Neoplasia
Lecture 2

CHARACTERISTICS OF BENIGN AND MALIGNANT NEOPLASMS

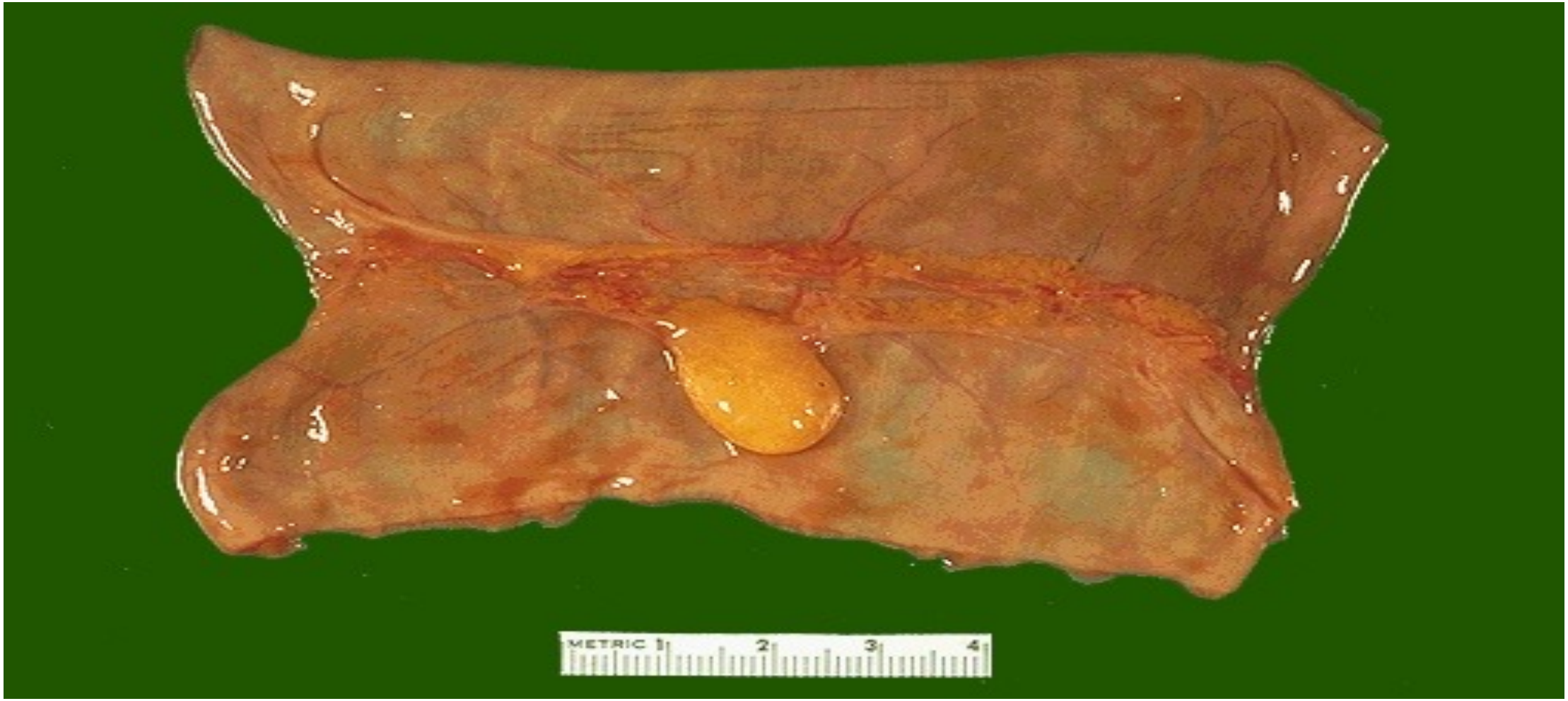
1. Differentiation and anaplasia

Differentiation refers to the extent to which neoplasms resemble their parenchymal cells of origin, both morphologically and functionall

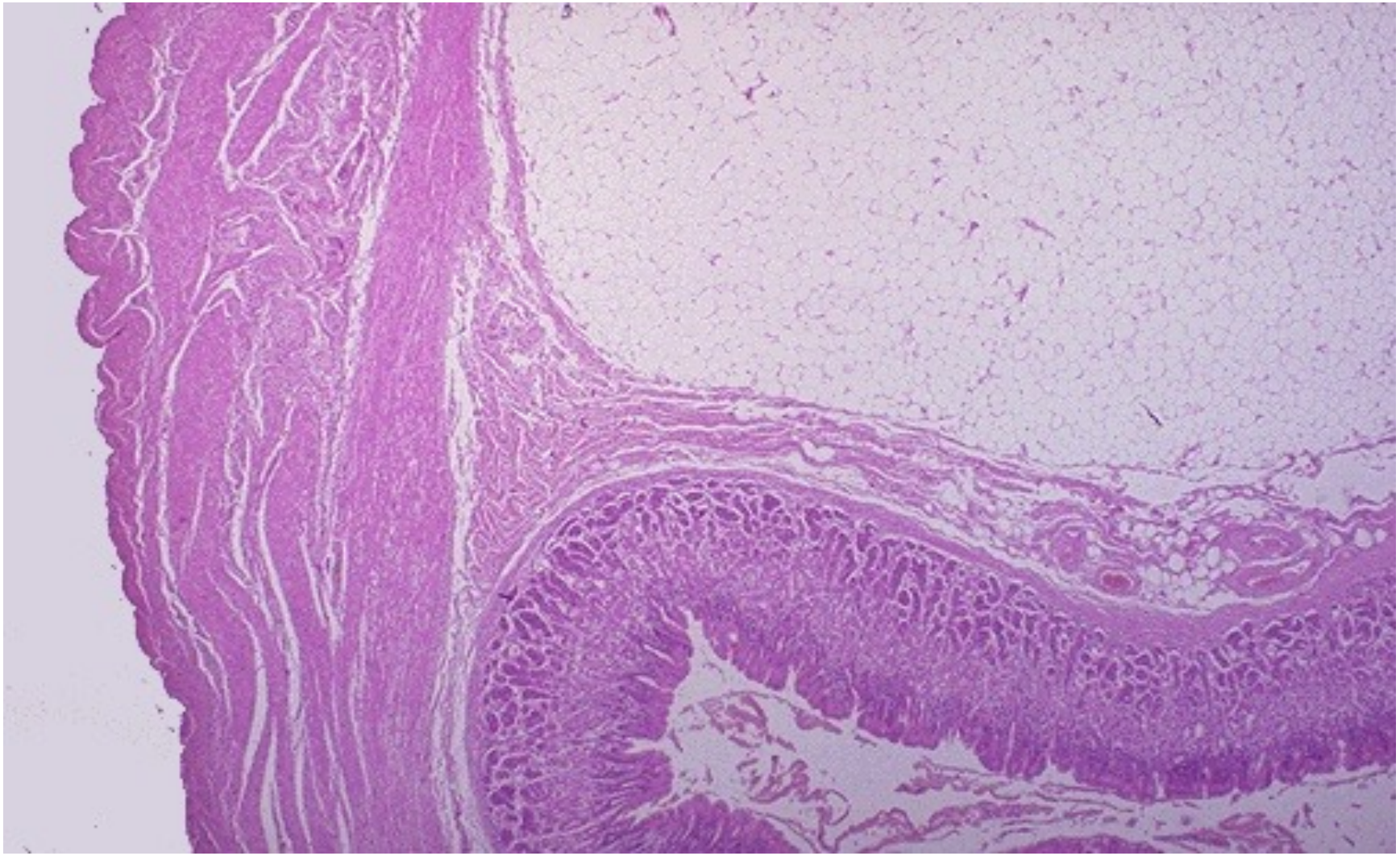
- **Lack of differentiation is called Anaplasia**

- **Benign neoplasms are composed of well-differentiated cells that closely resemble their normal counterparts.**
- **A lipoma is made up of mature fat cells laden with cytoplasmic lipid vacuoles, and a chondroma is made up of mature cartilage cells that synthesize their usual cartilaginous matrix—evidence of morphologic and functional differentiation.**
- **In well-differentiated benign tumors mitoses are usually rare and are of normal configuration.**

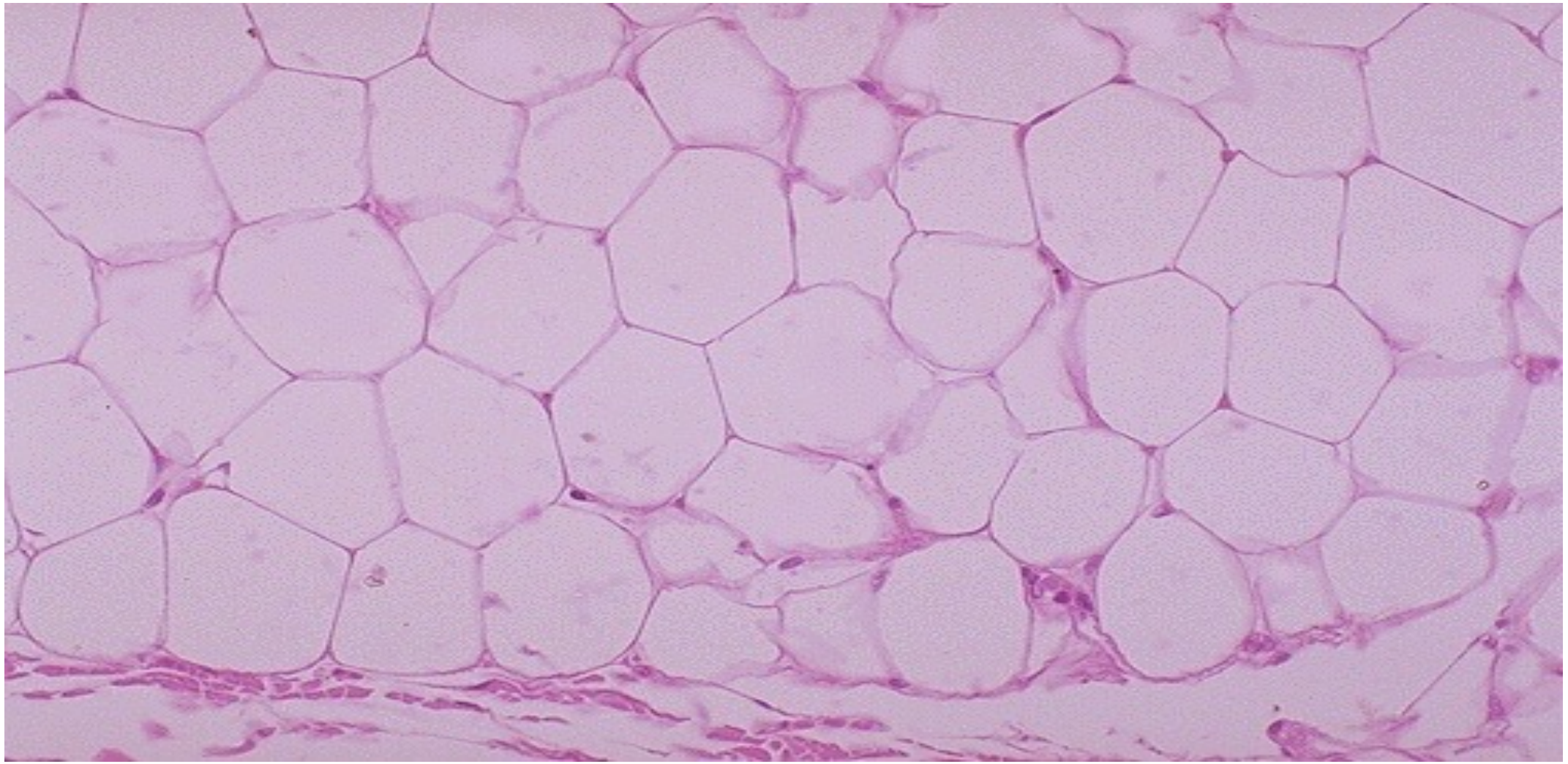
Lipoma



Lipoma



Mature adipose tissue (lipoma)



- **Malignant neoplasms exhibit a wide range of parenchymal cell differentiation most exhibit morphologic alterations**

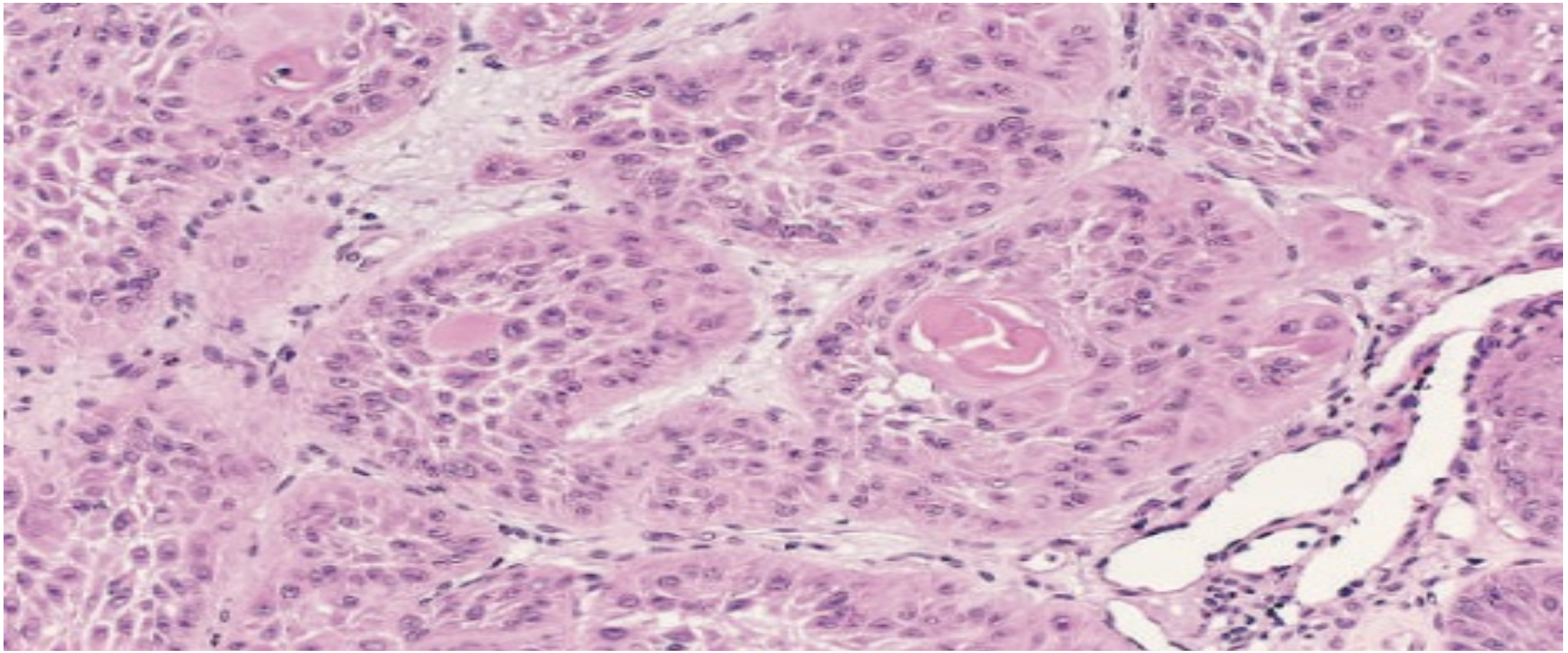
- **Malignant tumors can exhibit:**
- **Well differentiation**
- **Intermediate differentiation**
- **Poor differentiation**
- **Anaplasia (dedifferentiation, or loss of the structural and functional differentiation of normal cells)**

- **Malignant cells display the following:**
- **1. Nuclear Pleomorphism (variation in size and shape)**
- **2. Nuclear abnormalities (extreme hyperchromatism, variation in nuclear size & shape, or unusually prominent single or multiple nucleoli)**

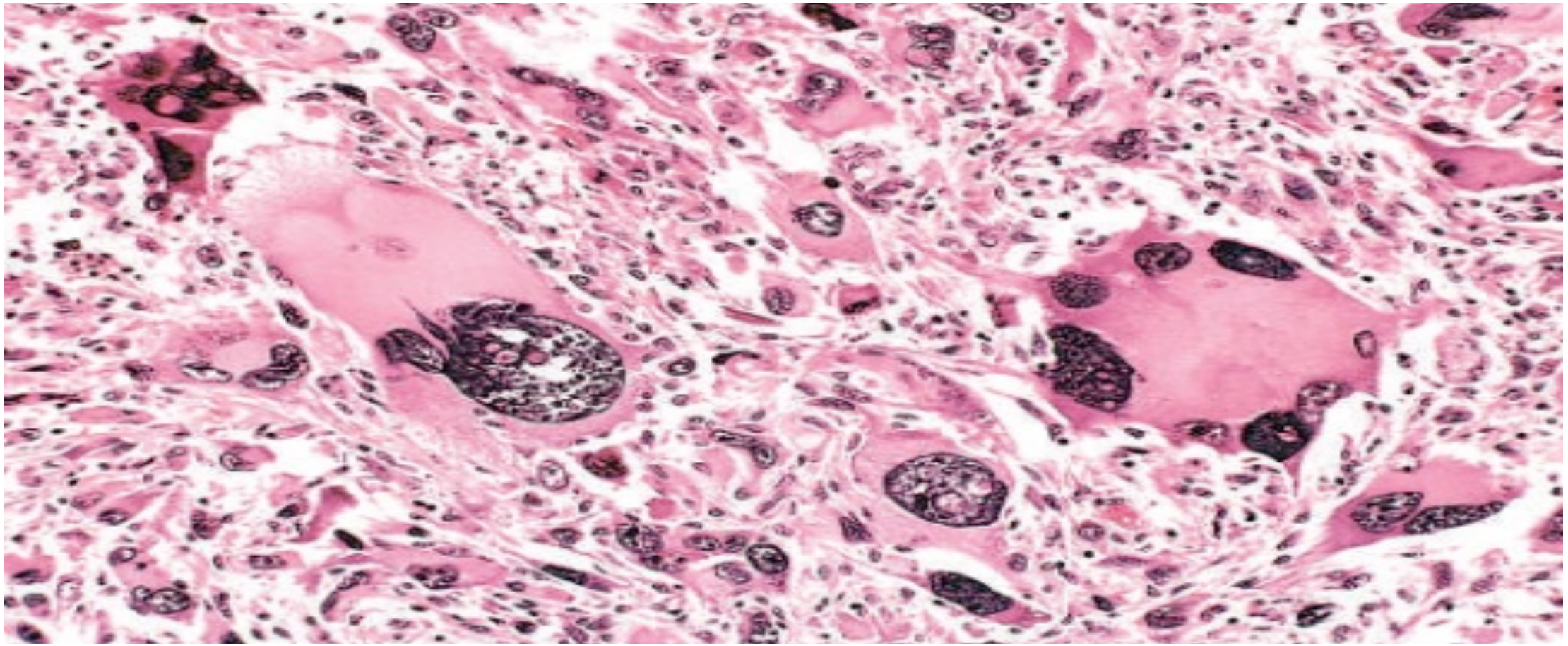
3. Increased nuclear-to-cytoplasmic ratio that approaches 1 :
4. instead of the normal 1 : 4 or 1 : 6.
5. Enlargement of the Nucleoli
6. Increased mitotic activity
7. Atypical mitoses (tripolar or quadripolar)
8. Tumor giant cells
9. Loss of polarity of tumor cells

10. Alteration or loss of functional capacity (paraneoplastic syndrome)

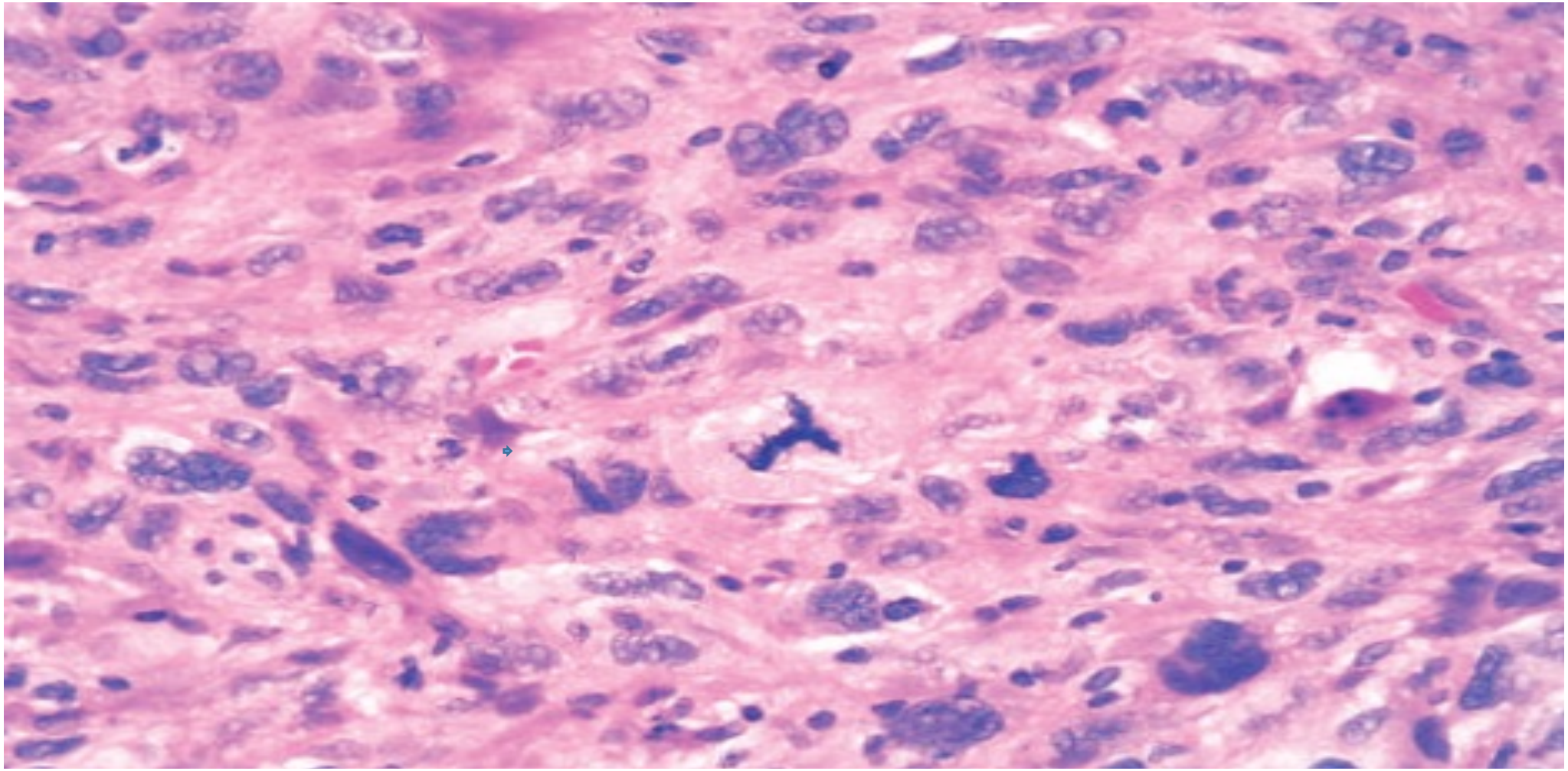
Well differentiated squamous cell carcinoma



Anaplasia



Abnormal mitosis

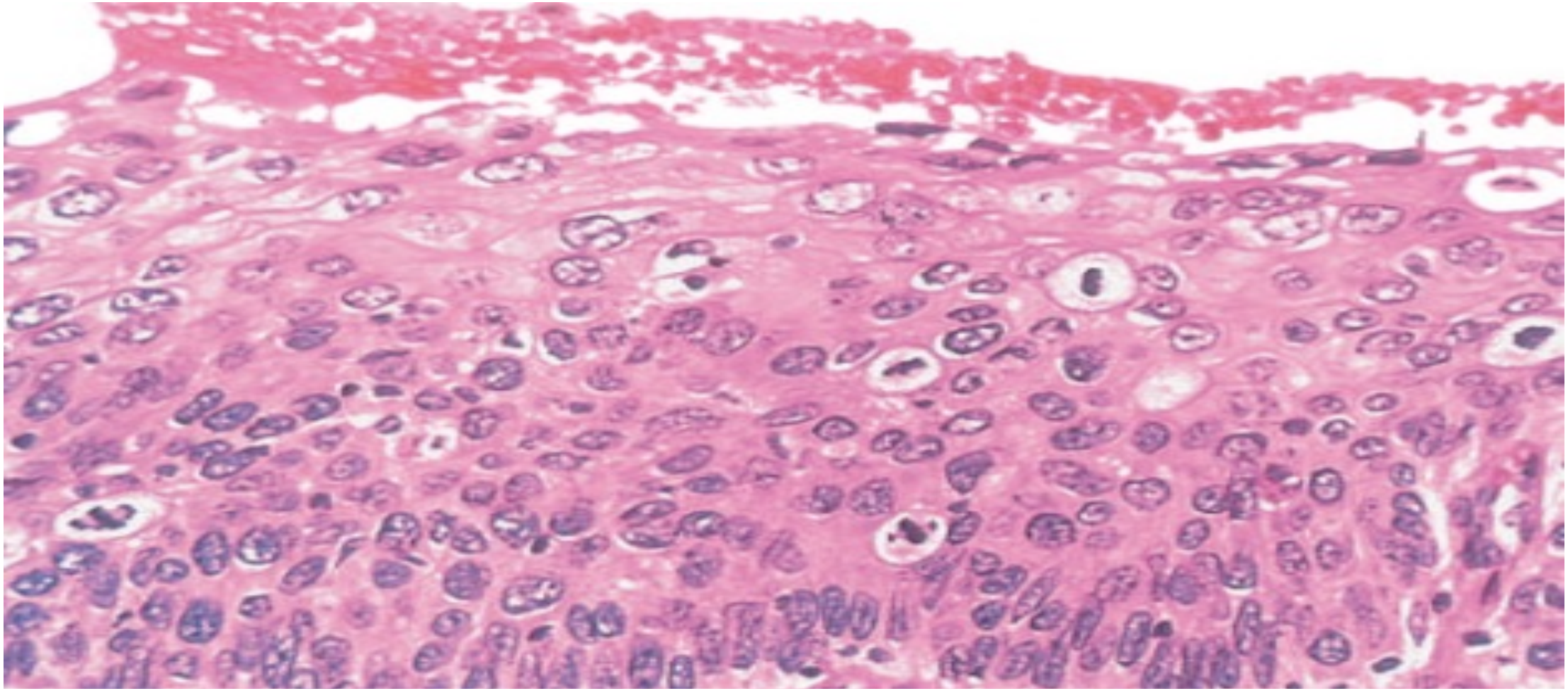


Dysplasia and carcinoma in-situ

- **Dysplastic epithelium is recognized by a loss in the uniformity of individual cells and in their architectural orientation**
- Dysplasia is not synonymous with cancer
- Mild to moderate dysplasias that do not involve the entire thickness of the epithelium sometimes regress completely, particularly if inciting causes are removed

- **When dysplastic changes are severe and involve the entire thickness of the epithelium, the lesion is referred to as *carcinoma in situ*, which is a preinvasive stage of cancer**

High-power view of another region
shows failure of normal differentiation, marked nuclear and cellular pleomorphism, and numerous mitotic figures extending toward the surface

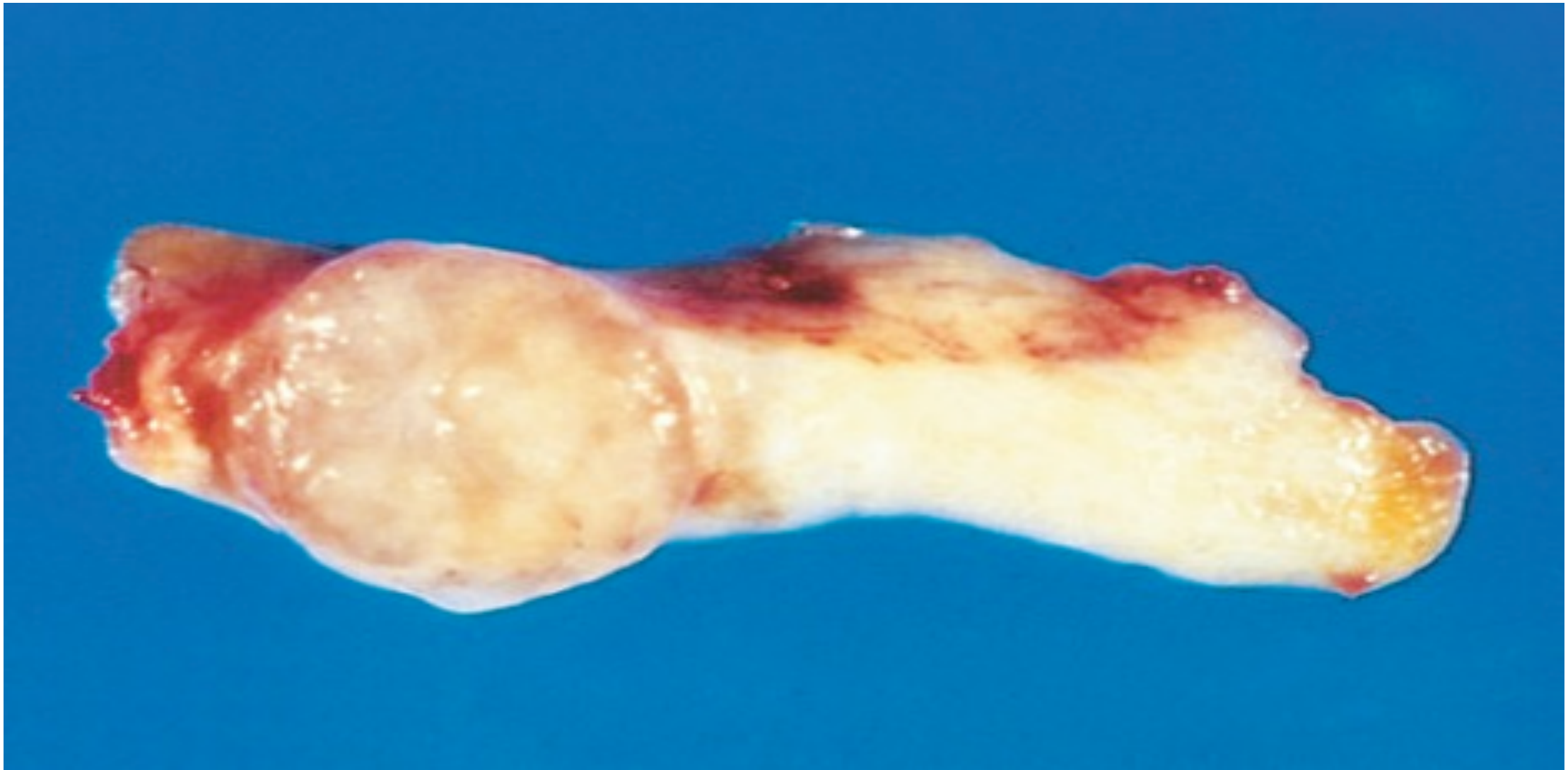


2. Local Invasion

- **The growth of cancers is accompanied by progressive infiltration, invasion, and destruction of surrounding tissues**
- **Most benign tumors grow as cohesive expansile masses that remain localized to their sites of origin**

- **Benign tumors grow and expand slowly**
- **Usually develop a rim of compressed fibrous tissue (capsule)**
- **This capsule consists largely of extracellular matrix that is deposited by stromal cells such as fibroblasts which are activated by hypoxic damage to parenchymal cells resulting from compression by the expanding tumor.**

Fibroadenoma of the breast.
The tan-colored, encapsulated small tumor is sharply demarcated from the whiter breast tissue



- **Encapsulation creates a tissue plane that makes the tumor discrete, moveable (non-fixed), and readily excisable by surgical enucleation**
- **However, not all benign neoplasms are encapsulated**
- **For example,**

- leiomyoma of the uterus is discretely demarcated from the surrounding smooth muscle by a zone of compressed and attenuated normal myometrium but lacks a capsule.

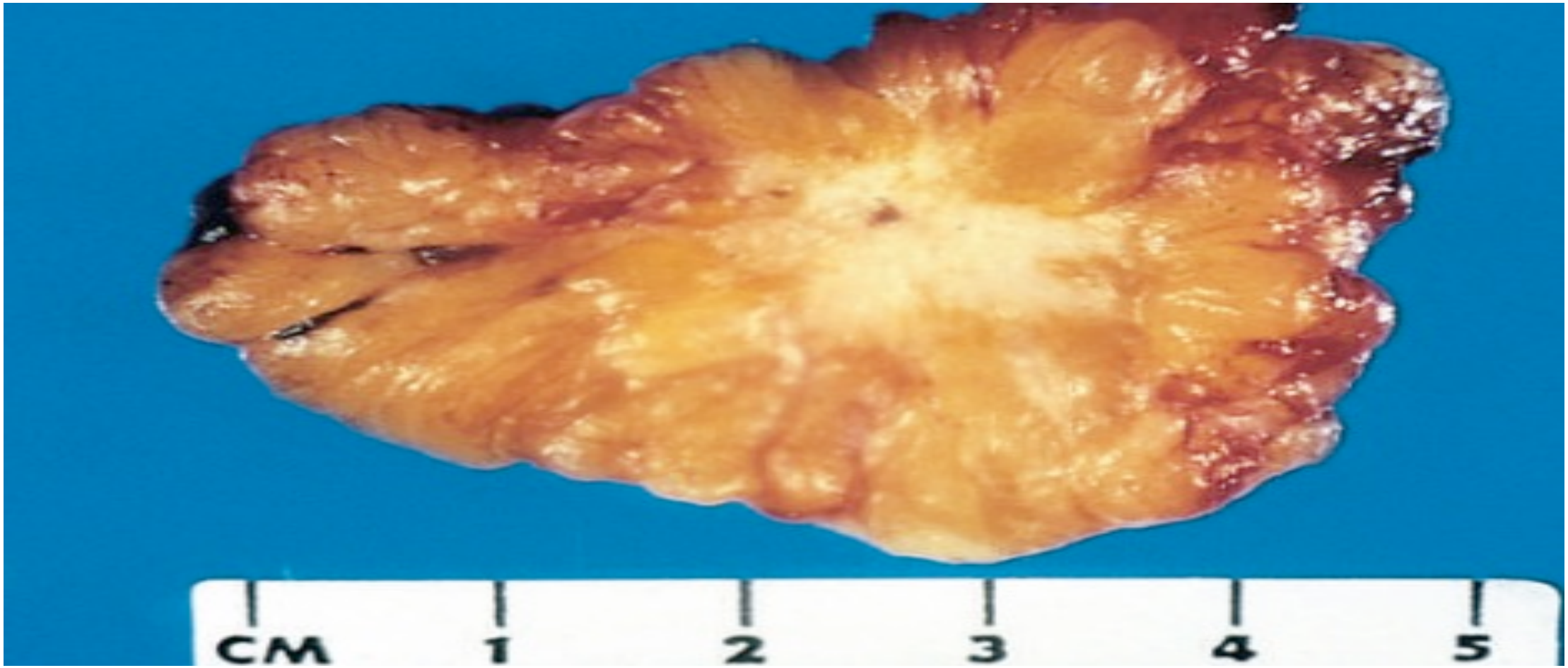
- **A few benign tumors are neither encapsulated nor discretely defined**
- For example

Benign vascular neoplasms (hemangiomas)

lack of demarcation makes them difficult to be excised

- **Malignant tumors lack well defined capsules**
- **Microscopic examination reveals tiny crablike feet penetrating the margin and infiltrating adjacent structures**
- **Malignant tumors are difficult to be removed totally**

Cut section of invasive ductal carcinoma of the breast. The lesion is retracted infiltrating the surrounding breast substance



3. Metastasis

- **The spread of a tumor to sites that are physically discontinuous with the primary tumor**
- **It unequivocally marks a tumor as malignant**
- **Benign neoplasms do not metastasize.**

- **30% of patients with newly diagnosed solid tumors (excluding skin cancers other than melanomas) present with clinically evident metastases**
- **20% have occult (hidden) metastases at the time of diagnosis**

- **The more anaplastic and the larger the primary neoplasm, the more likely is metastatic spread**
- **Exceptions**

Extremely small cancers have been known to metastasize while some large and ominous-looking lesions may not

- **Basal cell carcinomas of the skin and most primary tumors of the central nervous system are highly locally invasive but rarely metastasize**
- **Leukemias and lymphomas are taken to be disseminated diseases at diagnosis and are always considered to be malignant**

Pathways of metastasis

- **(1) Seeding within body cavities**
- **(2) Lymphatic spread**
- **(3) Hematogenous spread**

Seeding

- **Spread by seeding occurs when neoplasms invade a natural body cavity.**
- **For Example**

-Cancers of the ovary which often cover the peritoneal surfaces widely

-Neoplasms of the central CNS such as a medulloblastoma or ependymoma, may penetrate the cerebral ventricles and be carried by the cerebrospinal fluid to reimplant on the meningeal surfaces either within the brain or in the spinal cord.

Lymphatic spread

- **Lymphatic spread is more typical of carcinomas whereas hematogenous spread is favored by sarcomas.**
- **All forms of cancer may disseminate through either or both systems**
- **The pattern of lymph node involvement depends principally on the site of the primary neoplasm and the natural pathways of local lymphatic drainage.**

- **For example**
- **Lung carcinomas arising in the respiratory passages metastasize first to the regional bronchial lymph nodes and then to the tracheobronchial and hilar nodes**
- **Upper outer quadrant breast lesions first spread to the axillary nodes.**
- **Medial breast lesions may drain through the chest wall to the nodes along the internal mammary artery.**

- **Then to supraclavicular and infraclavicular nodes**
- **Cancer cells can travel in lymphatic channels within the immediately proximate nodes to be trapped in subsequent lymph nodes producing so-called “skip metastases”**
- **The cells may traverse all of the lymph nodes ultimately to reach the vascular compartment by way of the thorasic duct.**

- **A “sentinel lymph node” is the first regional lymph node that receives lymph flow from a primary tumor.**
- **It can be identified by injection of blue dyes or radiolabeled tracers near the primary tumor.**
- **Biopsy of sentinel lymph nodes allows determination of the extent of spread of tumor and can be used to plan treatment.**

Hematogenous spread

- **It is the favored pathway for sarcomas**
- **Carcinomas use it as well.**
- **Arteries are penetrated less readily than are veins.**
- **With venous invasion the bloodborne cells follow the venous flow draining the site of the neoplasm**
- **Liver and lungs are the most frequently involved secondary sites in hematogenous dissemination**
- **Liver is the commonest secondary organ to be receive metastatic deposits from organs with portal venous drainage**

- **Lungs are the most common site to receive metastatic deposits from organs with caval venous drainage**
- **Cancers arising near the vertebral column often embolize through the paravertebral plexus as vertebral metastases of carcinomas of the thyroid and prostate glands.**

A liver with metastatic cancer

- **Certain carcinomas have a propensity to grow within veins.**
- **Renal cell carcinoma often invades the renal vein to grow in a snakelike fashion up the inferior vena cava reaching the right side of the heart.**
- **Hepatocellular carcinomas often penetrate and grow within the radicles of portal and hepatic veins reaching reaching the main venous channels.**

- **The anatomic localization of a neoplasm and its venous drainage cannot explain the systemic distributions of metastases.**
- **<u>For example</u>**

Prostatic carcinoma preferentially spreads to bone

Bronchogenic carcinoma tends to involve the adrenal glands

Neuroblastoma spreads to the liver and bones

Skeletal muscles, although rich in capillaries, are rarely sites of tumor metastases