CLASSIFICATION OF TUMORS

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Objectives

- Compare between benign & malignant tumors in terms of differentiation, rate of growth, local invasion & metastases.
- Identify the morphological features that differentiate between benign & malignant tumors.
- Define the terms: differentiation & anaplasia.
- List the pathways by which malignant tumors spread.
- Define the terms: dysplasia & carcinoma in situ.

Introduction

- Features to distinguish between benign & malignant tumors:
  - Differentiation & anaplasia
  - Rate of growth
  - Local invasion
  - Metastasis

Differentiation & Anaplasia

- Differentiation & anaplasia are characteristics seen only in the parenchymal cells that constitute the transformed elements of neoplasms.

- *Differentiation*: the extent to which the parenchymal cells of the tumor resemble their normal counterparts morphologically and functionally

Differentiation & Anaplasia

- Differentiation:
  - Well differentiated = closely resemble their normal counterparts
  - Moderately differentiated
  - Poorly differentiated
  - Undifferentiated (*Anaplasia*)

Differentiation & Anaplasia

- Benign neoplasms are composed of well-differentiated cells that closely resemble their normal counterparts.
  - Lipoma: mature fat cells laden with cytoplasmic lipid vacuoles.
  - Chondroma: 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.

Differentiation & Anaplasia

- The more differentiated the tumor cell, the more completely it retains the functional capabilities of its normal counterparts.
  - e.g. benign neoplasms and even well-differentiated cancers of endocrine glands frequently elaborate the hormones characteristic of their origin.

Differentiation & Anaplasia

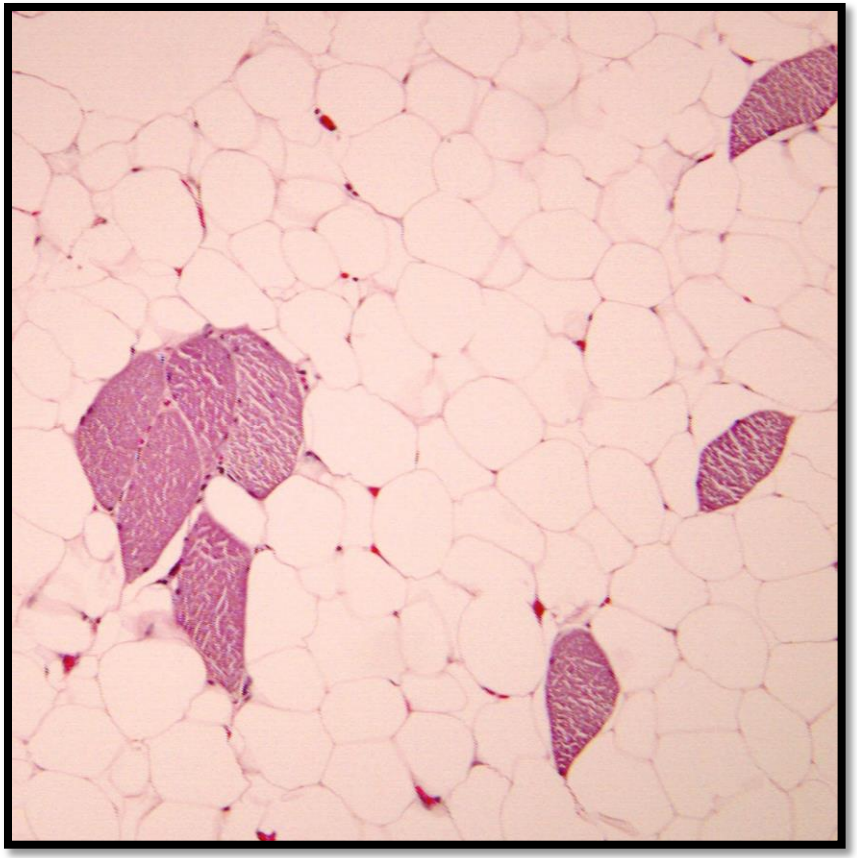
- The stroma carrying the blood supply is crucial to the growth of tumors but does not aid in the separation of benign from malignant ones.

- However the amount of stromal connective tissue determines the consistency of a neoplasm.

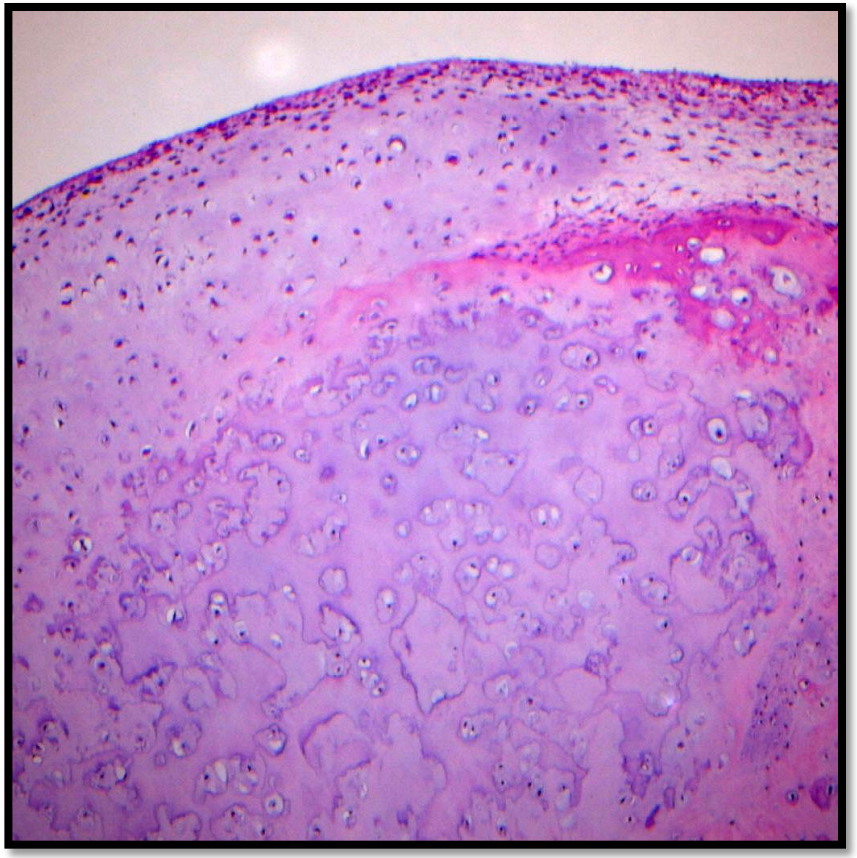
  - e.g. certain cancers induce a dense, abundant fibrous stroma (*desmoplasia*), making them hard, so-called *scirrhous* tumors.

Differentiation & Anaplasia

Lipoma



Chondroma



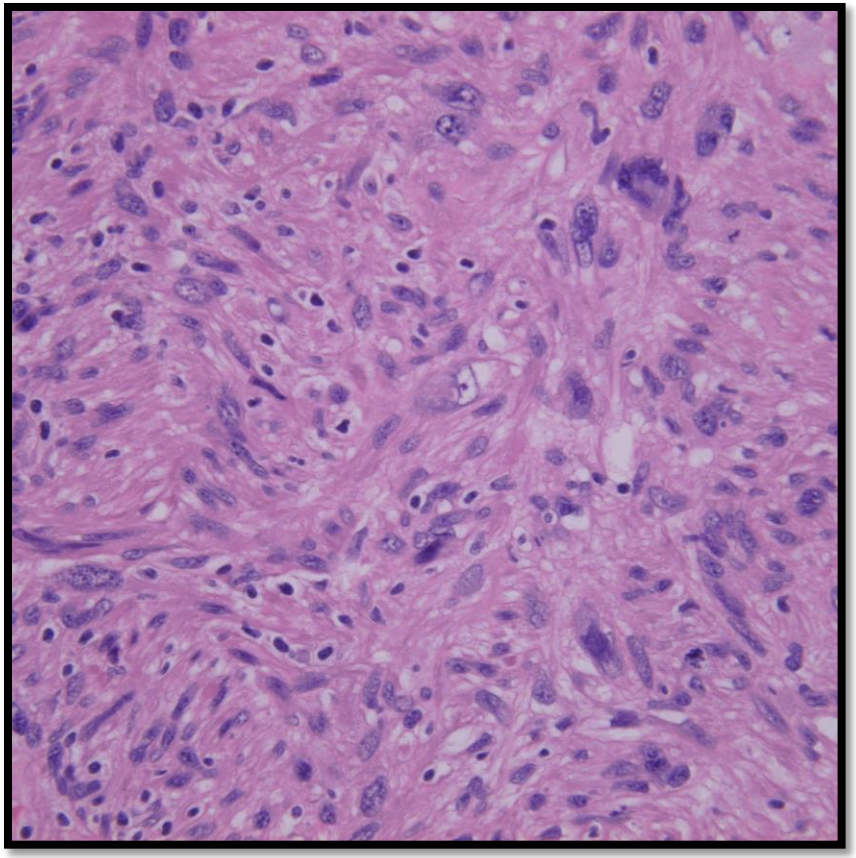
Differentiation & Anaplasia

- Malignant neoplasms are characterized by a wide range of parenchymal cell differentiation: from well differentiated to completely undifferentiated.

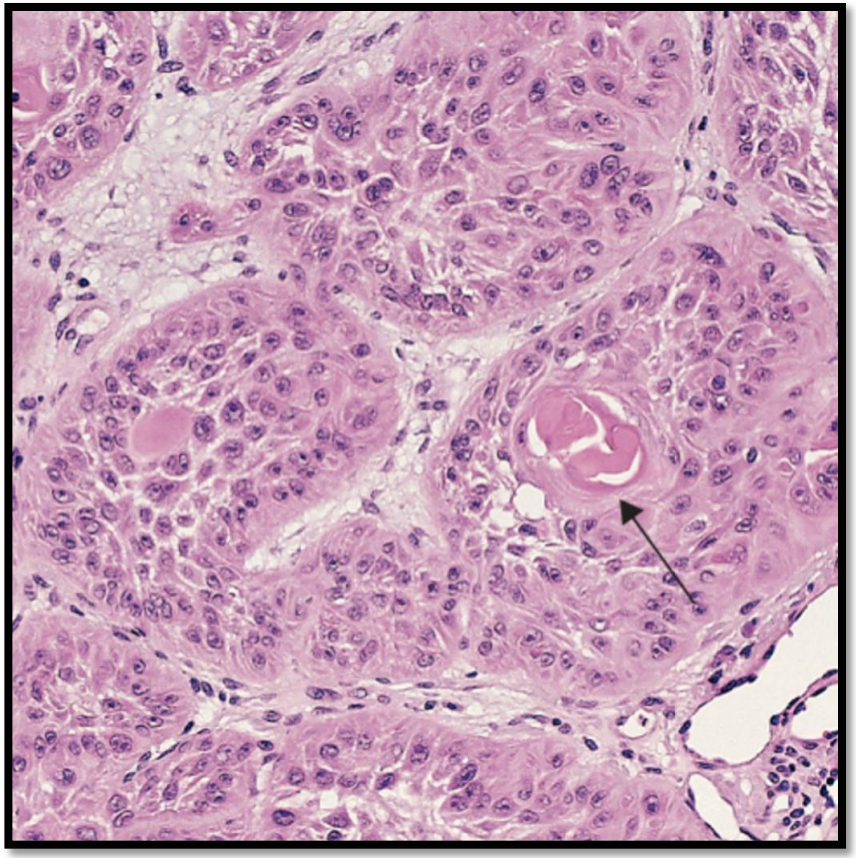
- Between the two extremes lie tumors loosely referred to as moderately differentiated.

Differentiation & Anaplasia

Leiomyosarcoma



Squamous cell carcinoma

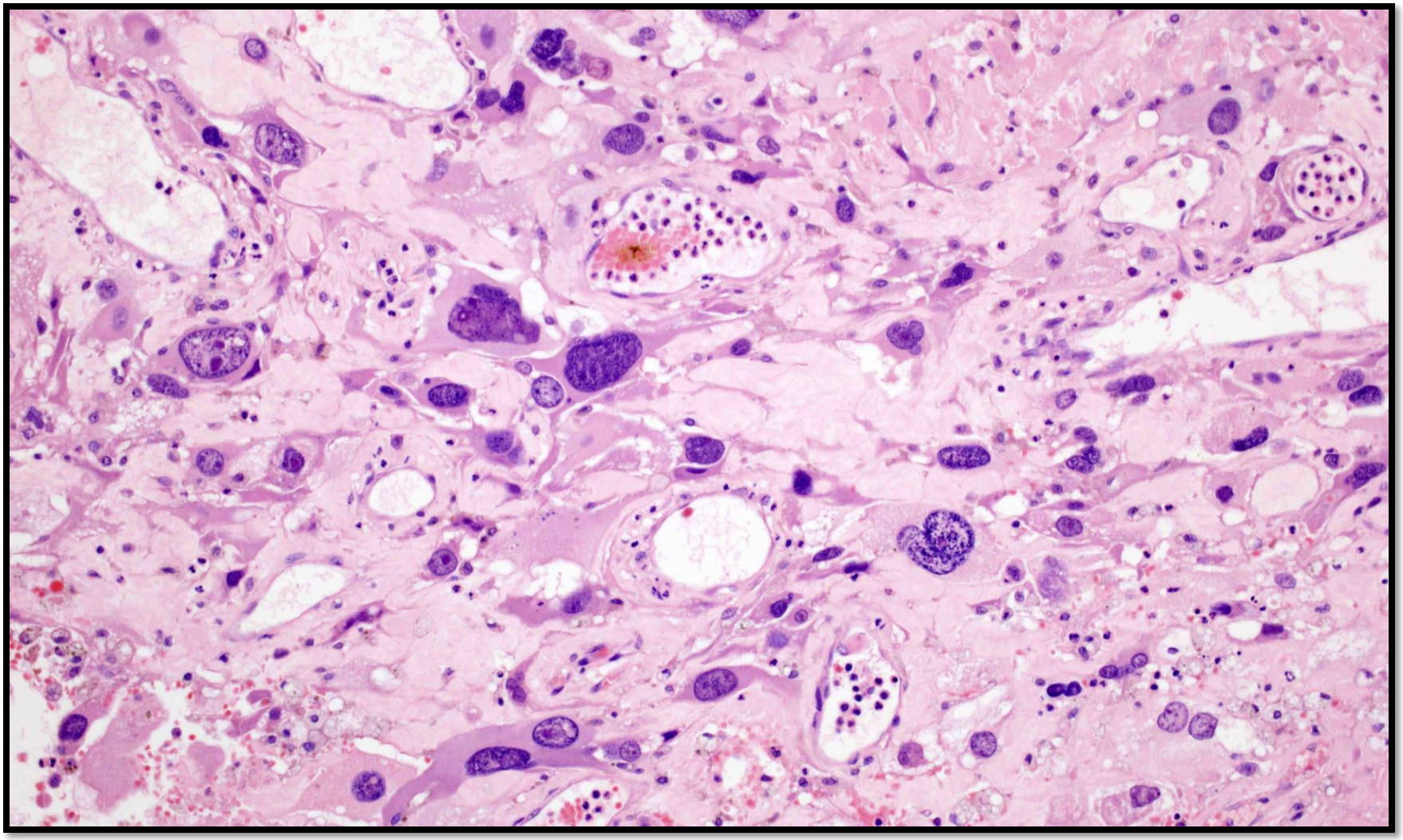


Differentiation & Anaplasia

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

- Anaplasia: loss of the structural and functional differentiation. It is a hallmark of malignancy.

Differentiation & Anaplasia

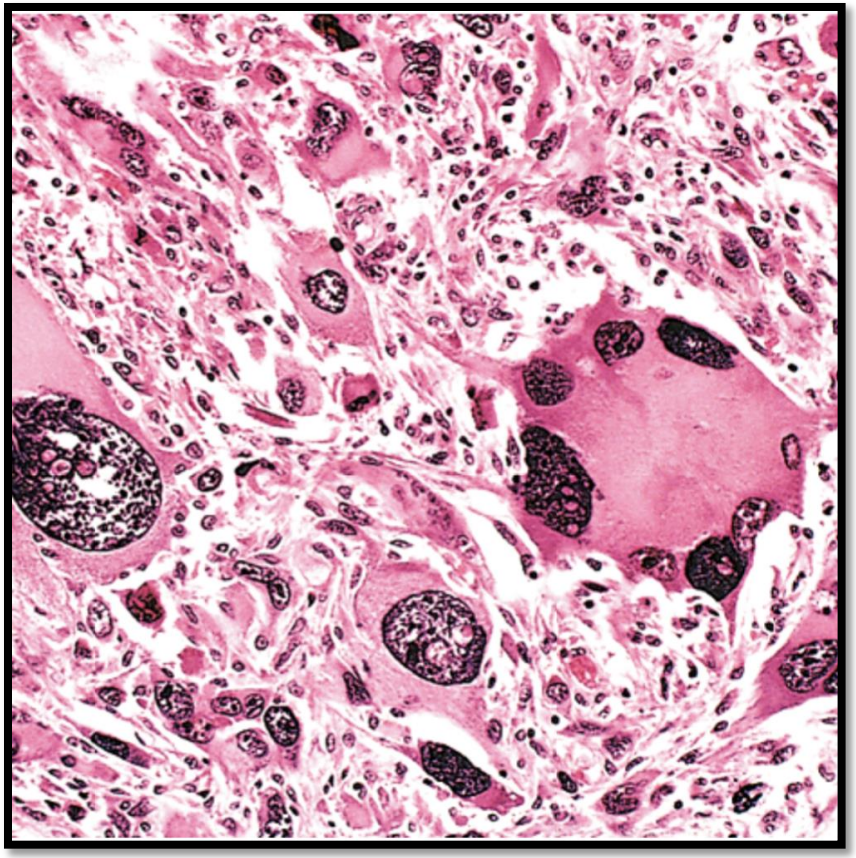


Differentiation & Anaplasia

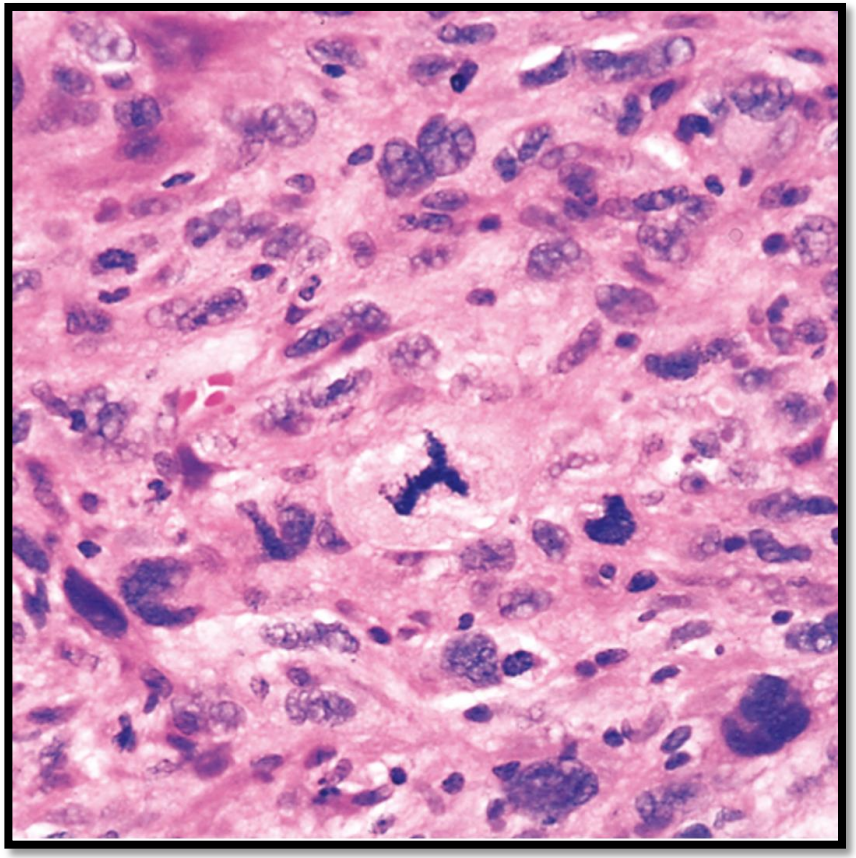
- It is important to recognize the following histopathological features in any neoplasm:
  - Pleomorphism: variation in size and shape
  - Enlarged nuclei resulting in an increase of nuclear to cytoplasm ratio (that may approach 1:1 instead of the normal 1:4 or 1:6)
  - Hyperchromasia (dark nuclei) due to coarse & clumped chromatin
  - Prominent nucleoli
  - Mitoses (typical or atypical forms)
  - *Giant cells*: larger than their neighbors & possess either one enormous nucleus or several nuclei.

Differentiation & Anaplasia

Tumor Giant Cells



Atypical Mitosis



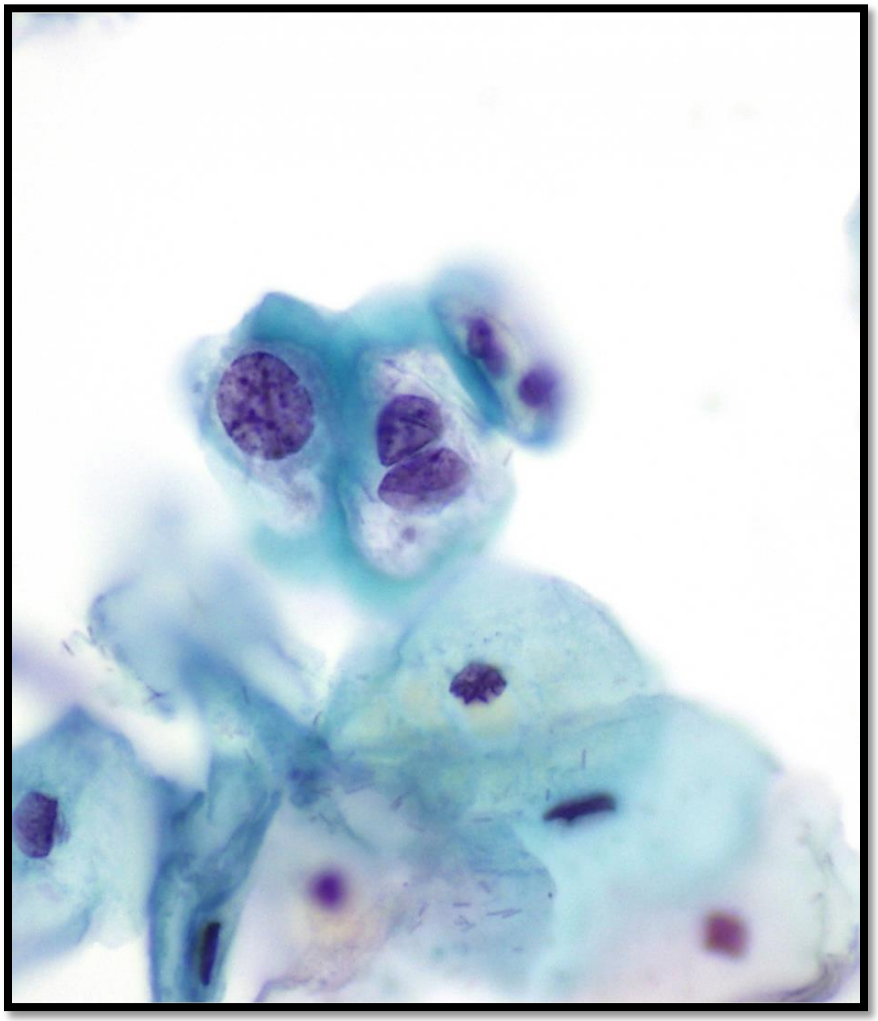
Dysplasia

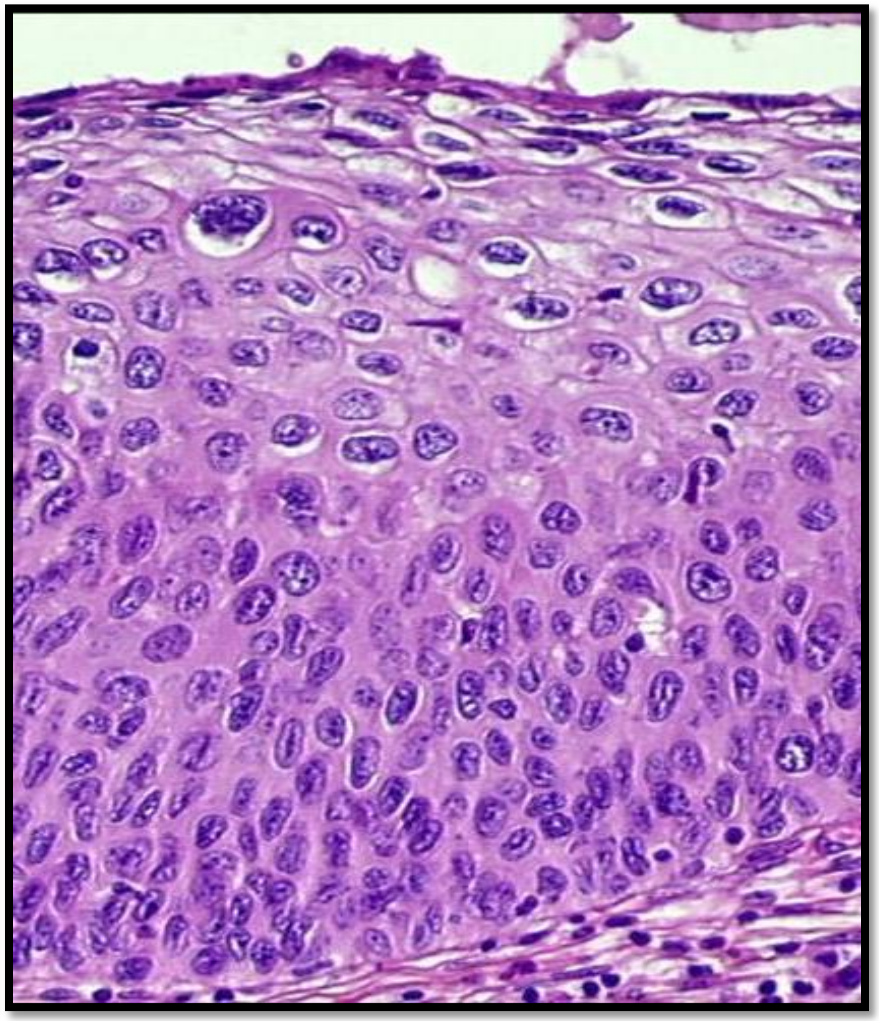
- Definition: a loss in the uniformity of the individual cells and a loss in their architectural orientation.
- It is a non-neoplastic process but a premalignant condition.
- It occurs mainly in the epithelia.
- Dysplastic cells show a degree of: pleomorphism, ↑N:C ratio, hyperchrmasia, irregular nuclei, increased mitoses, loss of polarity & a disordered maturation or total failure of maturation.

Dysplasia

- Dysplasia does not mean cancer.
- Dysplasia does not necessarily progress to cancer.
- Dysplasia may be reversible.
- The risk of invasive cancer varies with:
  - grade of dysplasia (mild, moderate, severe)
  - duration of dysplasia
  - site of dysplasia

Dysplasia





Dysplasia

- Differences between dysplasia & cancer:
  - Lack of invasiveness.
  - Reversibility

Carcinoma in Situ

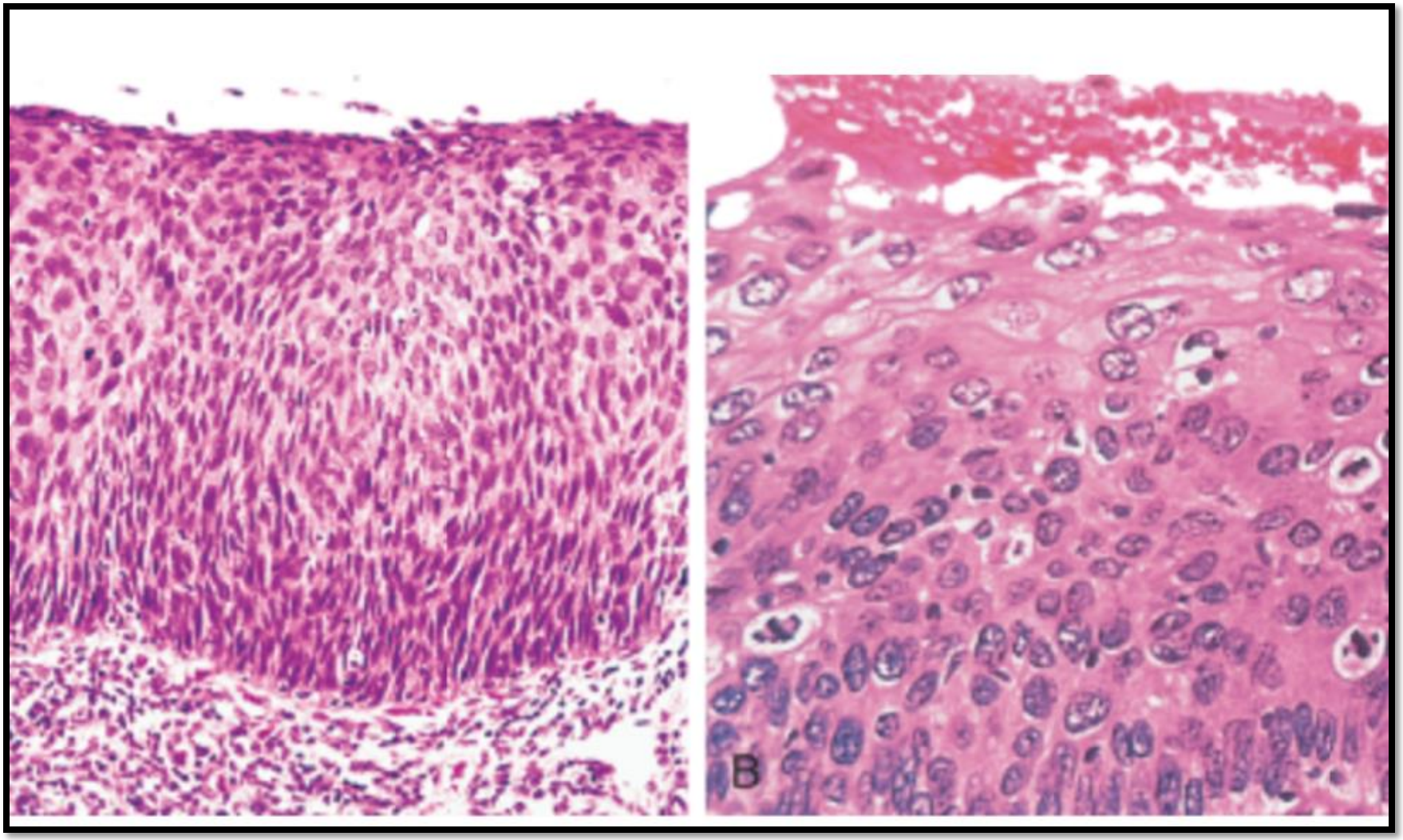
- If dysplastic changes involve the entire thickness of the epithelium it is called: *carcinoma in-situ.*

- Definition: an intraepithelial malignancy in which malignant cells involve the entire thickness of the epithelium without penetration of the basement membrane.

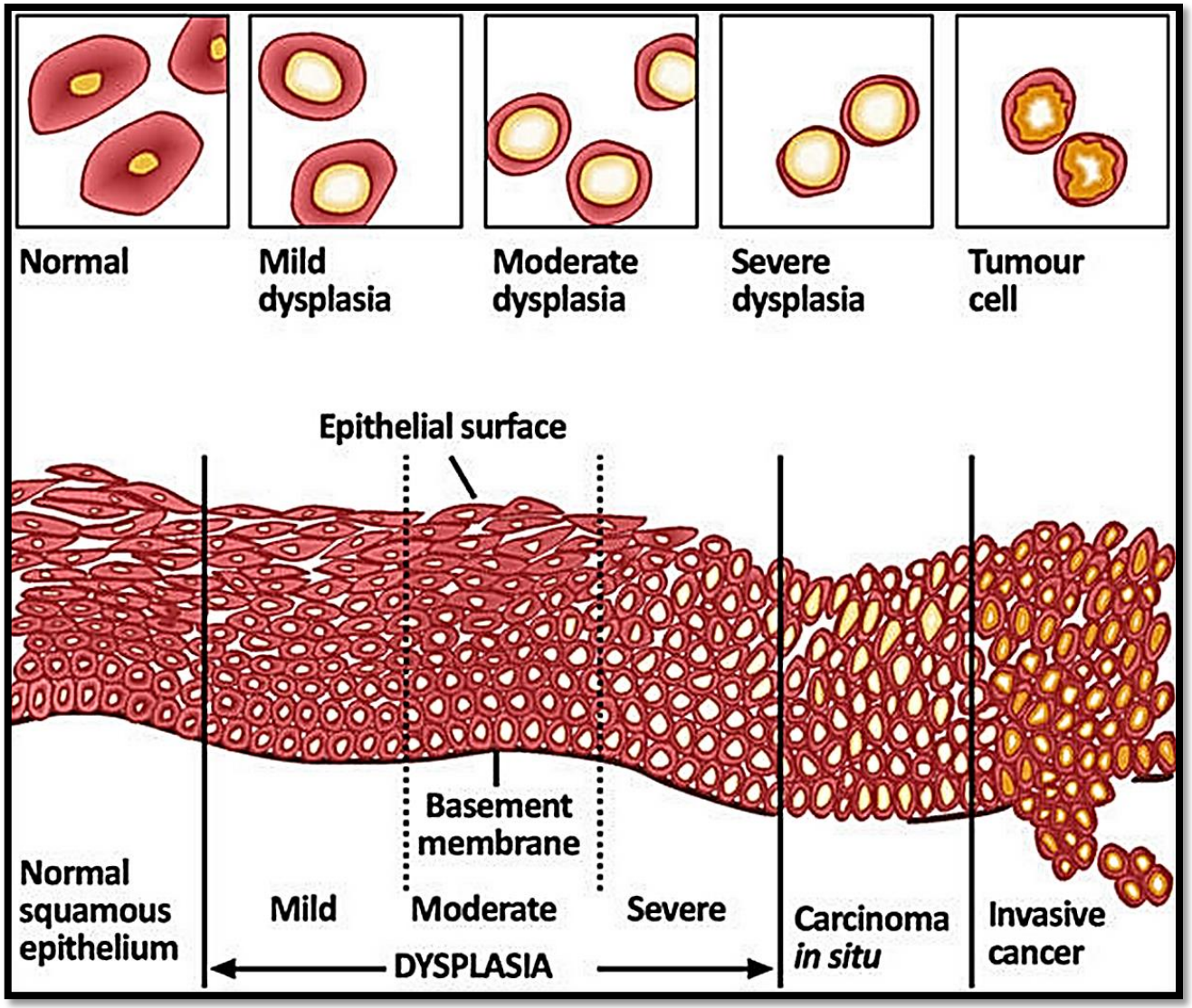
Carcinoma in Situ

- It is applicable only to epithelial neoplasms.
- It is a true neoplasm with all of the features of malignant neoplasm except invasiveness.
- It displays the cytological features of malignancy without invading the basement membrane.

Carcinoma in Situ



Dysplasia & Carcinoma in Situ



Reminder…

- Features to distinguish between benign & malignant tumors:
  - Differentiation & anaplasia
  - Rate of growth
  - Local invasion
  - Metastasis

Rate of Growth

- Benign tumors:
  - They usually grow slowly.
  - Their growth is affected by: adequate blood supply, location or hormones e.g. leiomyoma of the uterus.

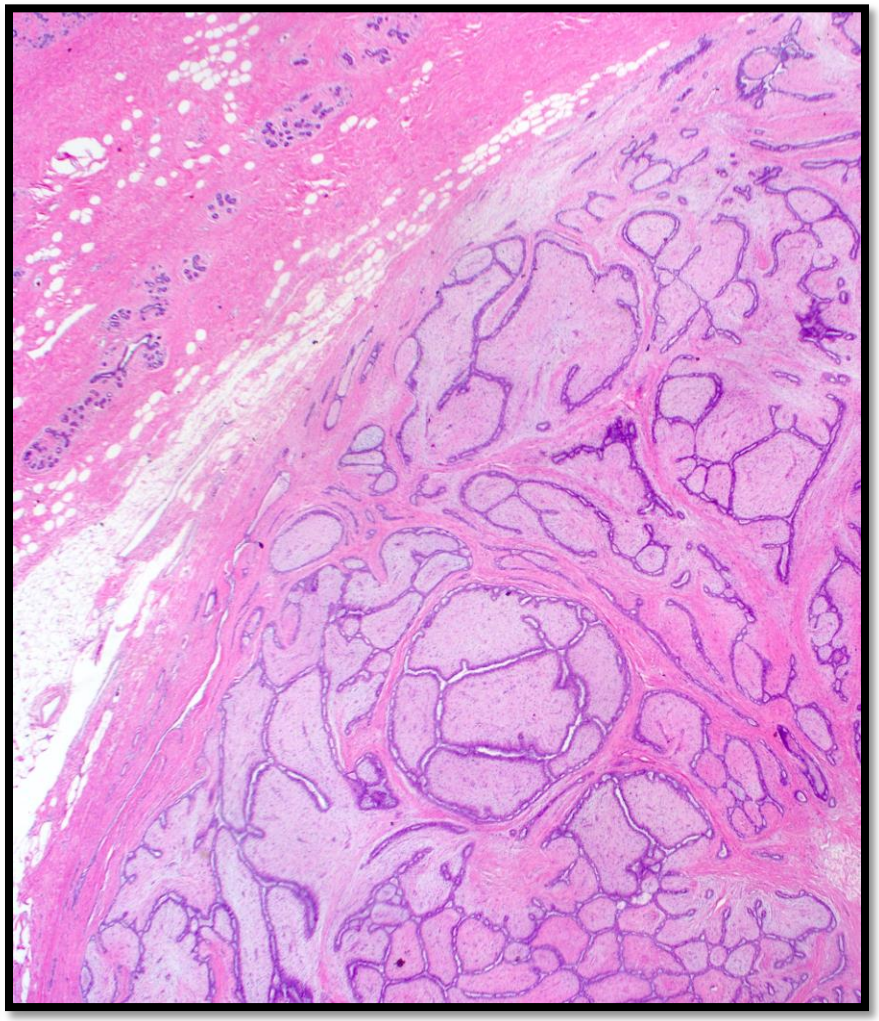
Rate of Growth

- Malignant tumors:
  - They usually grow fast.
  - The rate of growth of malignant tumors usually correlates inversely with their level of differentiation.

Local Invasion

- Benign tumors:
  - They remain localized.
  - They cannot invade.
  - They are *usually* encapsulated.

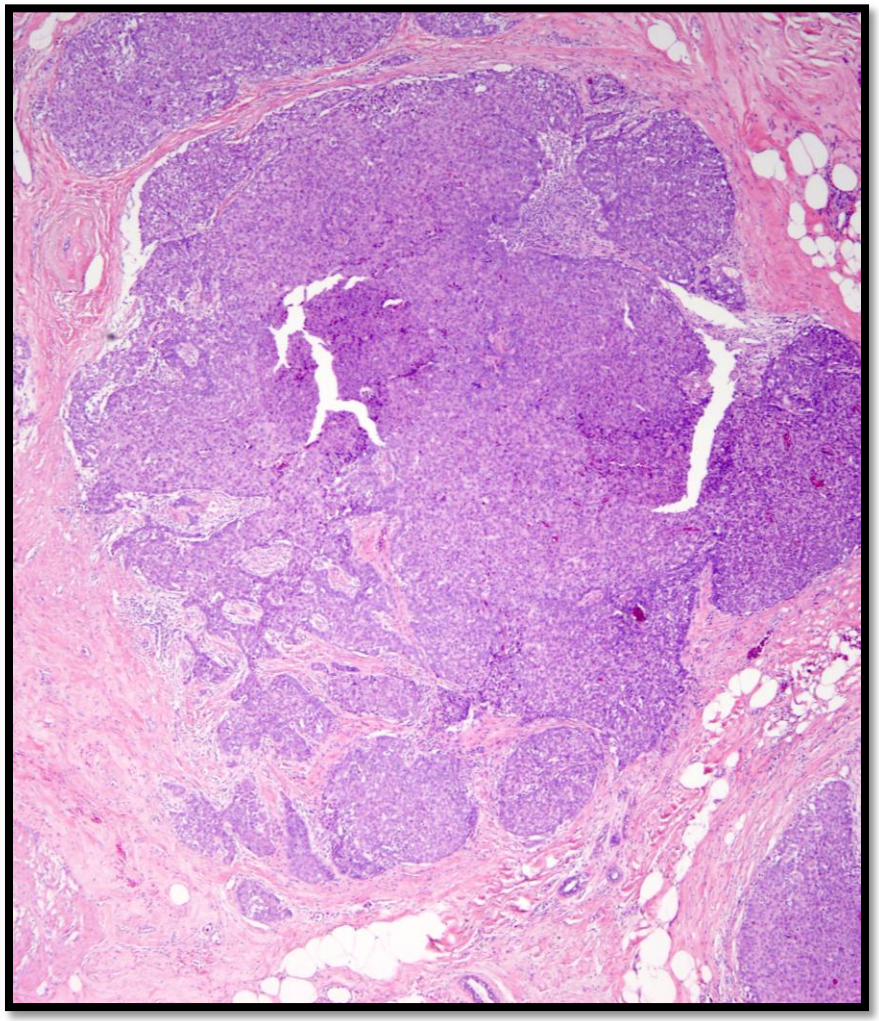
Local Invasion



Local Invasion

- Malignant tumors:
  - They invade the underlying basement membrane or stroma.
  - They are destructive.
  - They are *usually* not encapsulated.

Local Invasion*



Metastasis

- Definition: it is the development of secondary implants of a tumor that are discontinuous with the primary tumor & located in remote tissues.

- More than any other attribute, the property of metastasis identifies a neoplasm as malignant.

Metastasis

- Cancer have different ability to metastasize.
- Approximately 30% patients present with clinically evident metastases.
- Generally, the more anaplastic and the larger the primary tumor, the more likely it metastasizes.

Metastasis

- Malignant neoplasms disseminate by one of three pathways:
  - (1) seeding within body cavities
  - (2) lymphatic spread
  - (3) hematogenous spread

Metastasis

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

- This mode of dissemination is particularly characteristic of cancers of the ovary, which often cover the peritoneal surfaces widely.

Metastasis

- Lymphatic spread is more typical of carcinomas.
  - Breast carcinoma → axillary lymph node
  - Lung carcinomas → bronchial lymph nodes

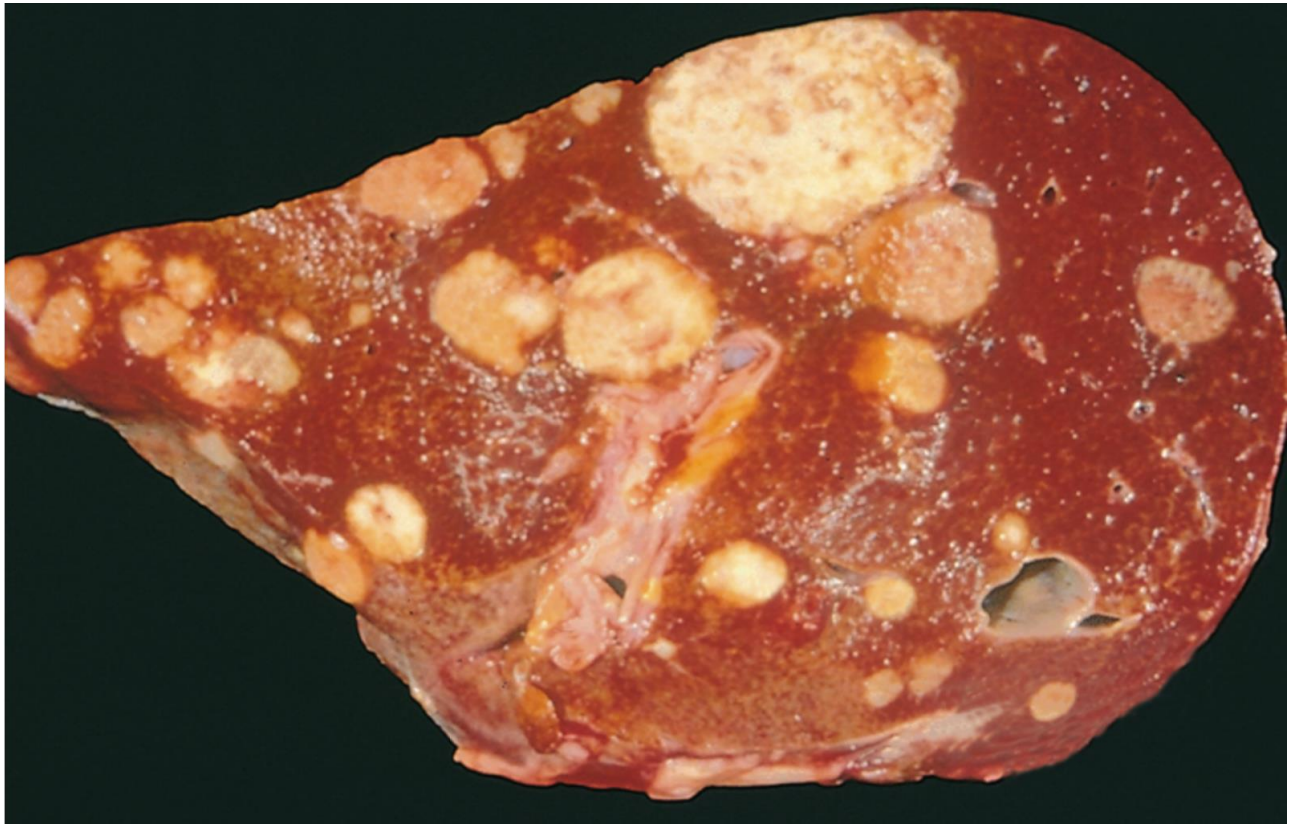
Metastasis

- Hematogenous spread is favored by sarcomas but can also occur in carcinomas.

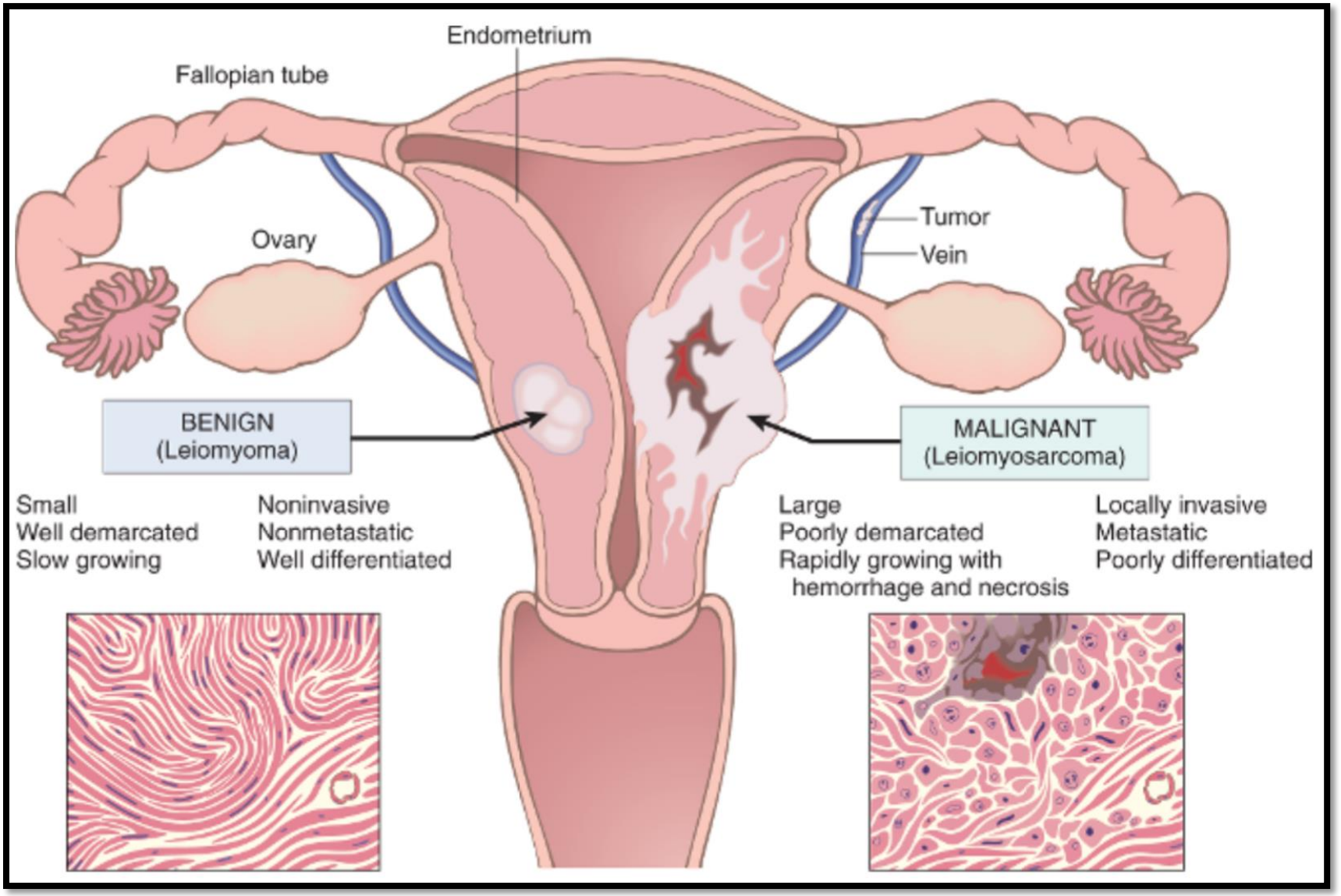
- Veins are more commonly invaded.

Metastasis

- The liver and lungs are the most frequently involved secondary sites.



Summary


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

Summary

SUMMARY

Characteristics of Benign and Malignant Tumors

- Benign and malignant tumors can be distinguished from one another based on the degree of differentiation, rate of growth, local invasiveness, and distant spread.
- Benign tumors resemble the tissue of origin and are well differentiated; malignant tumors are poorly or completely undifferentiated (anaplastic).
- Benign tumors are slow-growing, whereas malignant tumors generally grow faster.
- Benign tumors are well circumscribed and have a capsule; malignant tumors are poorly circumscribed and invade the surrounding normal tissues.
- Benign tumors remain localized to the site of origin, whereas malignant tumors are locally invasive and metastasize to distant sites.

Reference

- Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 9th ed. Elsevier; 2013. Philadelphia, PA.

END OF LECTURE

Thank You