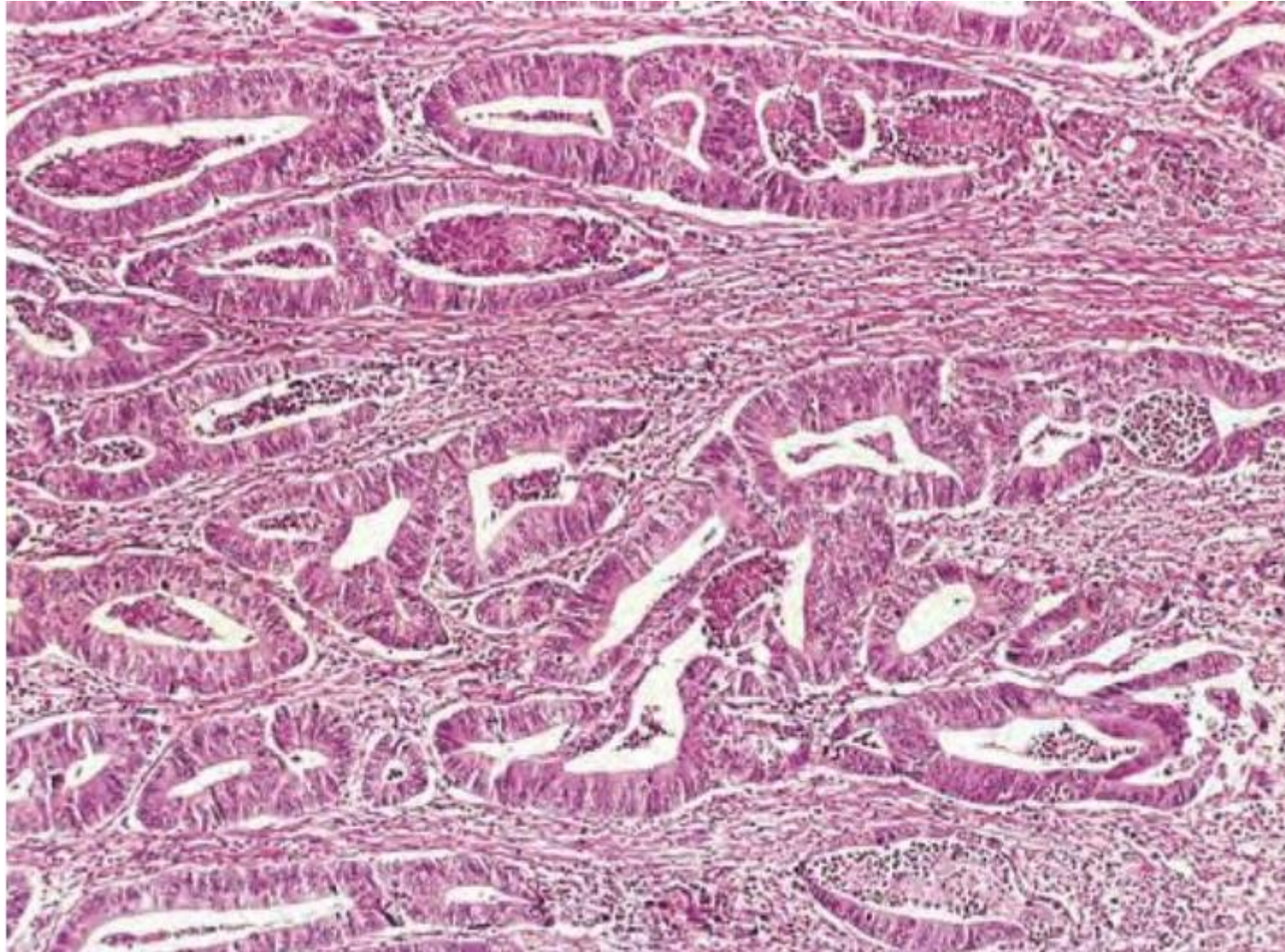


- Malignant neoplasms exhibit a wide range of parenchymal cell differentiation, most exhibit morphologic alterations that betray their malignant nature.
- There are exceptions , certain well-differentiated adenocarcinomas of the thyroid, for example, form normal-appearing follicles, and some squamous 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
- 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.

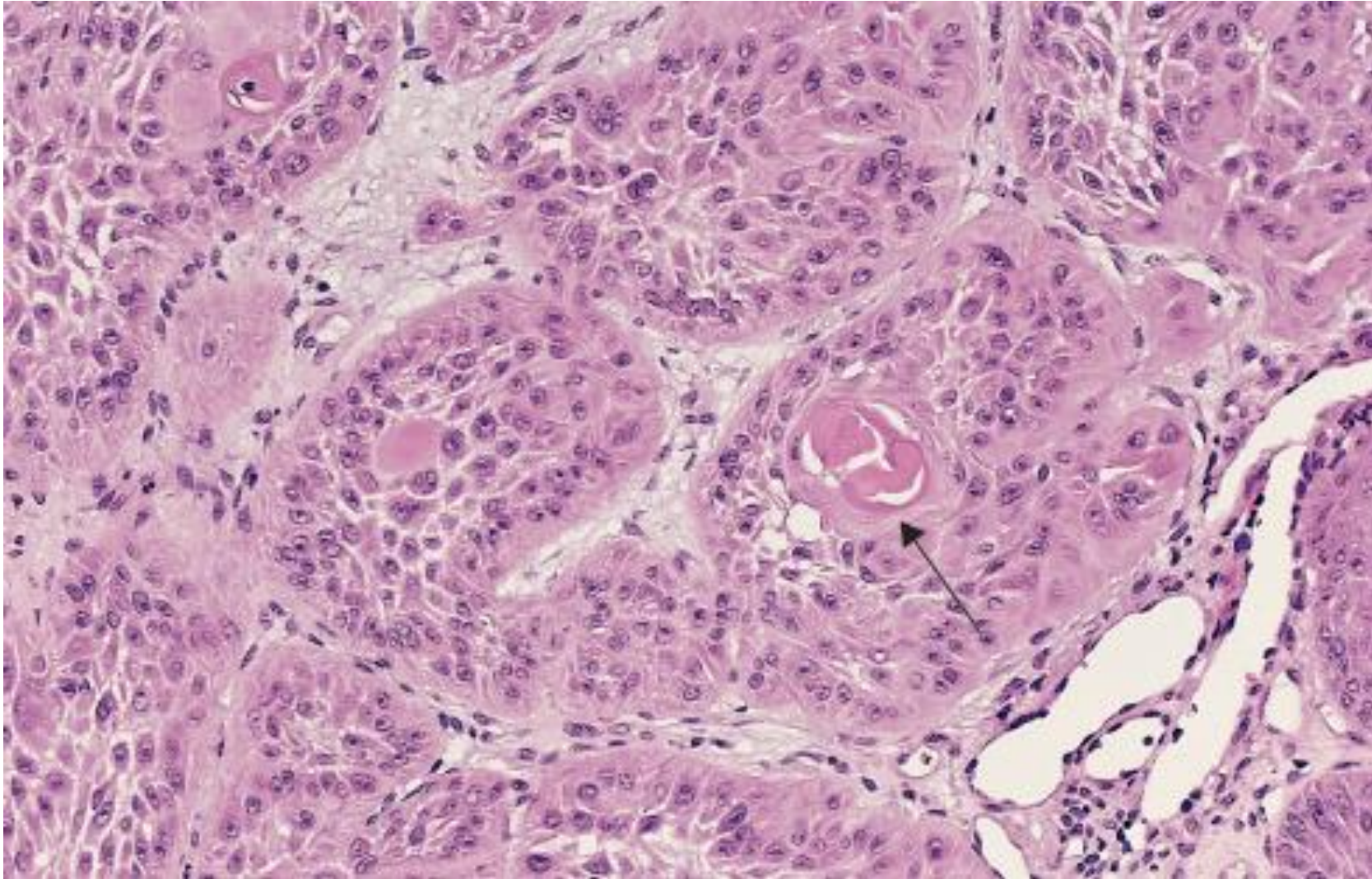
Normal colon



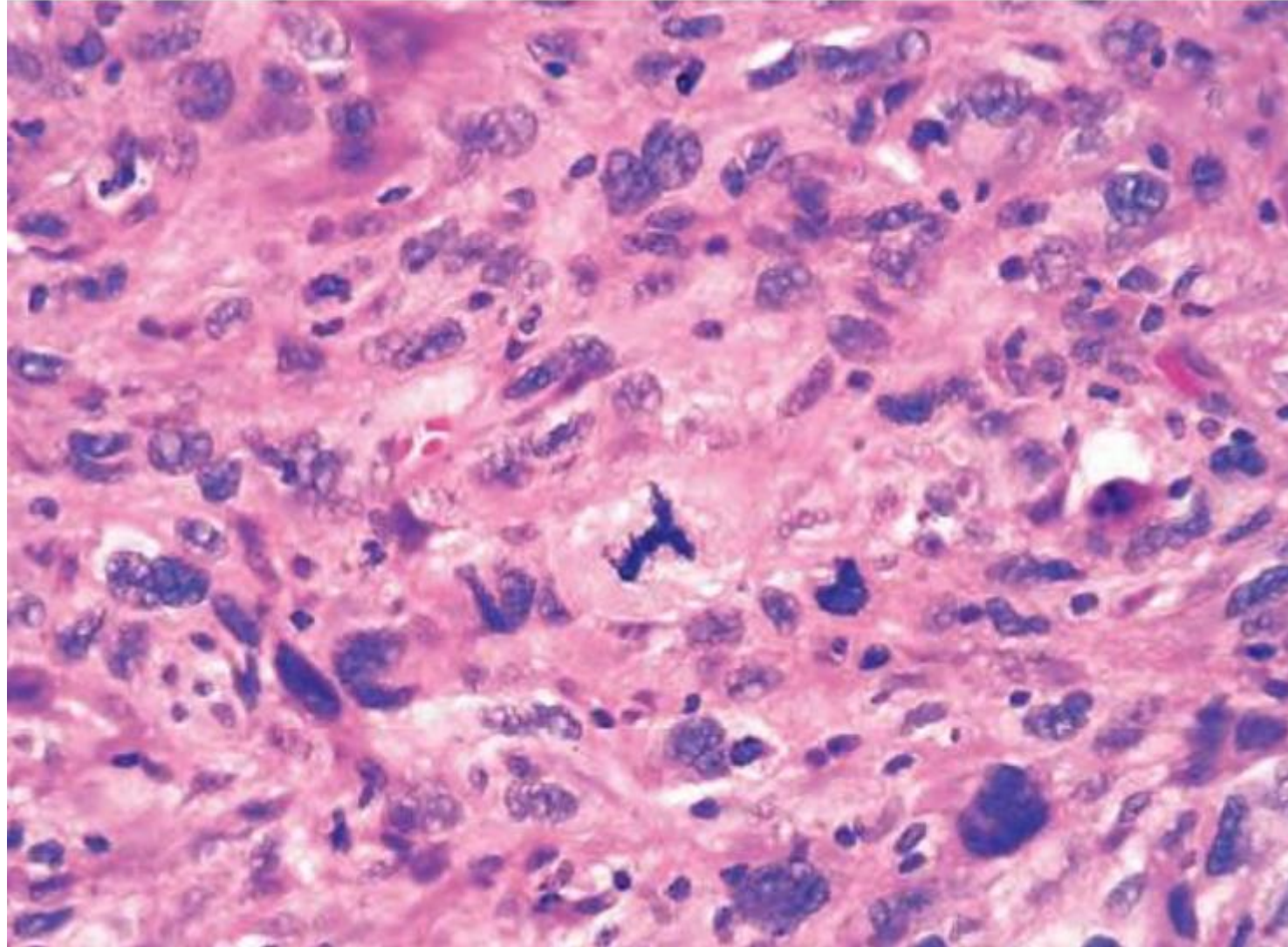
❖ Malignant tumor (adenocarcinoma) of the colon - Moderately differentiated



va Well-differentiated squamous cell carcinoma of the skin.



va Anaplastic tumor



❖ DIFFERENTIATION AND ANAPLASIA



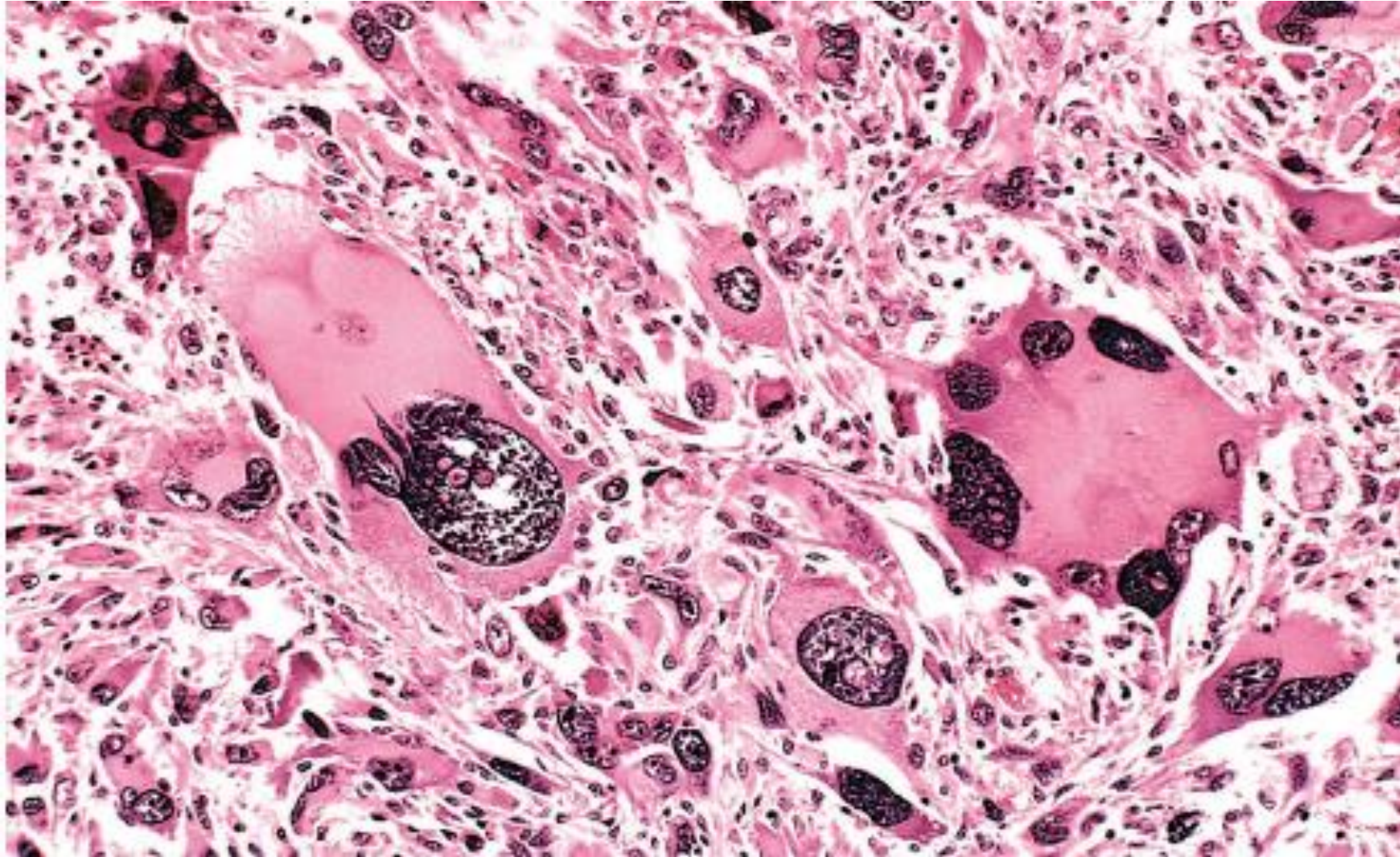
- Malignant neoplasms that are composed of poorly differentiated cells are said to be anaplastic.
- Lack of differentiation, or anaplasia, is considered a hallmark of malignancy. The term anaplasia means “to form backward,” implying a reversal of differentiation to a more primitive level.

❖ 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.

va Pleomorphic tumor of the skeletal muscle (rhabdomyosarcoma).



❖ Anaplasia



2. Abnormal nuclear morphology:

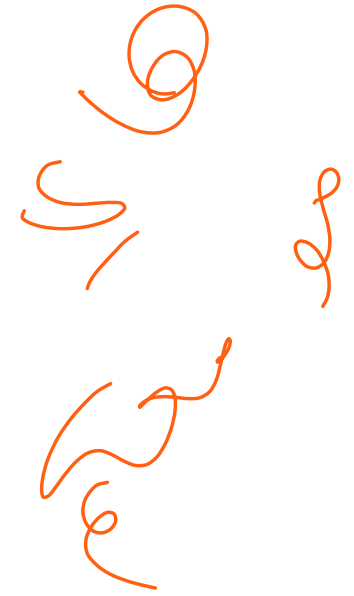
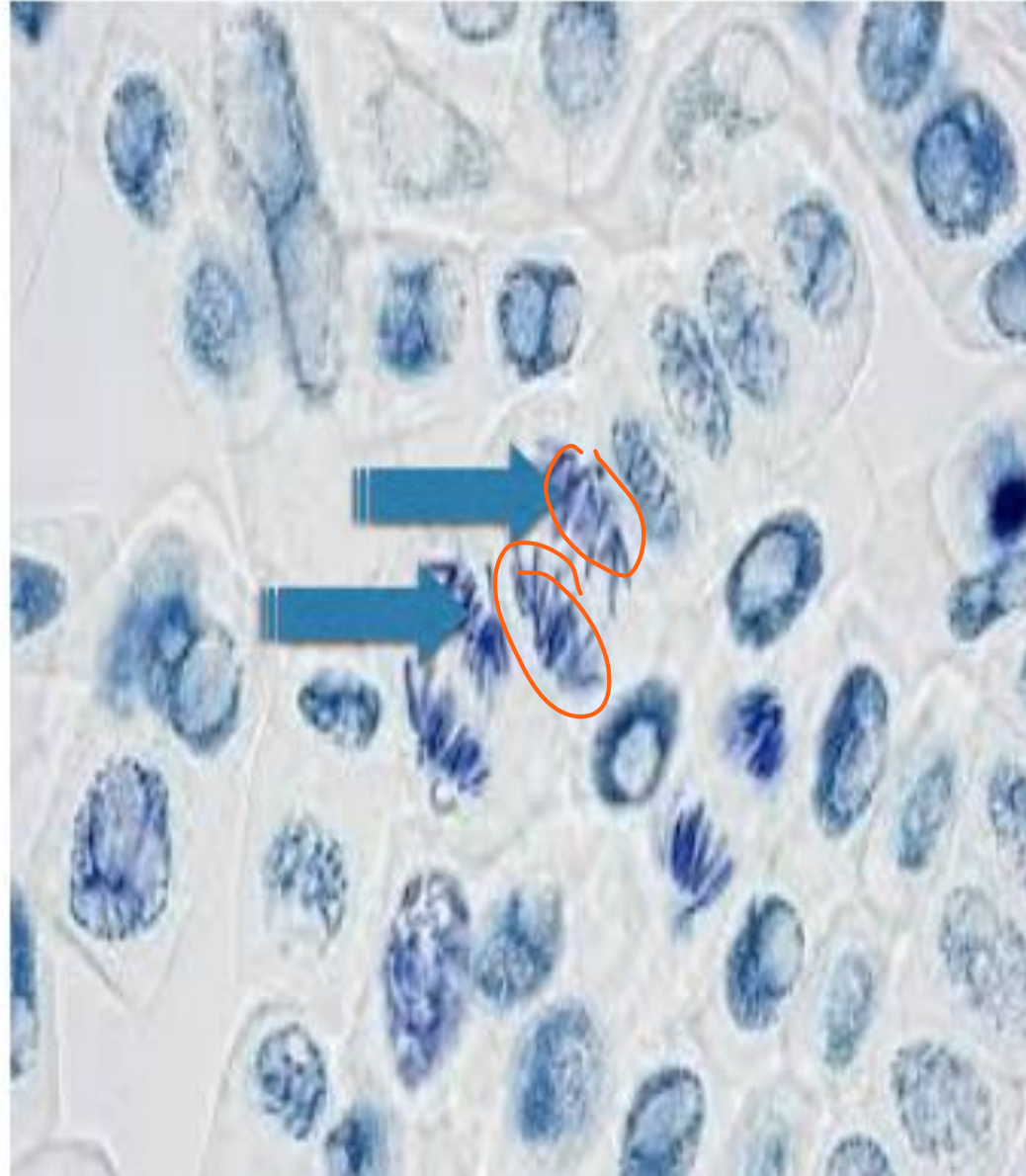
- The nuclei are disproportionately large for the cell, with a nuclear-to-cytoplasm ratio that may approach 1 : 1 instead of the normal 1 : 4 or 1 : 6.
- The nuclear shape is variable and often irregular, and the chromatin is often coarsely clumped and distributed along the nuclear membrane, or more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



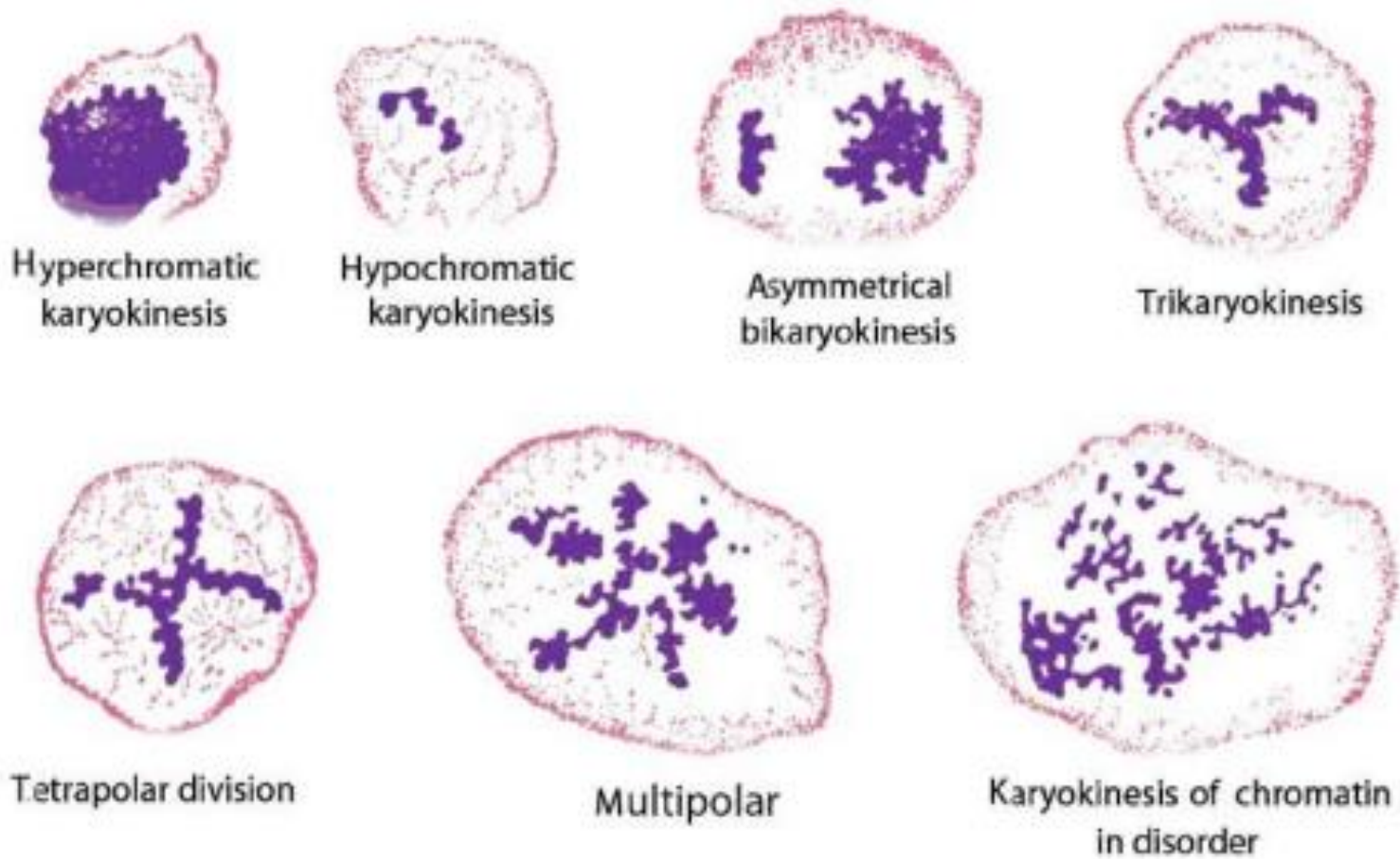
3. Mitoses:

- 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.

Normal mitotic figures



Abnormal mitotic figures



abnormal mitotic figures in malignant tumors

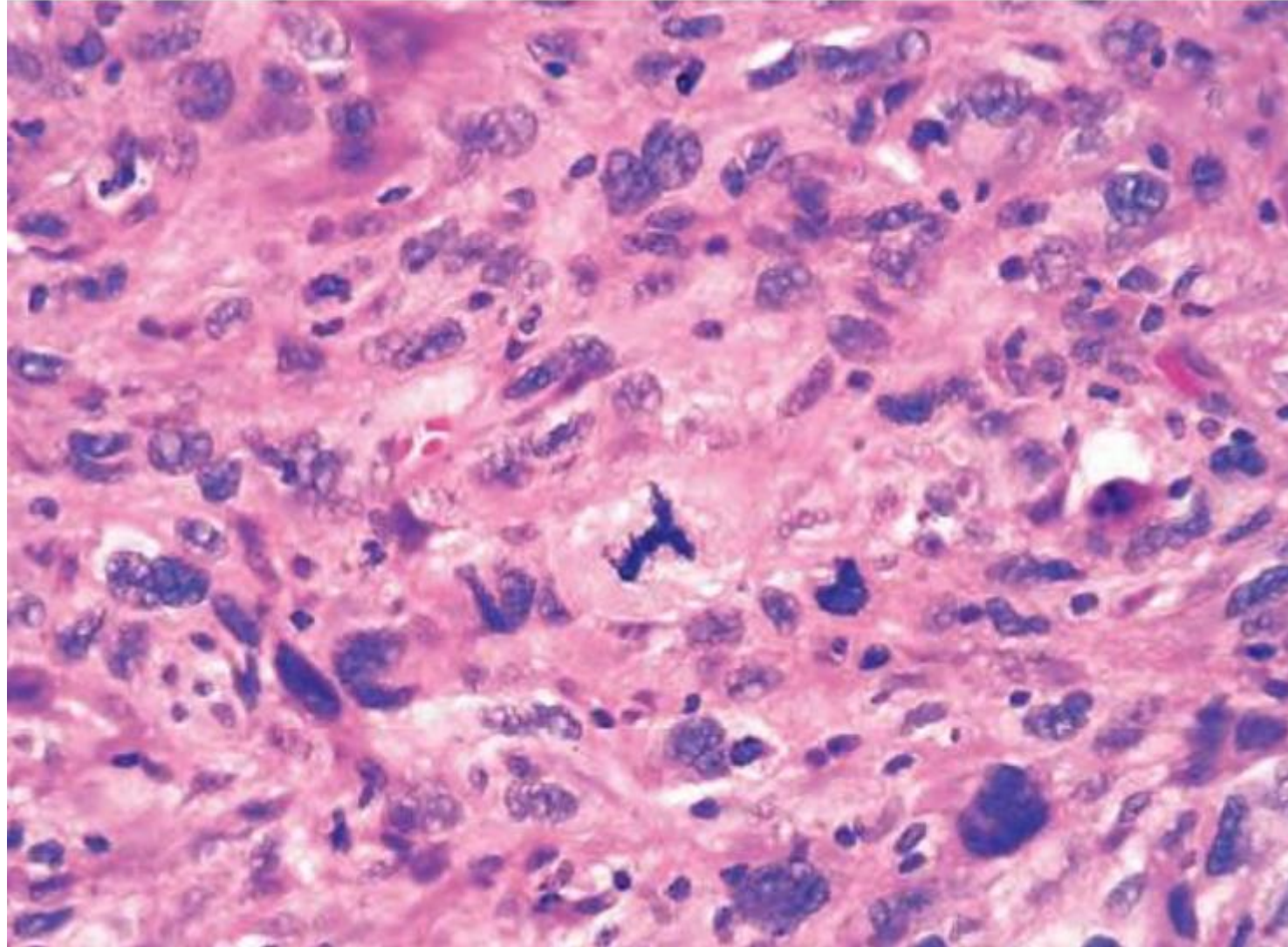
❖ Anaplasia



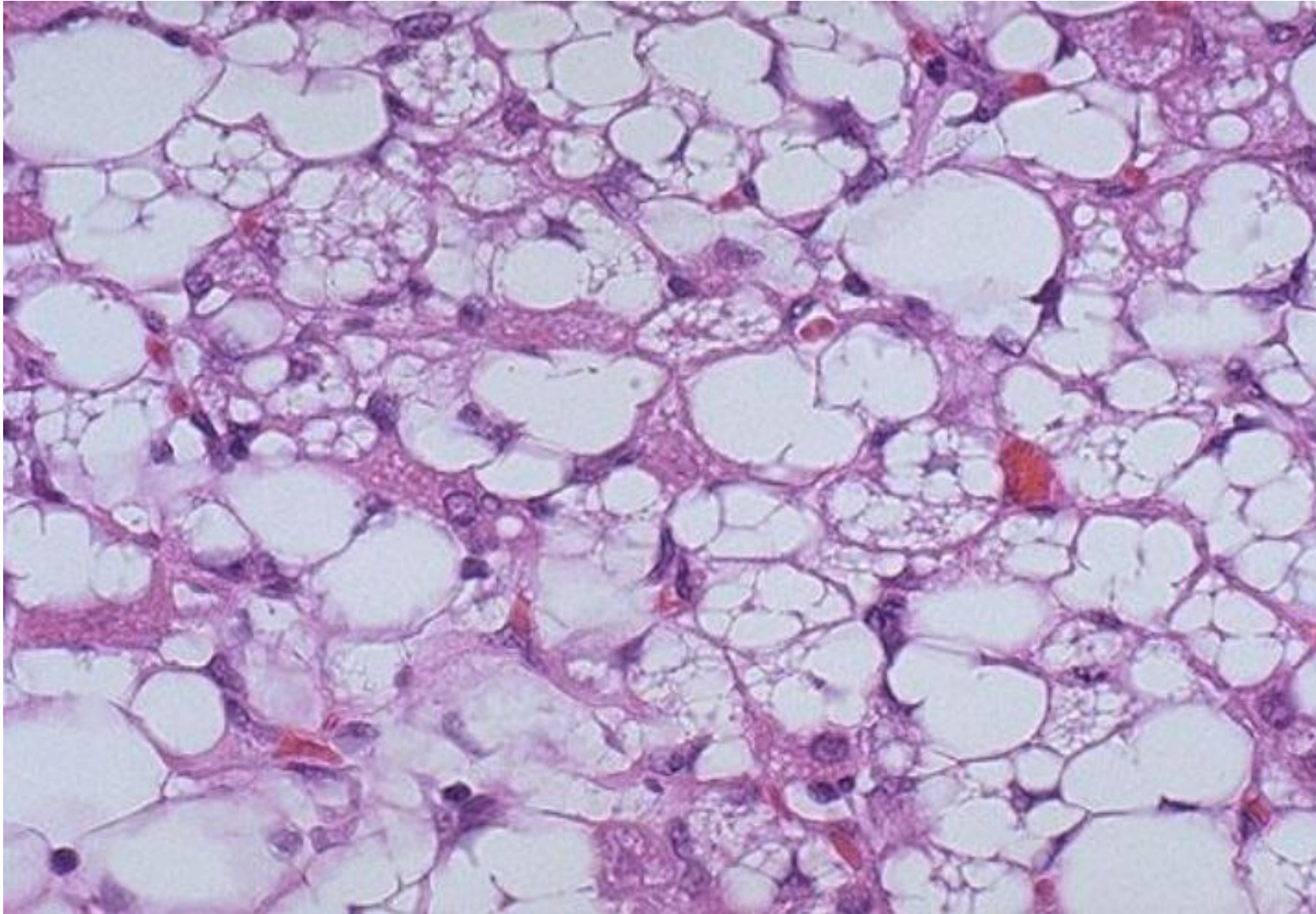
4. **Loss of polarity:**

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

va Anaplastic tumor



va Liposarcoma



❖ Anaplasia



- 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.

❖ 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.

❖ Anaplasia



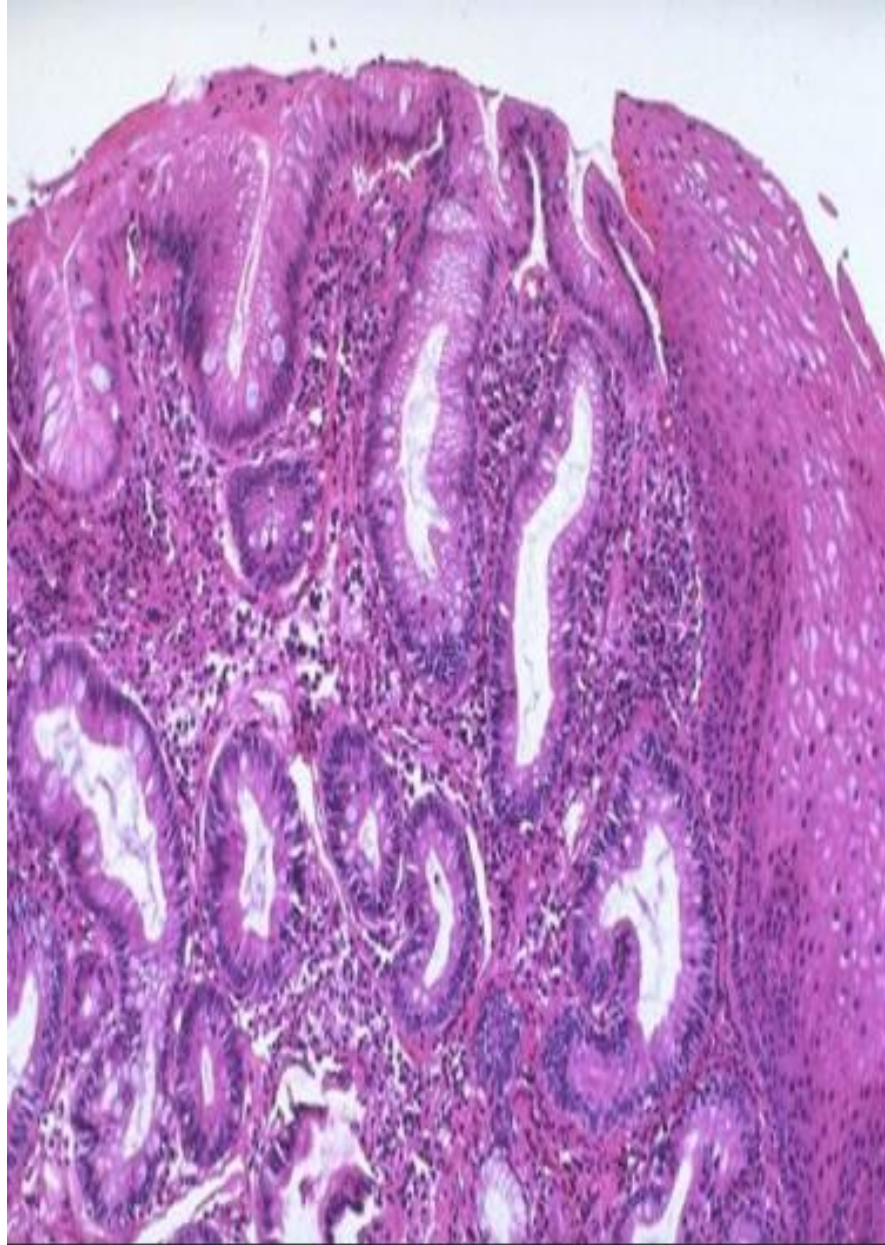
- In some instances, new and unanticipated functions emerge → Thus, some tumors express fetal proteins that are not produced by comparable cells in the adult, while others express proteins that are normally only found in other types of adult cells.
- For example, bronchogenic carcinomas may produce corticotropin, 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

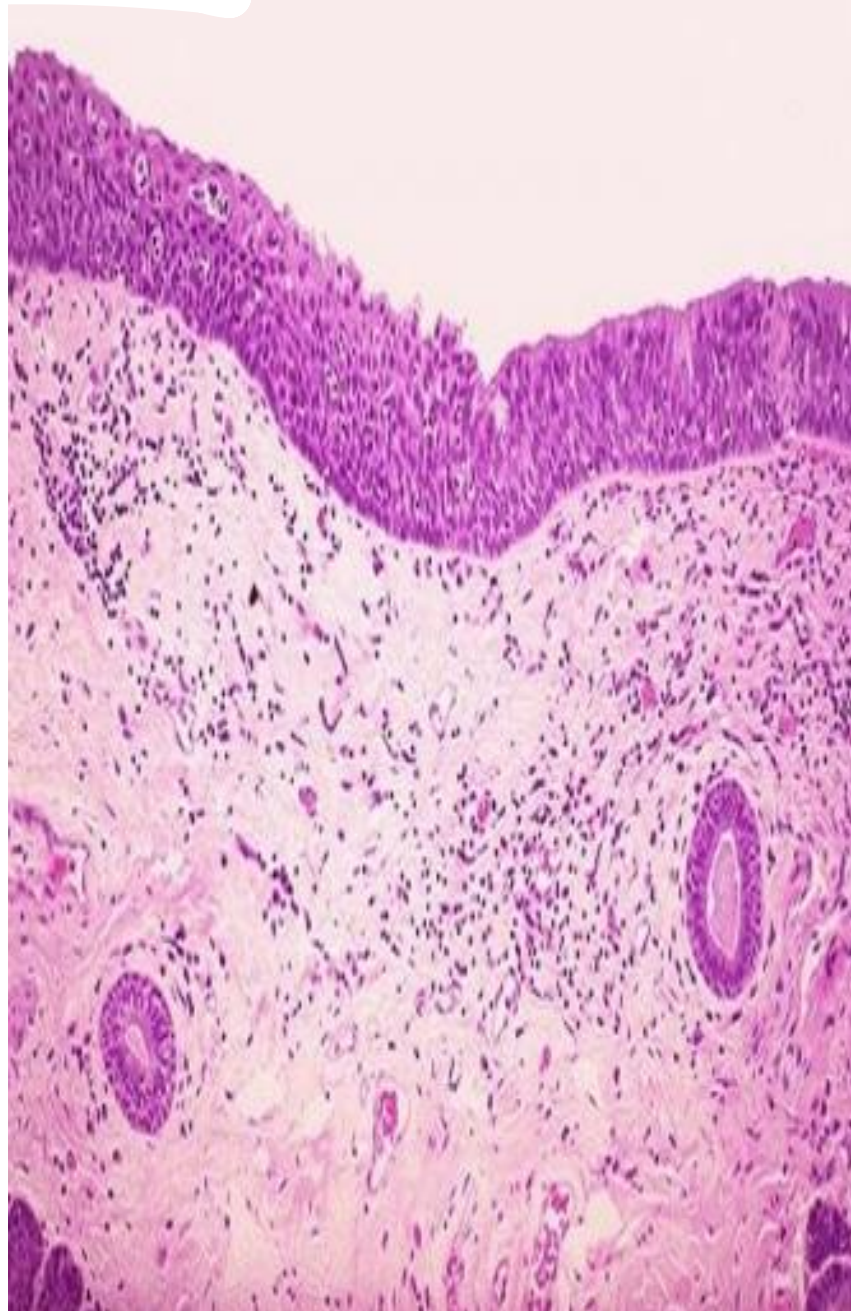


- **Metaplasia** is defined as the replacement of one type of cell with another type.
- Metaplasia is nearly always found in association with tissue damage, repair, and regeneration.
- Often the replacing cell type is better suited to some alteration in the local environment.
- For example, gastroesophageal reflux damages the squamous epithelium of the esophagus, leading to its replacement by glandular (gastric or intestinal) epithelium more suited to an acidic environment.

Intestinal metaplasia



Dysplasia



Normal epithelium



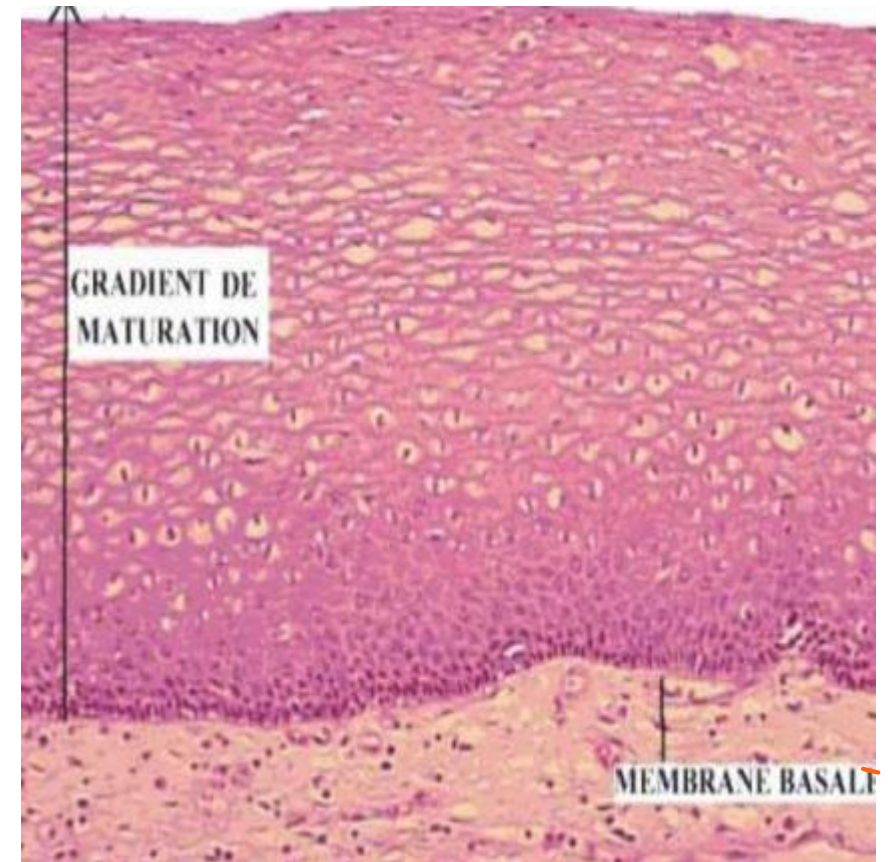
- Normal epithelium is well organized.
- It is composed of layers of cells that mature as we go up: towards the surface.
- Epithelial tissue regenerates all the time, so cells originate from the base of the epithelium and grow upwards.
- During this growth they mature.. and when they reach the surface they spend the rest of their lifespan as fully mature cells then they die by apoptosis.



Normal epithelium



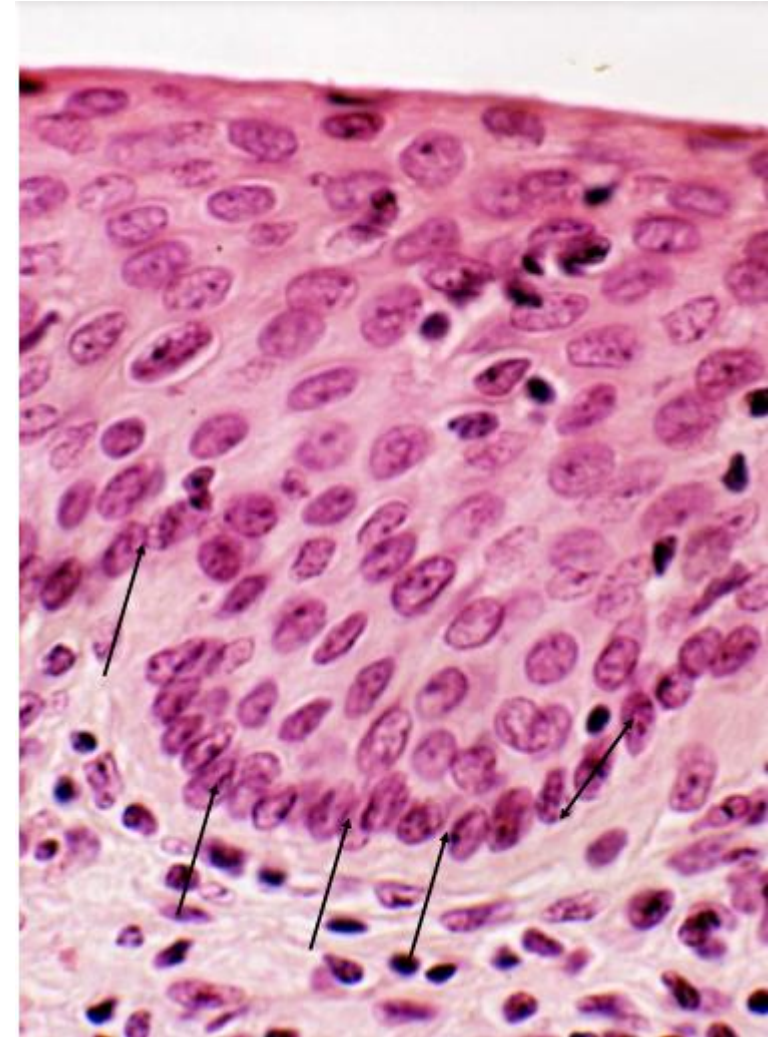
- Note that this epithelium is composed of several layers of squamous cells.
- They are all organized.
- The cells look similar with slight differences; they mature towards the top.
- There is an intact, non invaded, basement membrane.



Normal epithelium



- Basal layer in normal epithelium
- Note the cells with arrows at the base of this epithelium
- They are nice and intact and form a continuous, undisturbed layer



Metaplasia and Dysplasia



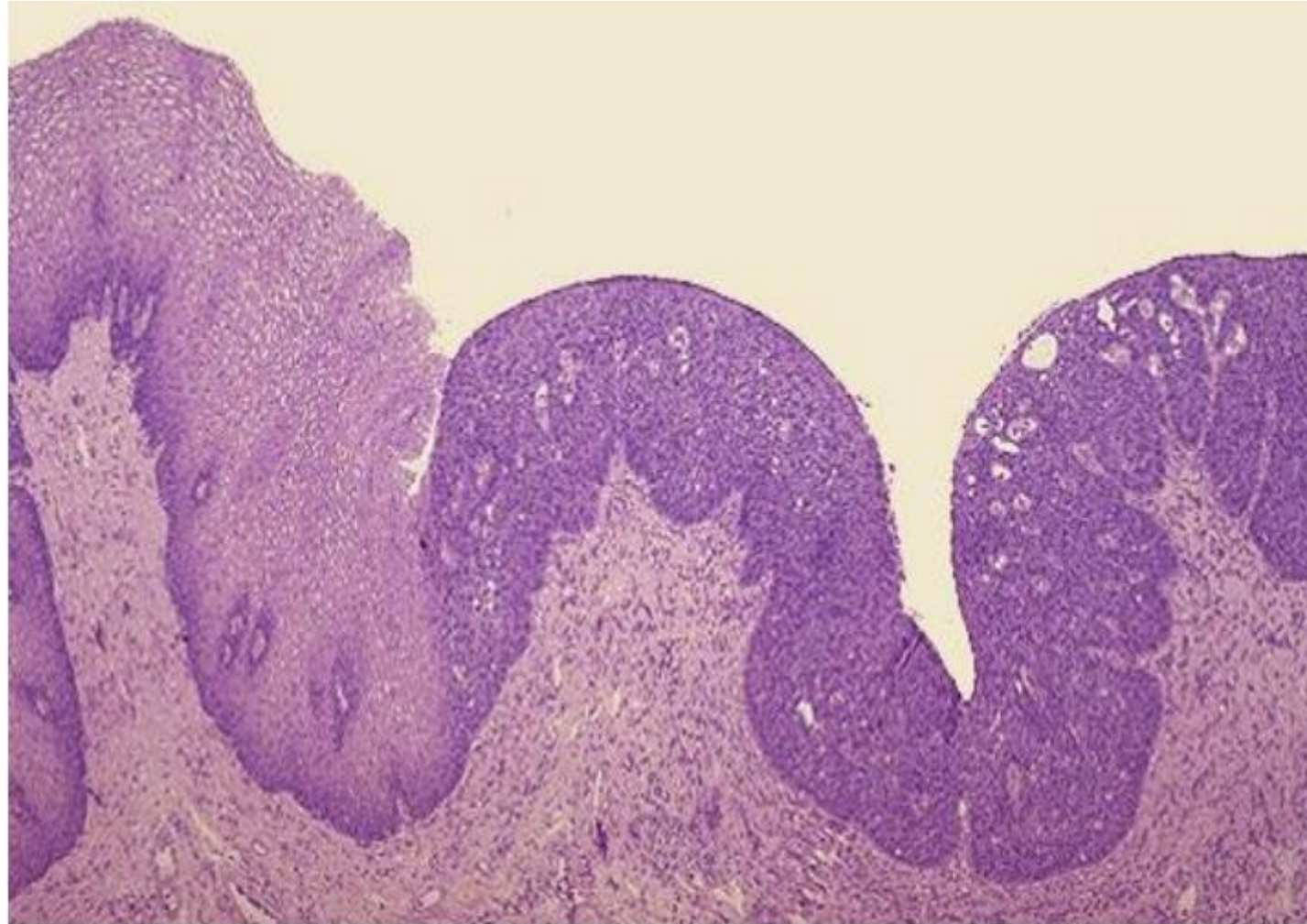
- **Dysplasia** means “disordered growth.”
- It is characterized by a constellation of changes that include a loss in the uniformity of the individual cells as well as a loss in their architectural orientation.
- For example, in dysplastic squamous epithelium the normal progressive maturation of tall 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

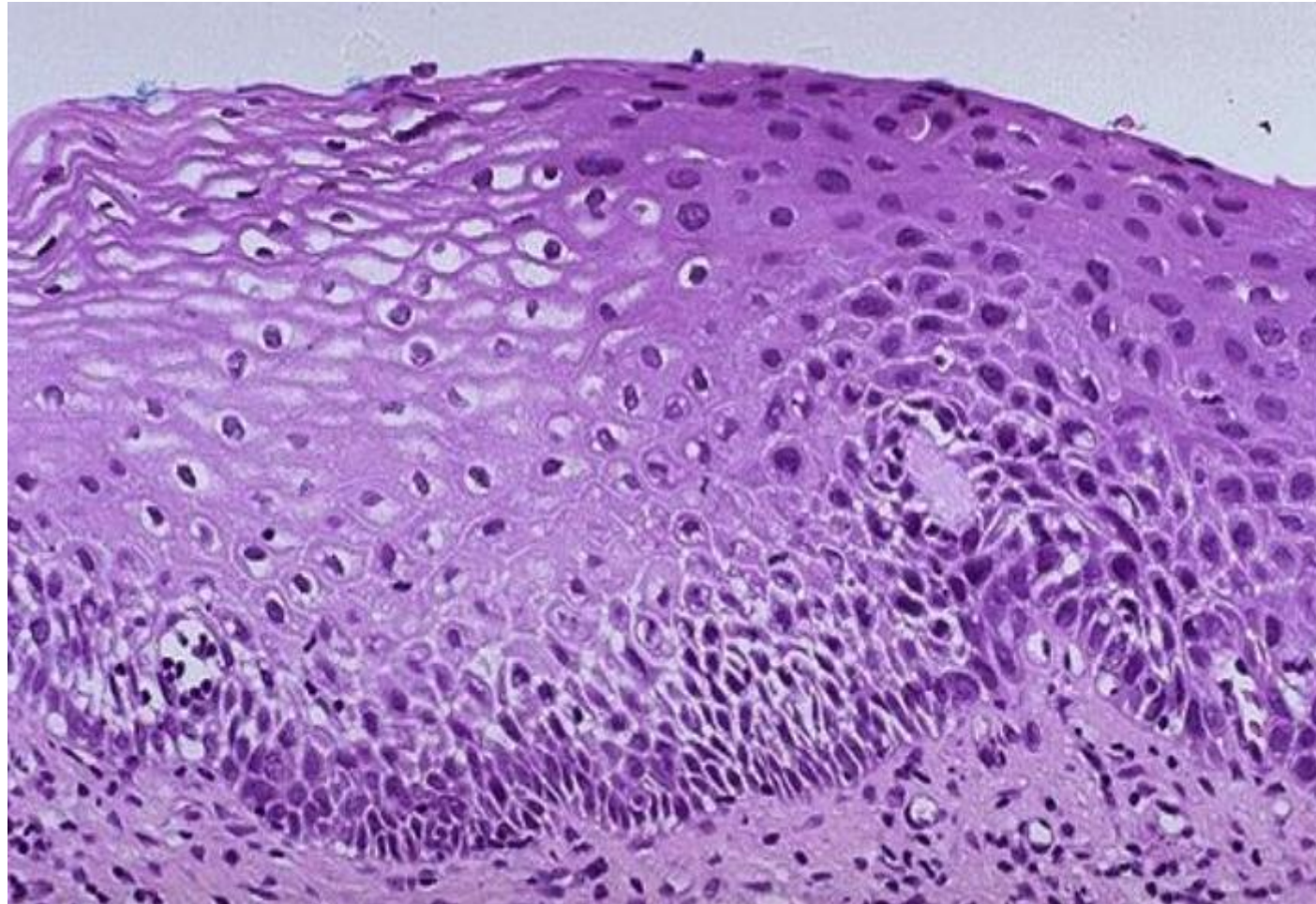


- When dysplastic changes are marked and involve the full thickness of the epithelium, but the lesion does not penetrate the basement membrane, it is considered a preinvasive neoplasm and is referred to as carcinoma in situ.
- Once the tumor cells breach the basement membrane, the tumor is said to be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

❖ Cervical dysplasia



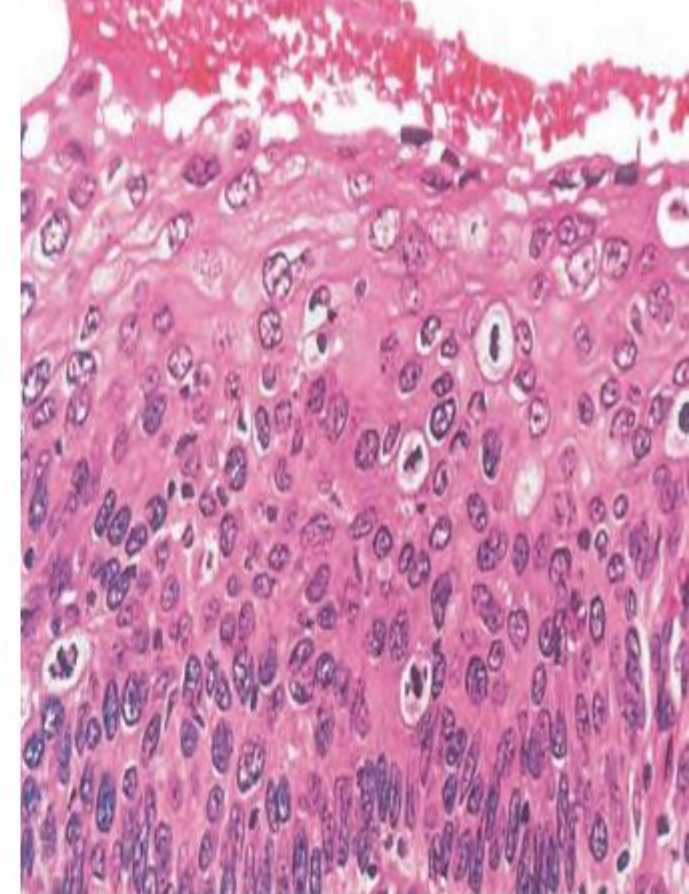
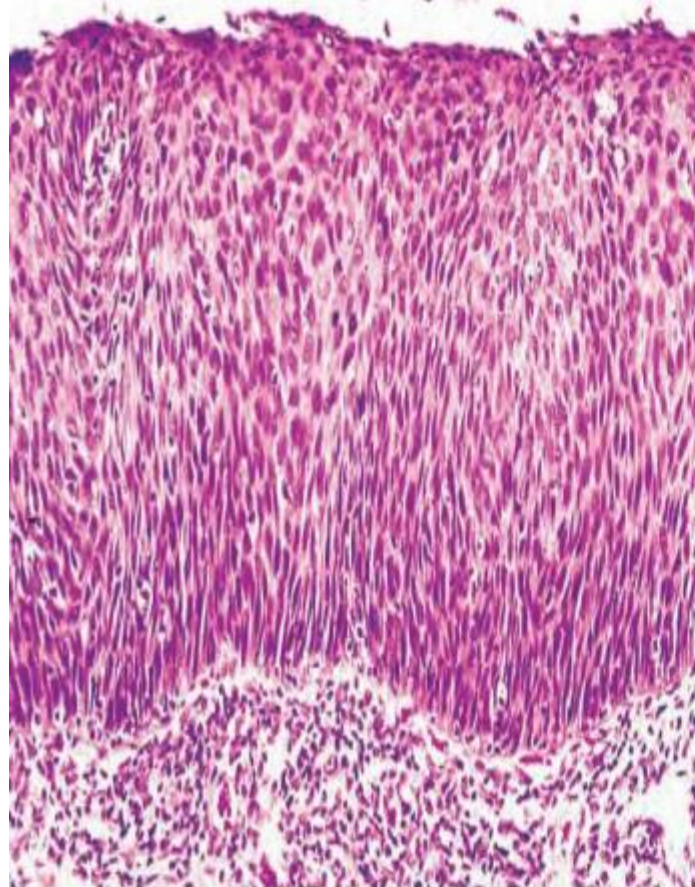
va Cervical dysplasia



VA Carcinoma in situ



- Carcinoma in situ. This low - power view shows that the entire thickness of the epithelium is replaced by atypical dysplastic cells.
- The basement membrane is intact.
- B, A high-power view of another region shows marked nuclear and cellular pleomorphism, and numerous mitotic figures extending toward the surface.





«Wherever the art of medicine is loved,
there is also a love of humanity.»

- Hippocrates-

