NEOPLASIA I.

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Neoplasia-definition

- Neoplasia-new growth
- Neoplasia-neoplasm-tumor
- Uncontrolled and uncoordinated growth of genetically altered cells, resulting in an abnormal tissue mass (that persists even after cessation of the stimuli that evoked its development)
- Clonal proliferation – from a single genetically altered cell

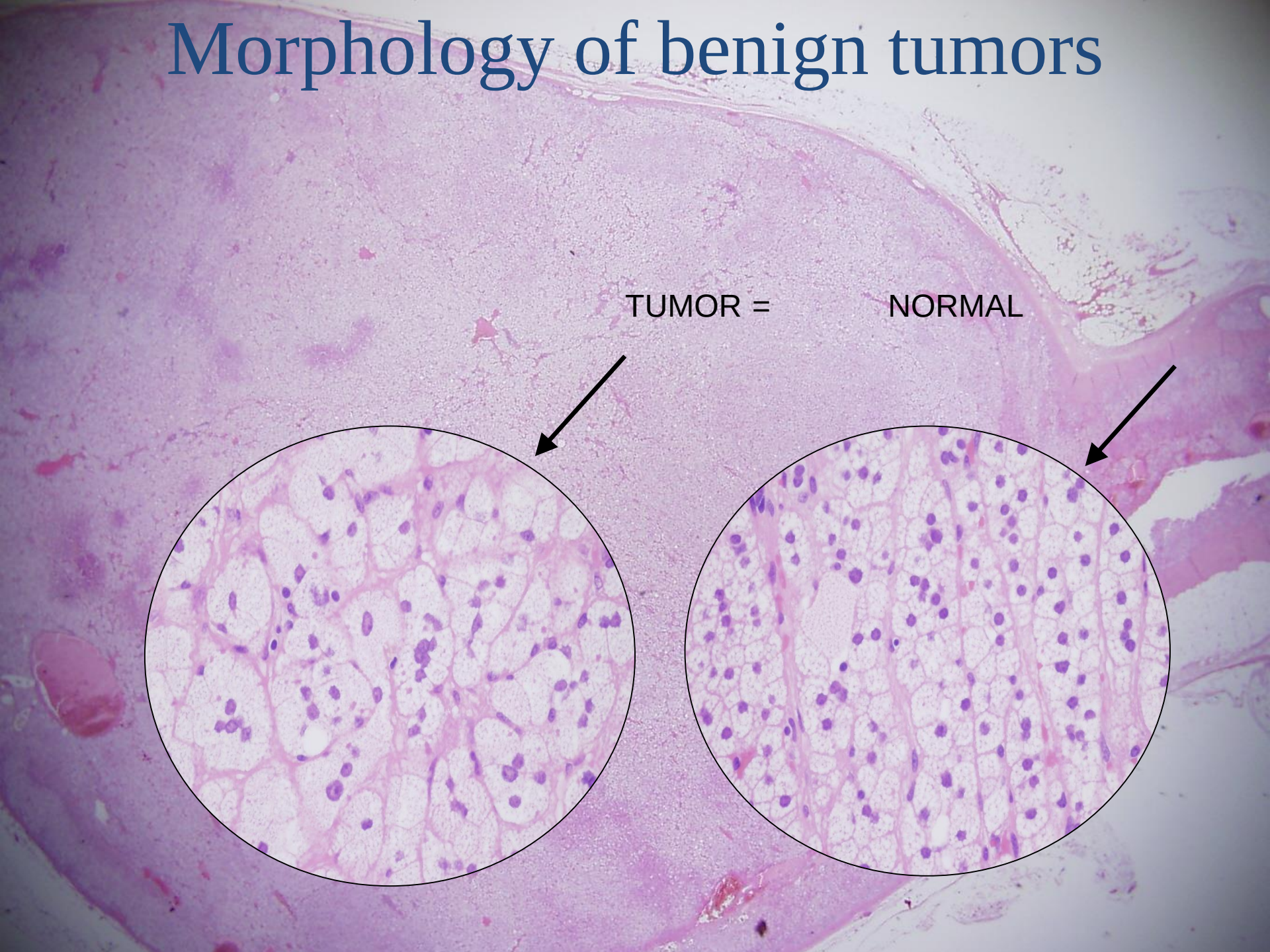
Neoplasm-general characteristics I.

- Benign or malignant
- Benign:
  - macroscopy and microscopy not alarming
  - Localized (no spread to surrounding structures, no distant spread)
  - Surgically removable (not always true)
  - Doesn't kill the host (not always true)

Adrenal gland- adenoma

Photo: 2nd Dept of Pathology,Semmelweis University

Morphology of benign tumors



Leiomyoma- uterine corpus

Photo: 2nd Dept of Pathology,Semmelweis University

Neoplasm-general characteristics II.

- Malignant:
  - Invasion (destruction of surrounding structures)
  - Metastasis (spread to distant sites)
  - May lead to death of the host
  - Cancer (crab)-general term
  - **Carcinoma** (e.g. squamous cell carcinoma, adenocarcinoma…)-malignant tumor of epithelial origin
  - **Sarcoma** (fibrosarcoma, leiomyosarcoma, angiosarcoma…)- malignant tumor of mesenchymal origin
  - **Leukemia, lymphoma, malignant melanoma, malignant teratoma** …

Laryngeal cancer (squamous cell carcinoma)

Photo: 2nd Dept of Pathology,Semmelweis University

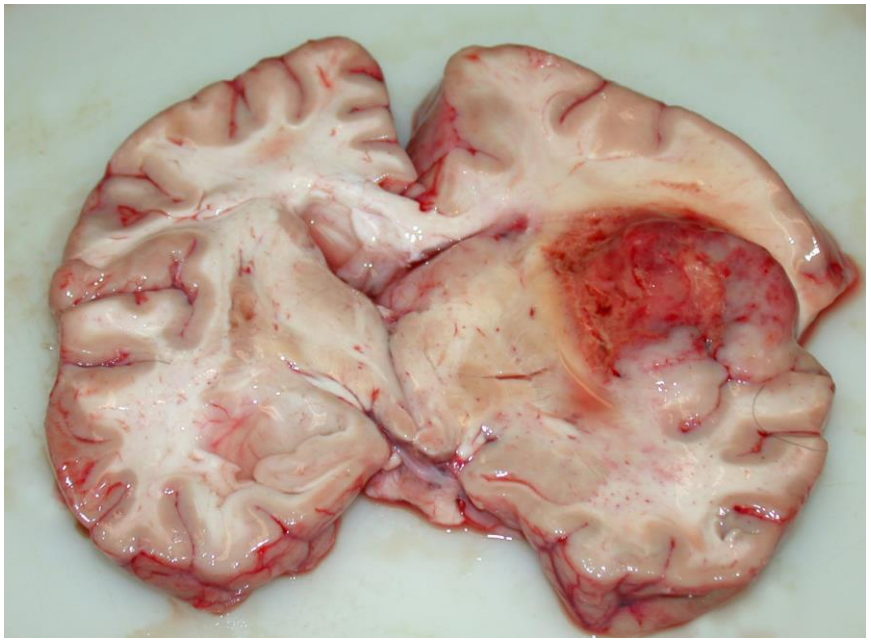
Pancreatic cancer (adenocarcinoma)

Photo: 2nd Dept of Pathology,Semmelweis University

Testicular malignancy (seminoma+teratoma)

Photo: 2nd Dept of Pathology,Semmelweis University

Brain- primary (Glioblastoma) and secondary (lung cancer metastasis) malignancy



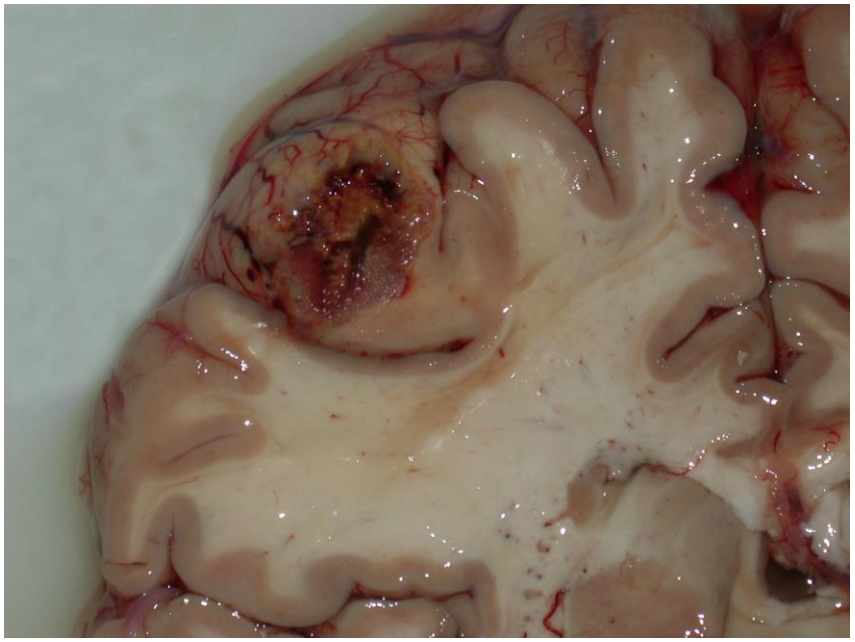
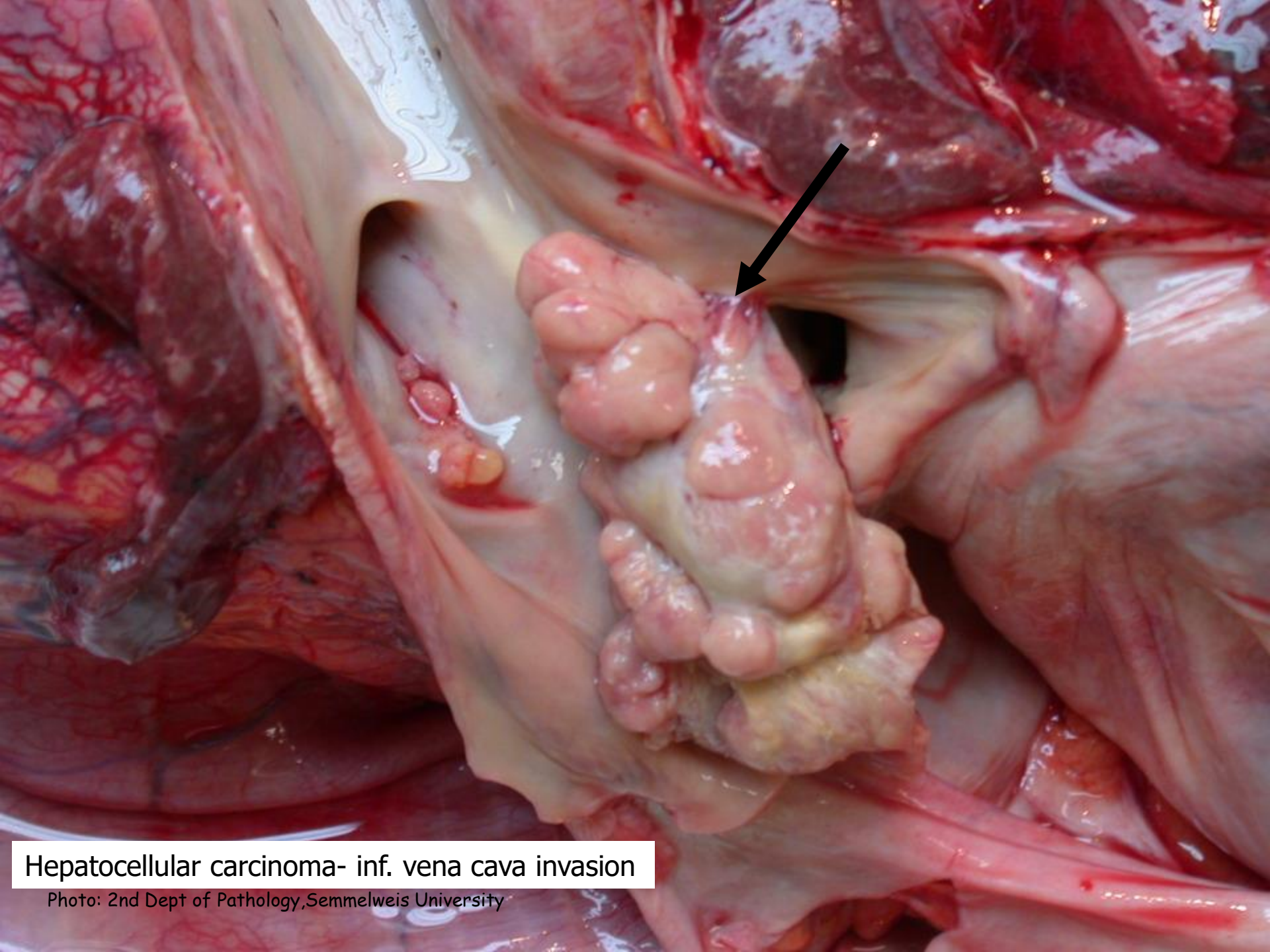


Photo: 2nd Dept of Pathology,Semmelweis University

Liver-primary (hepatocellular carcinoma) and secondary (CRC metastases) malignancy

Photo: 2nd Dept of Pathology,Semmelweis University



Hepatocellular carcinoma- inf. vena cava invasion

Photo: 2nd Dept of Pathology,Semmelweis University

Breast cancer

Photo: 2nd Dept of Pathology,Semmelweis University

Breast cancer- sentinel LN detection

Photo: 2nd Dept of Pathology,Semmelweis University

Breast cancer and fibroadenoma

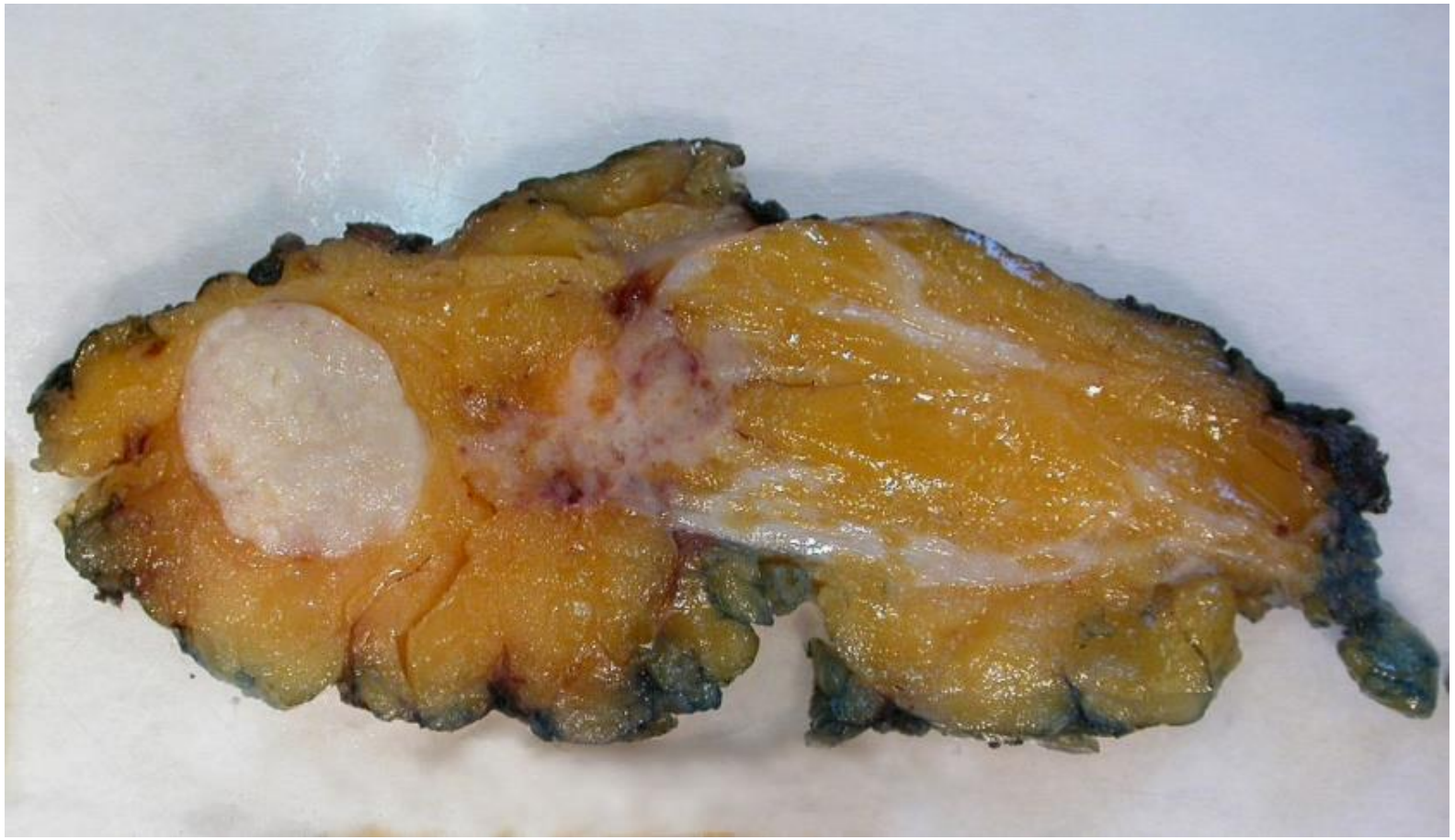
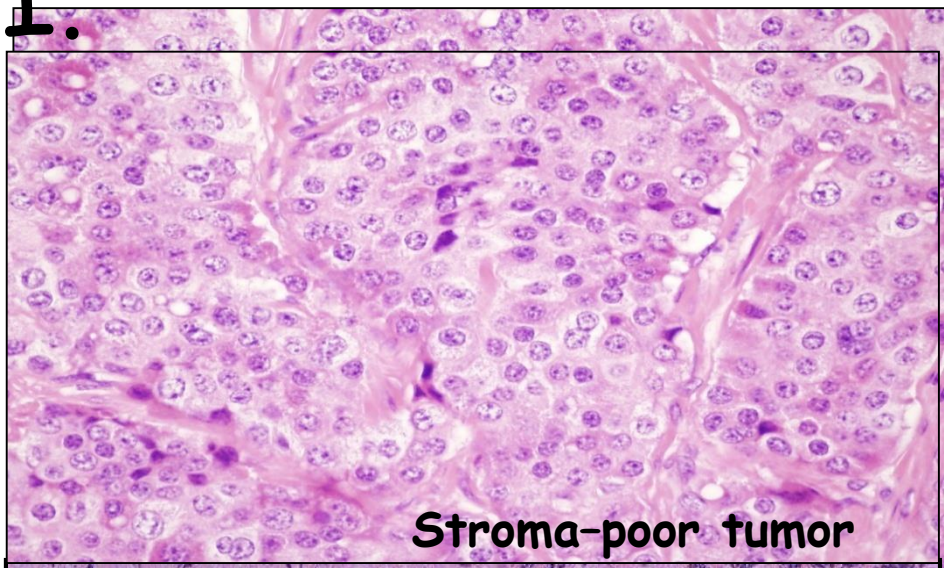
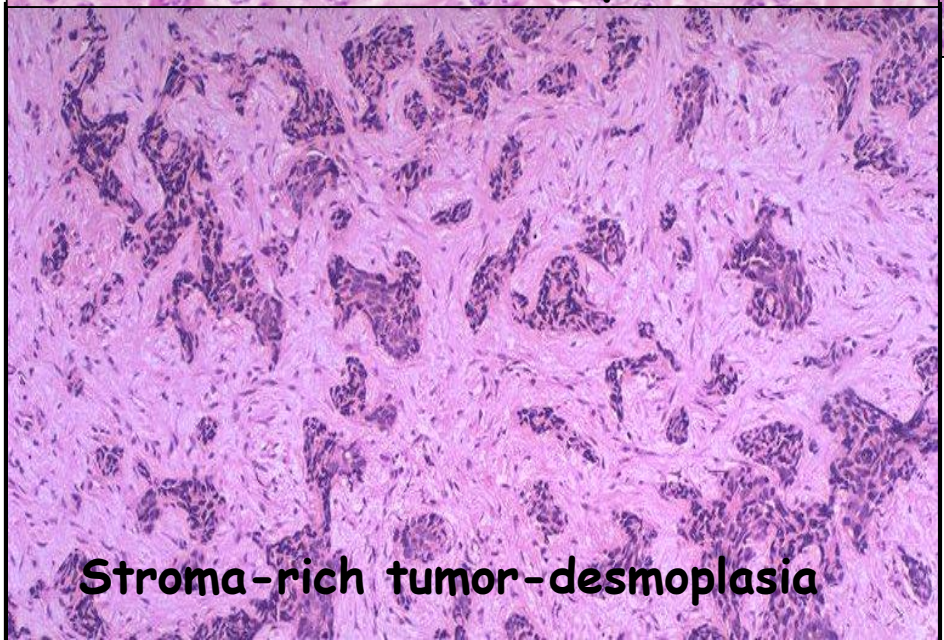


Photo: 2nd Dept of Pathology,Semmelweis University

Neoplasm- general characteristics III.

- Two basic components (benign and malignant tumors)
  - Parenchyma: clonal neoplastic cells
  - Stroma: connective tissue, blood vessels, inflammatory cells (ly, macrophages)
    - Usually reactive
    - Parenchyma depends on stroma (blood supply, connective tissue framework)
    - Cross-talk between parenchyma cells and stromal cells
    - Desmoplasia: abundant collagenous stroma (resulting in the stony hard consistency of the tumor- scirrhous- e.g. breast cancer, cholangiocellular cc)





Benign tumors- nomenclature I.

- -oma: (exceptions-lymphoma, melanoma…)
- Of mesenchymal origin: fibroma, osteoma, chondroma, lipoma
- Of muscles: rhabdomyoma, leiomyoma
- Of endothelial and related: hemangioma, lymphangioma

Benign tumors- nomenclature II.

- Of epithelial origin
  - Papilloma (from squamous cells or glandular epithelial cells-eg. Laryngeal papilloma)- finger-like projection
  - Adenoma (from glandular epithelium- but not necessary glandular in structures) e.g. tubular adenoma of the colon-glandular morphology, parathyroid adenoma, liver cell adenoma- solid)
  - Cystadenoma e.g serous cystadenoma-ovary

Benign tumors- nomenclature III.

- Of melanocytes: nevus
- More than one neoplastic cell type (usually from one germ cell layer): pleomorphic adenoma (mixed tumor)- e.g. within parotis
- More than one neoplastic cell type (from more than one germ cell layer): mature teratoma – e.g. ovarian teratoma, sacrococcygeal teratoma

Malignant tumors –nomenclature I.

- sarcoma
- Scant connective tissue stroma→→ fleshy consistency
- Fibrosarcoma, liposarcoma, chondrosarcoma, osteosarcoma
- Angiosarcoma, lymphangiosarcoma
- Leiomyosarcoma, rhabdomyosarcoma

Malignant tumors –nomenclature II.

- Leukemia, lymphoma
- Malignant melanoma
- Malignant teratoma

Malignant tumors –nomenclature III.

- Of epithelial origin: carcinoma
- From squamous cells: squamous cell carcinoma (e.g. cervix, esophagus, larynx, bronchi…)
- From glandular epithelial cells: adenocarcinoma (stomach, colon, cervix…)

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
Endothelial and Related Tissues		
Blood vessels Lymph vessels Synovium Mesothelium Brain coverings	Hemangioma Lymphangioma Meningioma	Angiosarcoma Lymphangiosarcoma Synovial sarcoma Mesothelioma Invasive meningioma
Blood Cells and Related Cells		
Hematopoietic cells Lymphoid tissue		Leukemias Lymphomas
Muscle		
Smooth Striated	Leiomyoma Rhabdomyoma	Leiomyosarcoma Rhabdomyosarcoma
Tumors of Epithelial Origin		
Stratified squamous Basal cells of skin or adnexa Epithelial lining of glands or ducts Respiratory passages Renal epithelium Liver cells Urinary tract epithelium (transitional) Placental epithelium Testicular epithelium (germ cells)	Squamous cell papilloma Adenoma Papilloma Cystadenoma Bronchial adenoma Renal tubular adenoma Liver cell adenoma Transitional-cell papilloma Hydatidiform mole	Squamous cell carcinoma Basal cell carcinoma Adenocarcinoma Papillary carcinomas Cystadenocarcinoma Bronchogenic carcinoma Renal cell carcinoma Hepatocellular carcinoma Transitional-cell carcinoma Choriocarcinoma 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 Renal anlage	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin 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

From Robbins Pathologic Basis of Disease 7th edition

„Dangerous" aspects of tumor growth

- Benign tumors
  - Localization (brain!!!)
  - Necrosis, hemorrhage
  - Production of a biologically active substance (parathormone production of **parathyroid adenoma**→→ bone resorption, hypercalcemia)
- Malignant tumors
  - Progressive growth (locally advanced disease) and metastasis
  - Necrosis and hemorrhage
  - Cachexia
  - Paraneoplastic syndromes

Breast cancer- Locally advanced disease

Photo: 2nd Dept of Pathology,Semmelweis University

Hemorrhage within metastatic foci of MM

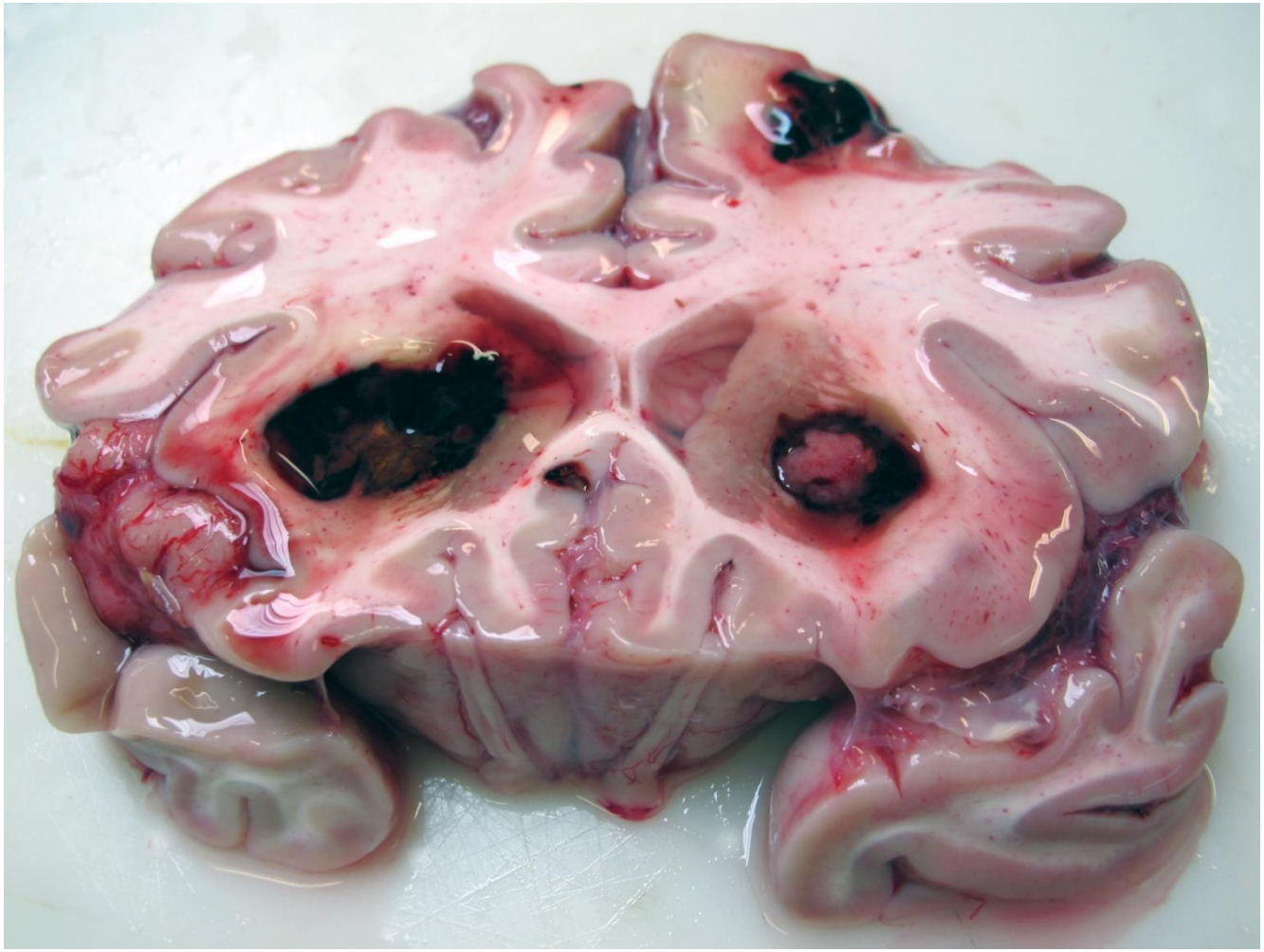
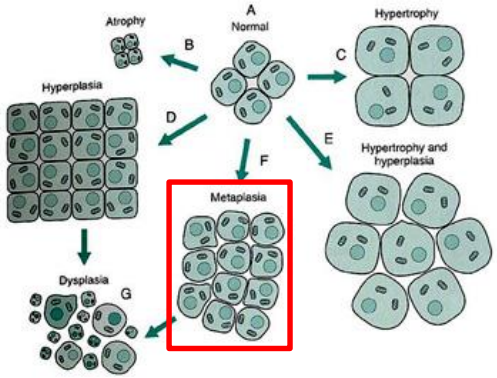


Photo: 2nd Dept of Pathology,Semmelweis University

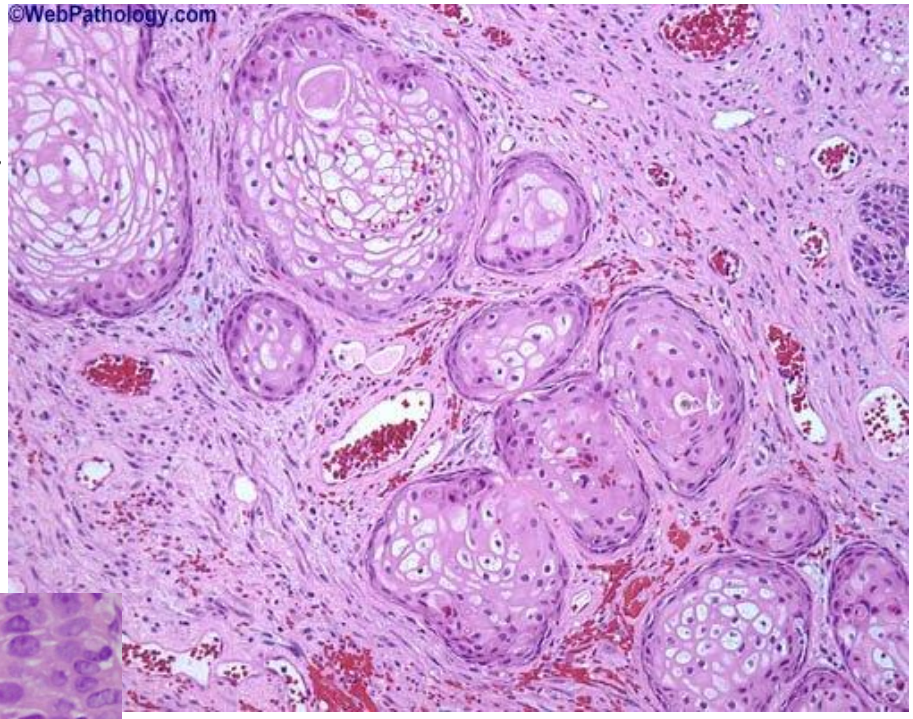
Terms not closely/or only eventually related to neoplasia

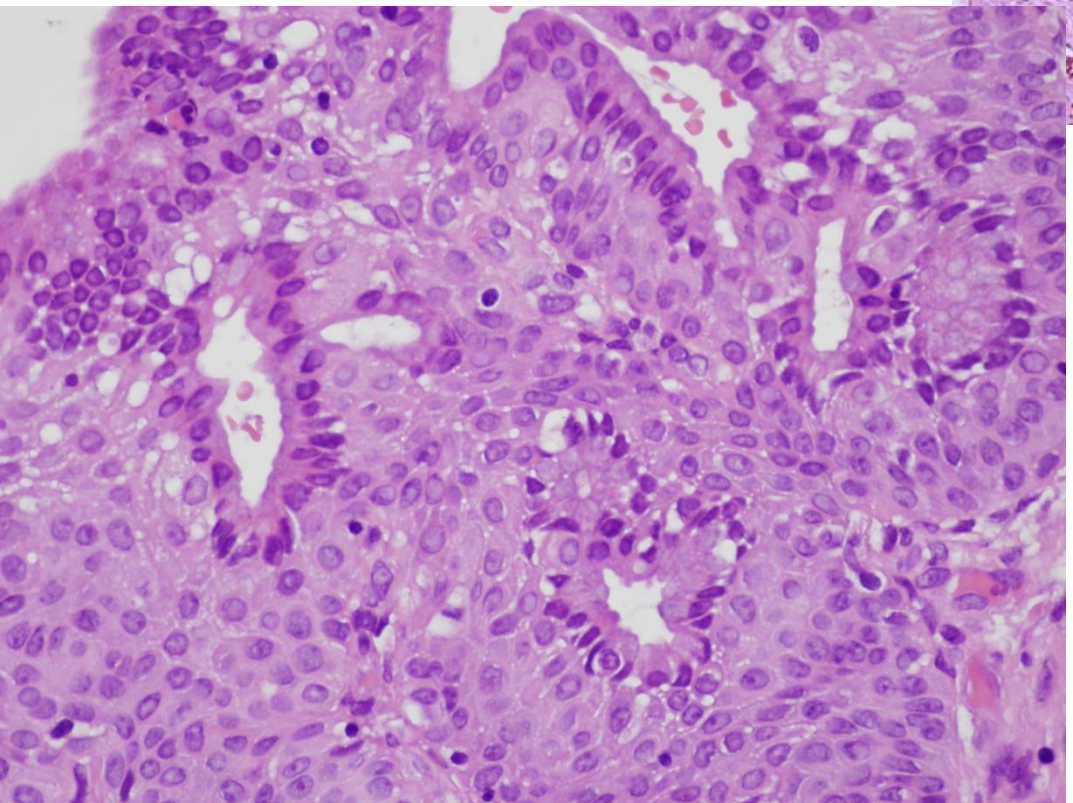
- Hamartoma- e.g. within lung, breast
- Choristoma/heterotopic tissue-e.g. pancreas within Meckel diverticulum (not a teratoma!!)

- Metaplasia:
  - An adult cell type is replaced by an other adult cell type
  - Reversible (adaptation)
  - Due to chronic irritation
  - Forms: Squamous mtpl. (resp. epithelium, prostate, cervix, urinary bladder)
    Columnar mtpl. (Barett's esophagus)
    Mesenchymal (osseous, chondroid, etc)

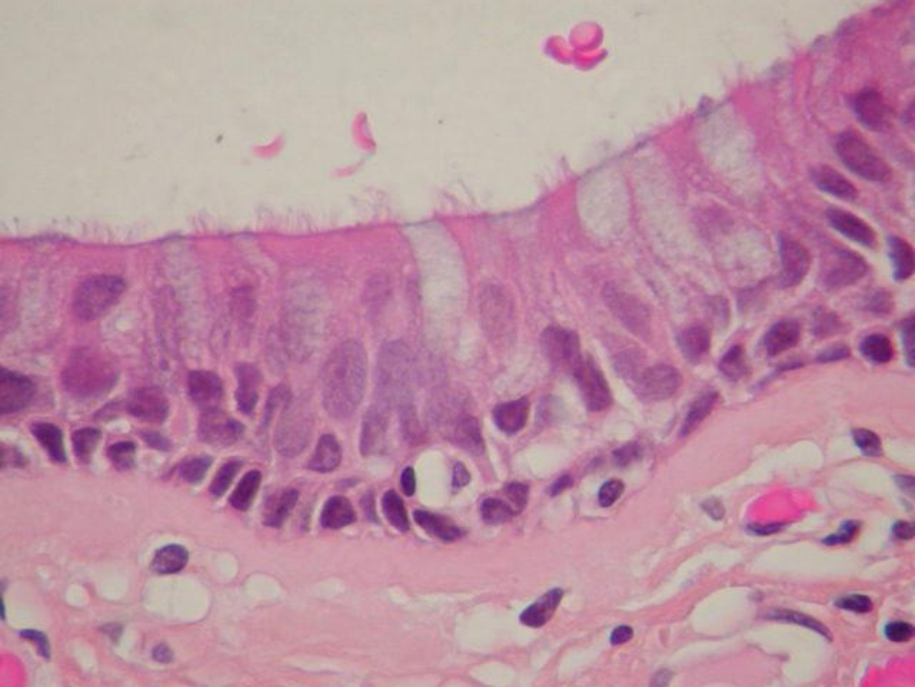


Squamous metaplasia in the prostate…

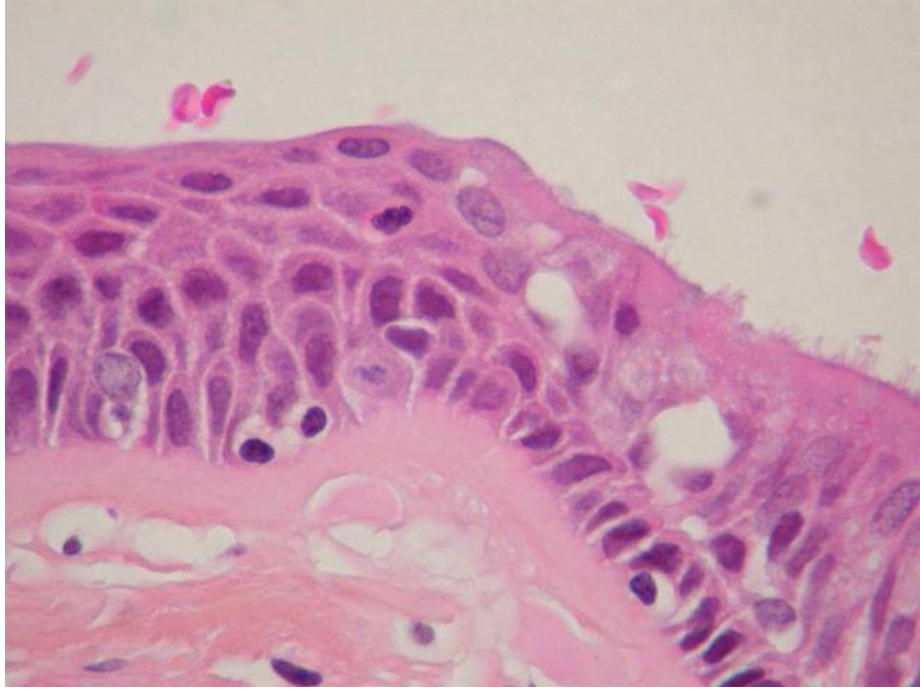




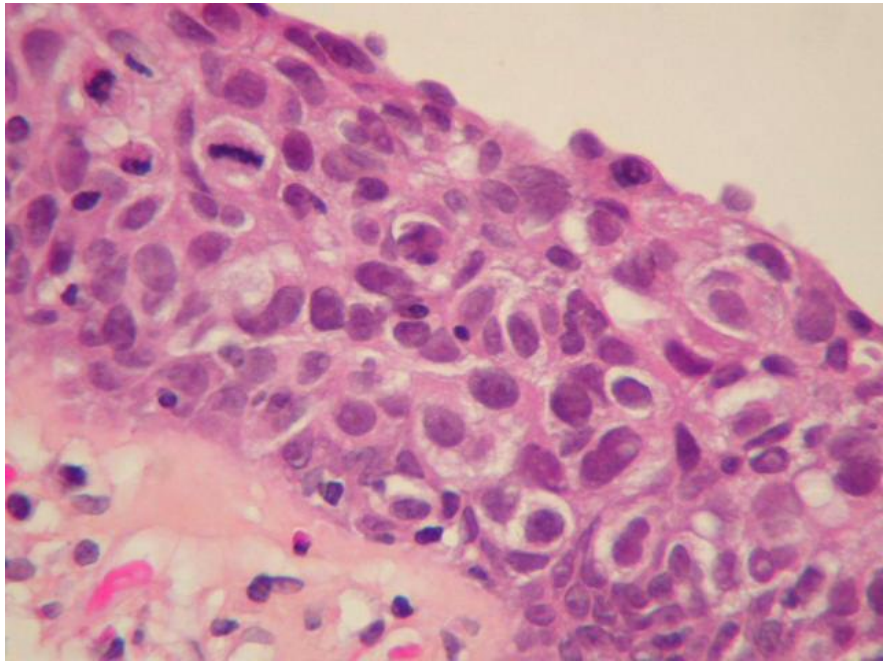
and in the endocervix



normal bronchial epithelium

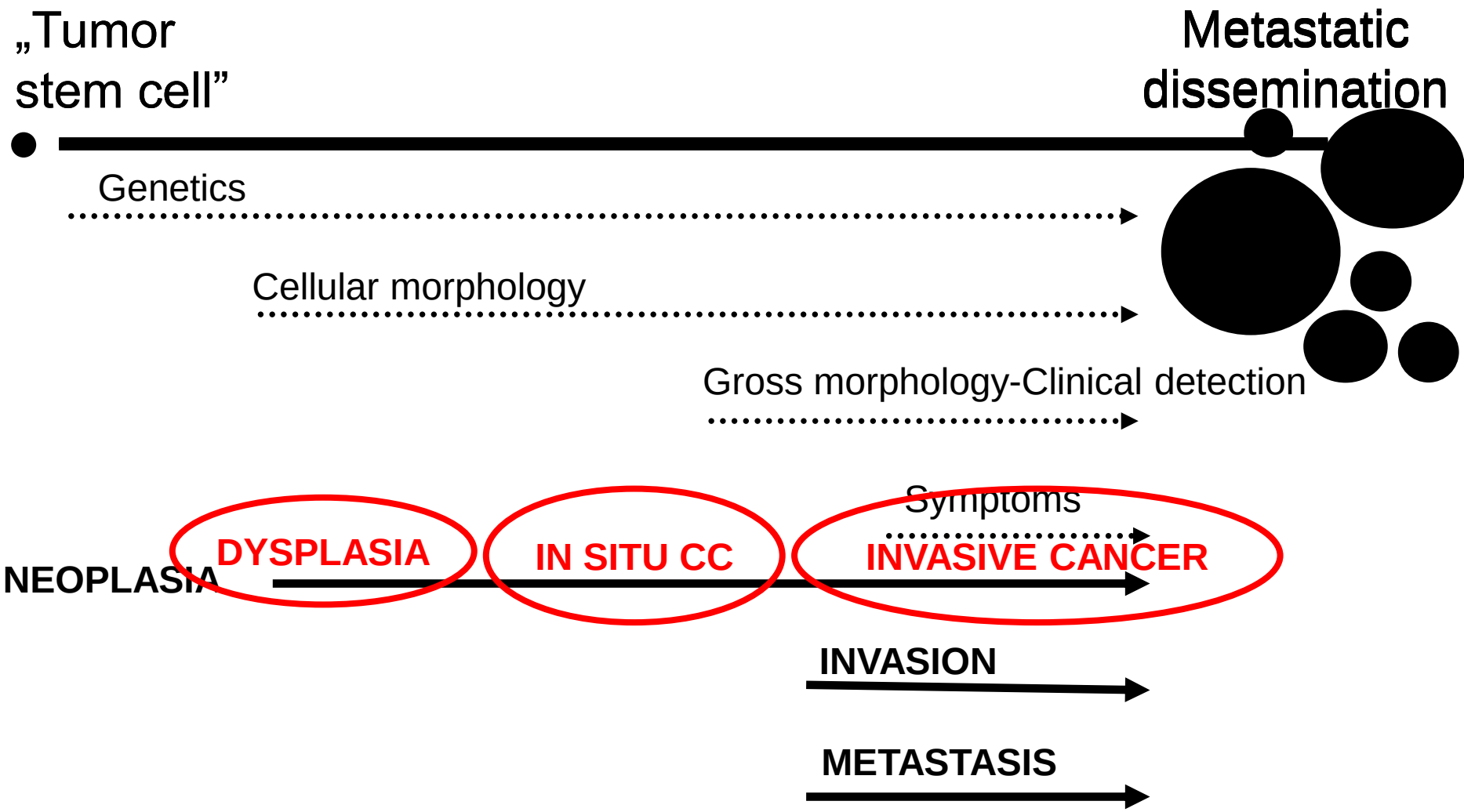


metaplasia



cc. in situ

Carcinogenesis



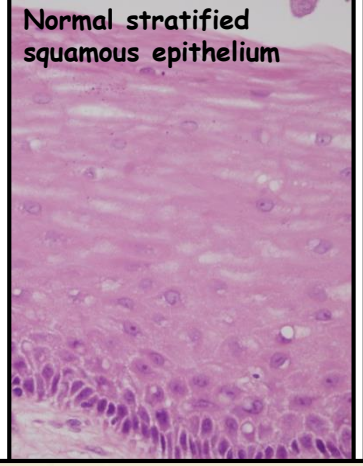
Courtesy Dr Kovács KA

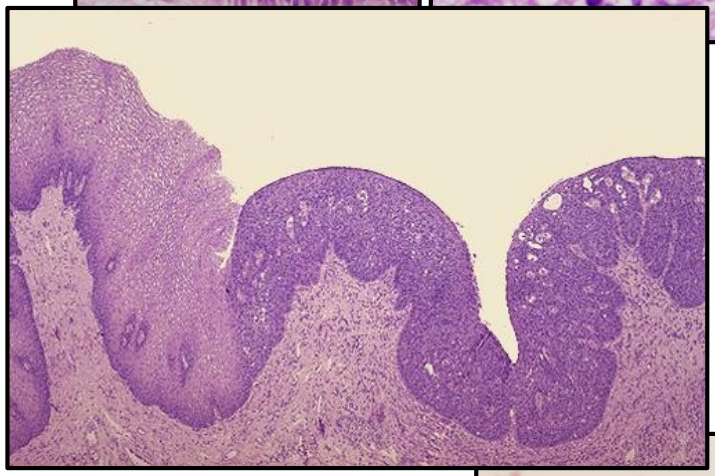
Carcinogenesis-morphology I.

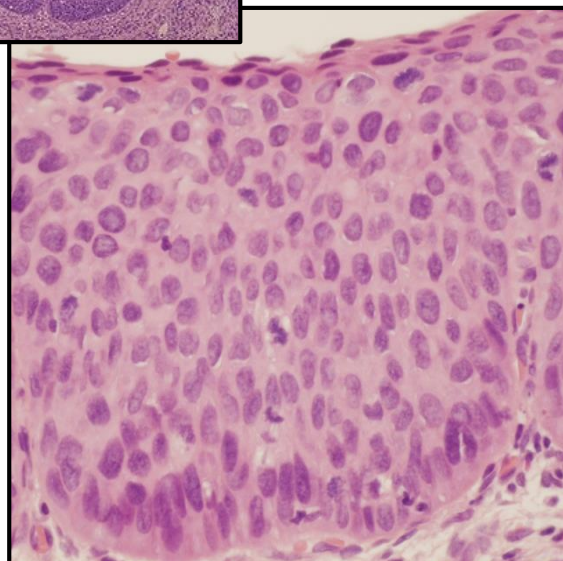
- Dysplasia
  - Within stratified epithelia
  - Loss of normal cellular orientation/polarity
  - Polymorphism: different nuclear size, shape and staining properties
  - Increased mitotic count
  - Mitotic figures in superficial epithelial layers (not only in basal layer)
  - May be a precursor lesion of carcinoma in situ, invasive cancer (but not necessarily!!!)

Dysplasia

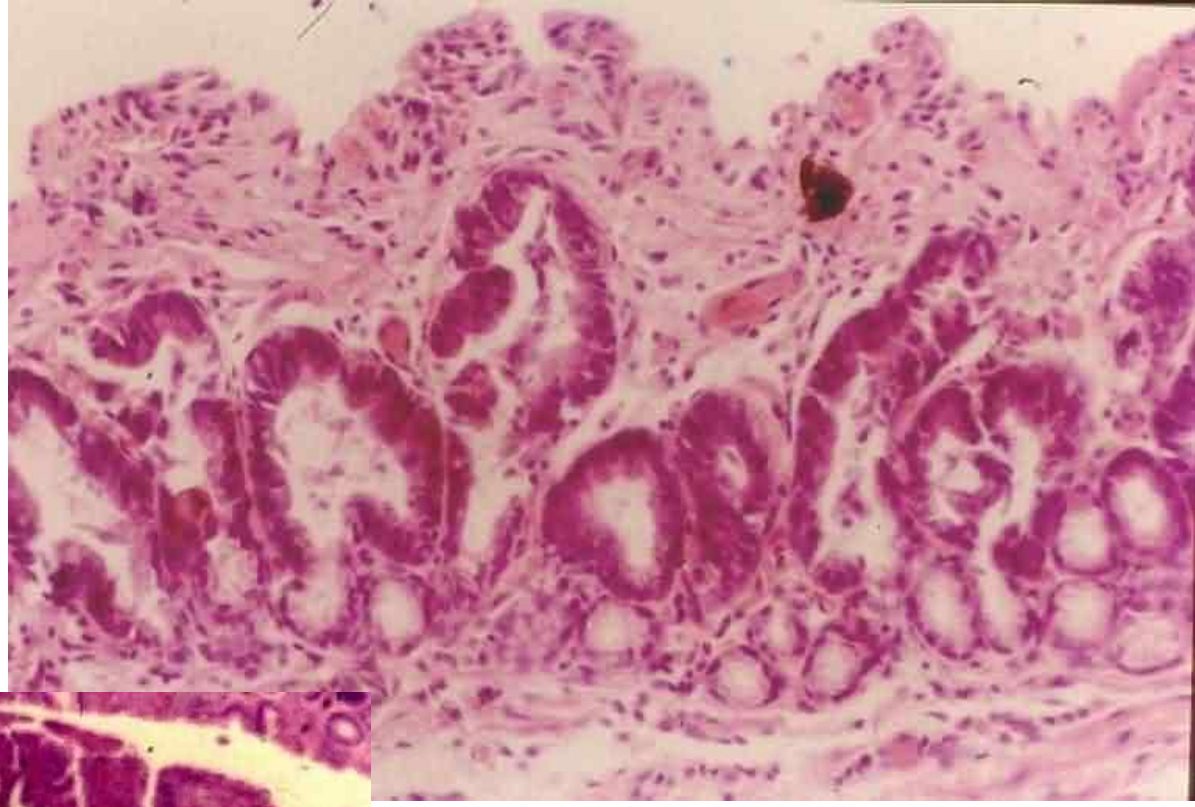
Loss of cellular orientation
Cells resembling basal cells
Increased nuclear size
(N/C ratio increased)
Hyperchromasia
Nucleoli
MI in abnormal location
Increased MI
Occasional bizarre cells
Polymorphism

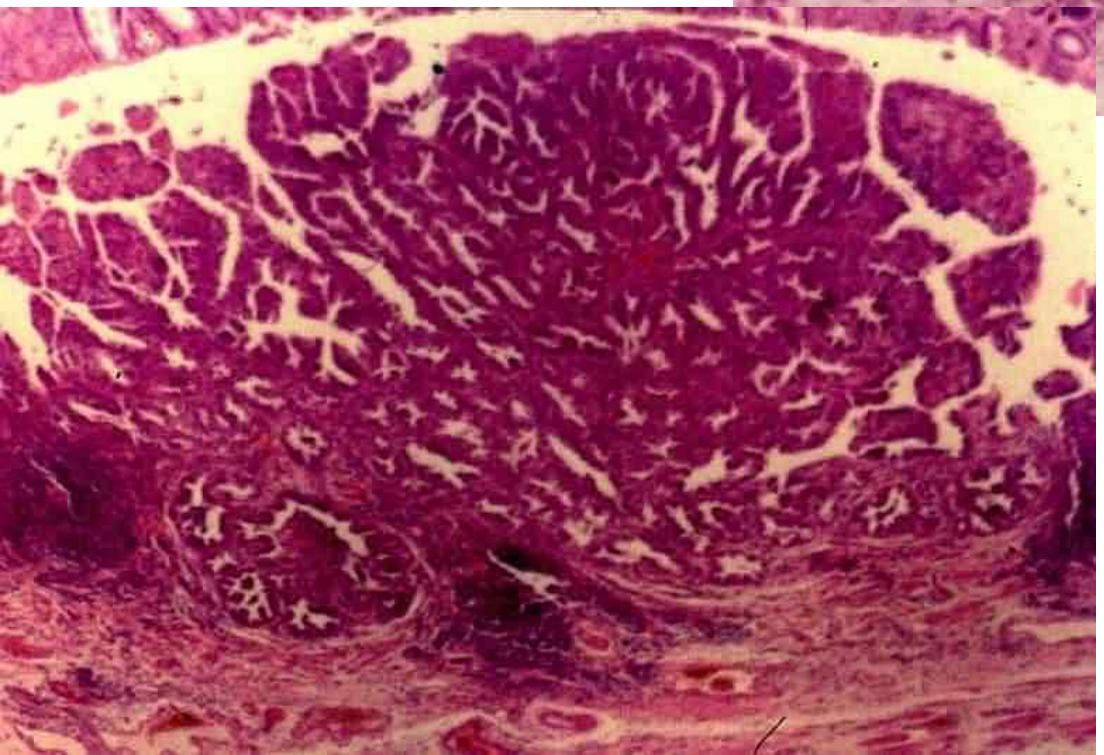






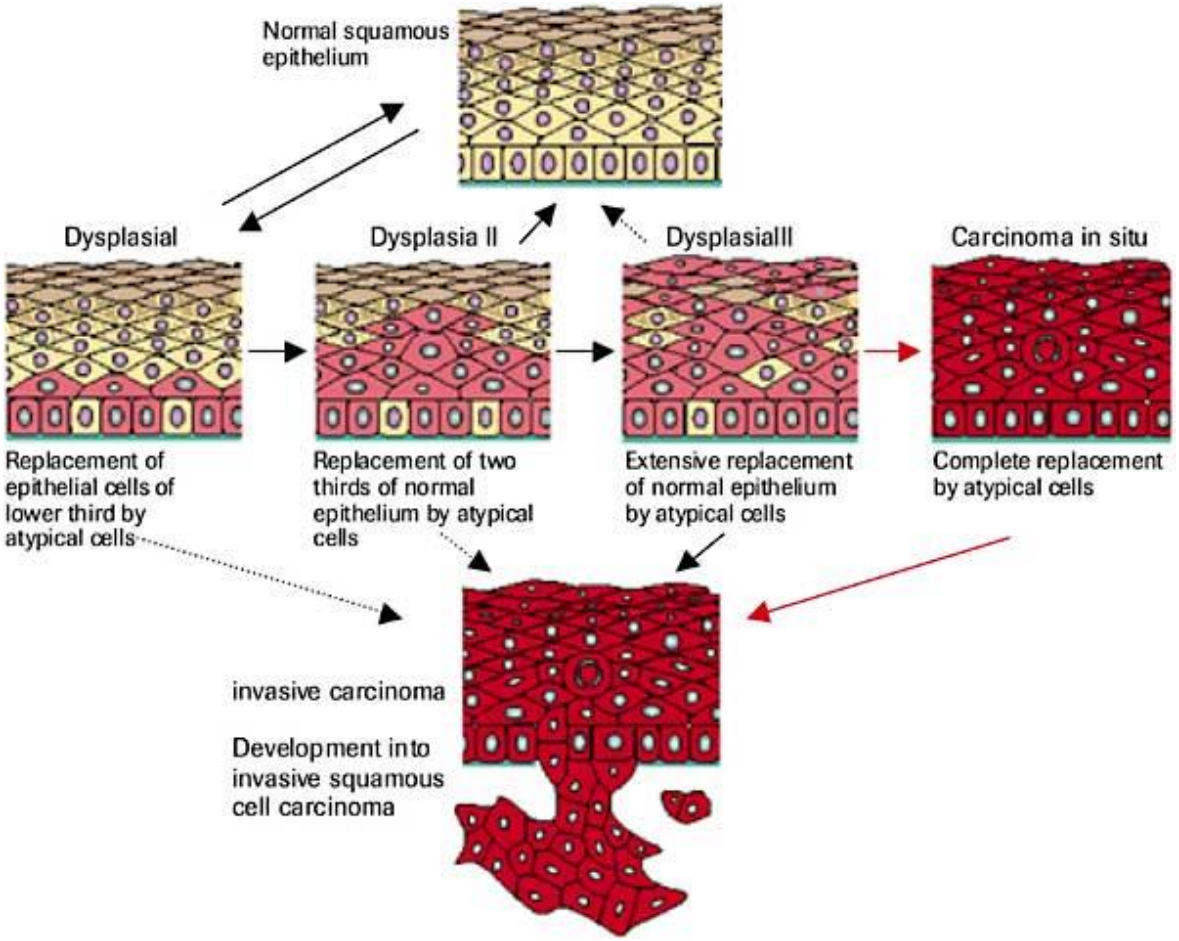
Barrett-dysplasia esophagus





Barrett-adenocarcinoma

Possible outcomes of dysplasia



Carcinogenesis-morphology II.

- In situ carcinoma
  - Basal membrane intact→→ no signs of invasion
  - Neoplastic proliferation confined to the epithelial layer

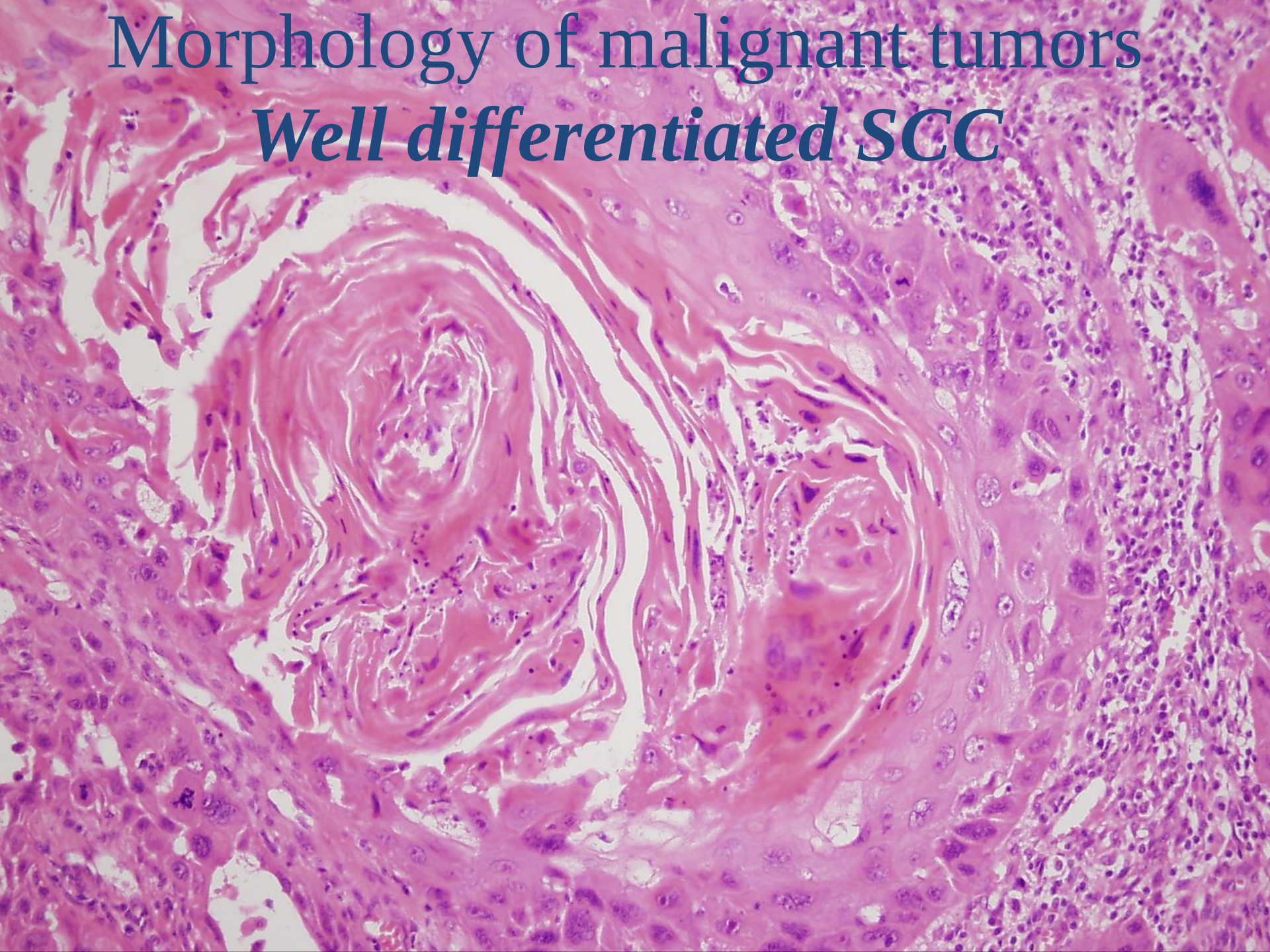
Carcinogenesis-morphology III.

- Invasive carcinoma
  - The tumor is seen within subepithelial connective tissue /lamina propria and beyond
  - Differentiation↔anaplasia
  - Differentiation: how far the tumor resembles its original counterpart in morphology and function
    - Well differentiated
    - Moderately differentiated
    - Poorly differentiated (anaplastic)

    GRADE
  - Anaplasia: lack of differentiation

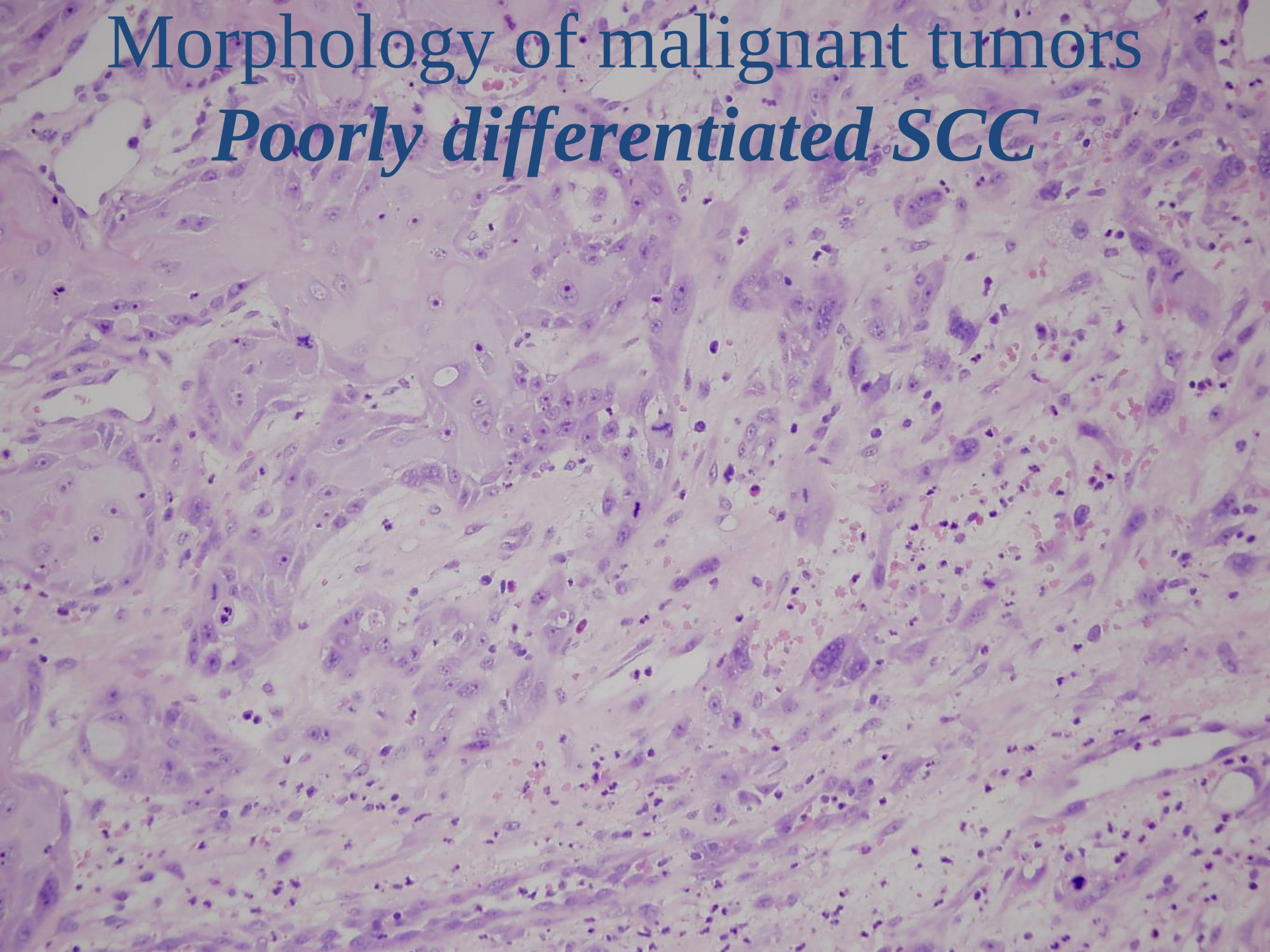
Morphology of malignant tumors

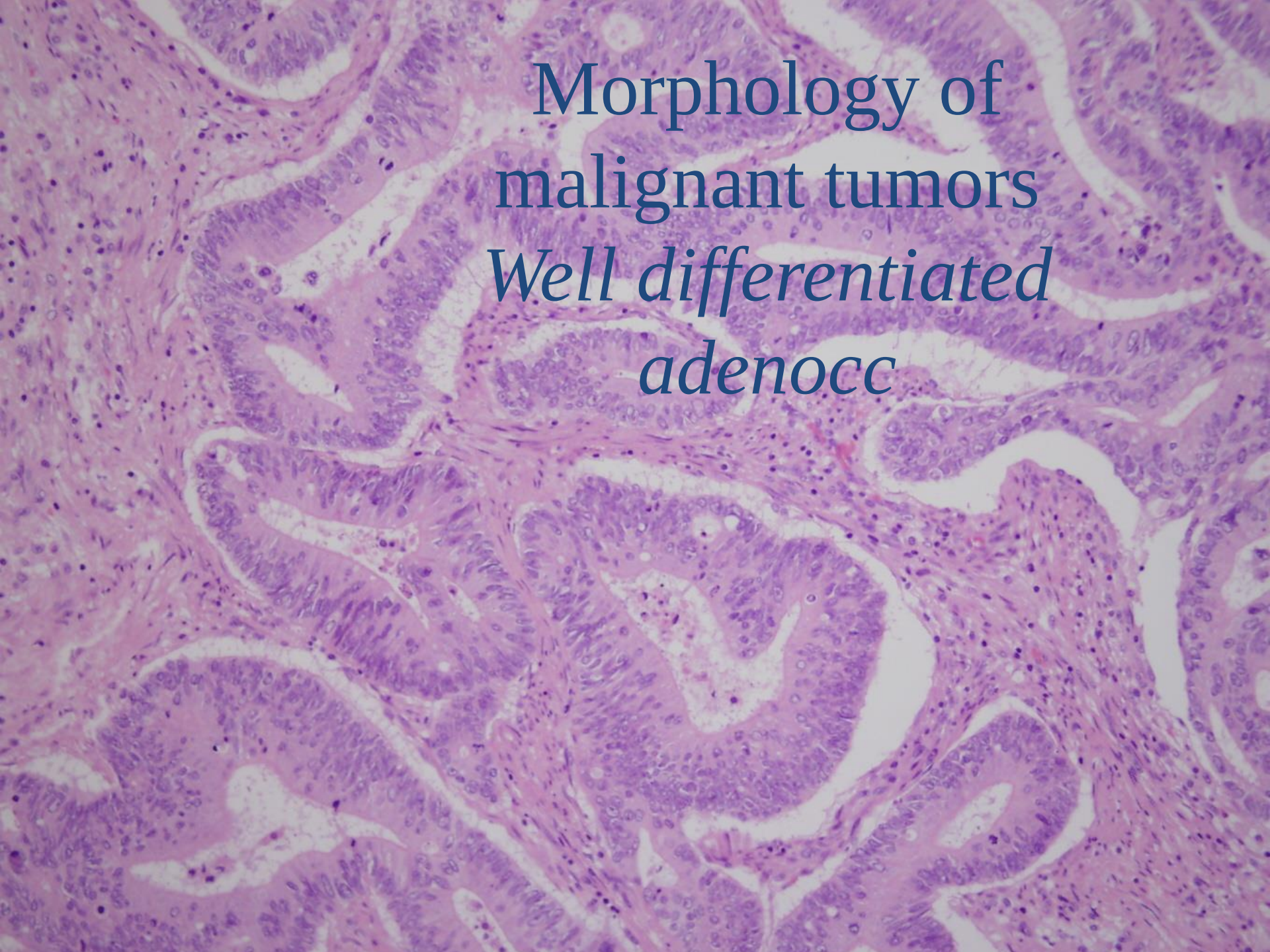
Well differentiated SCC



Morphology of malignant tumors

Poorly differentiated SCC



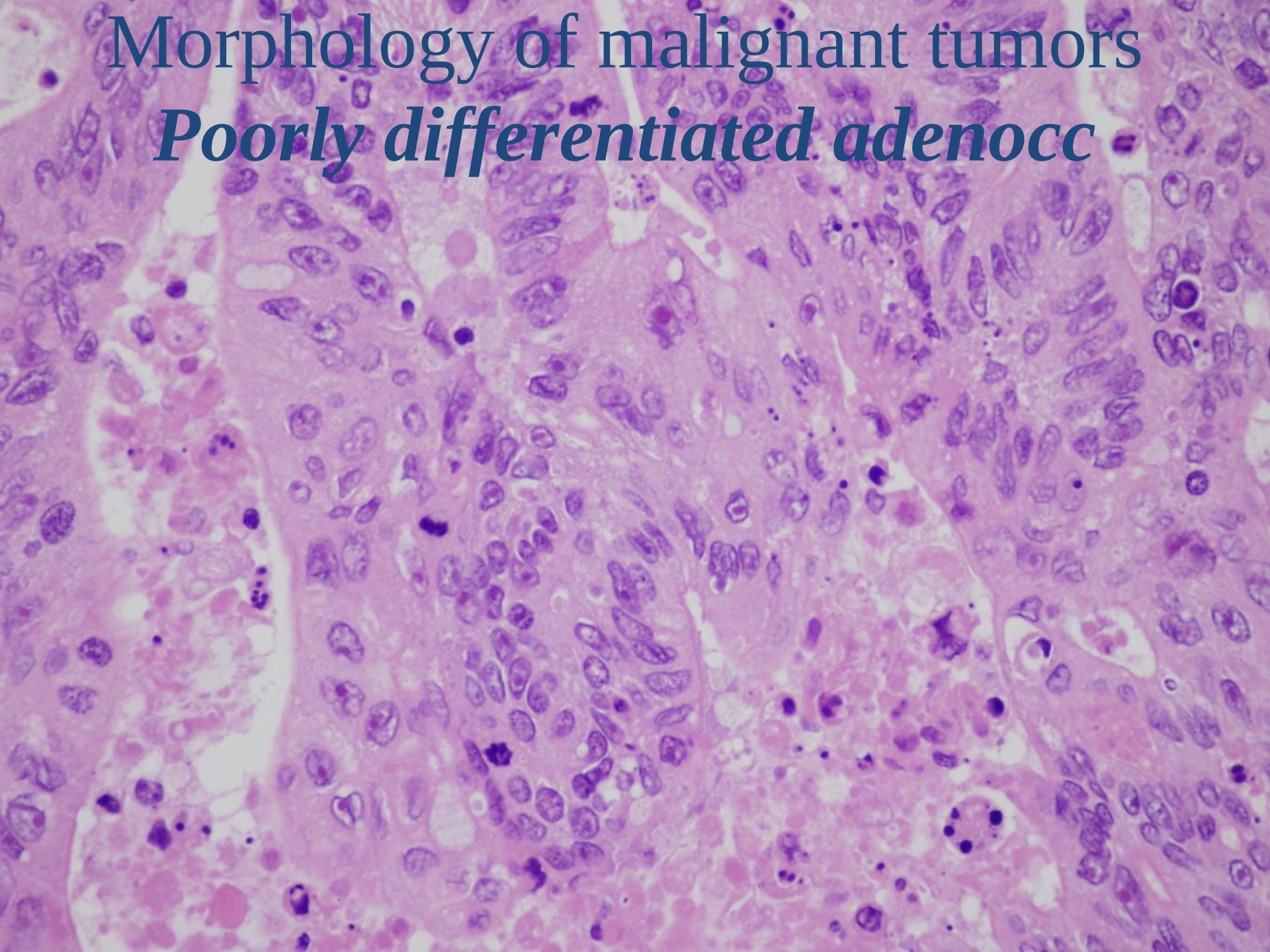


Morphology of malignant tumors

Well differentiated adenocc

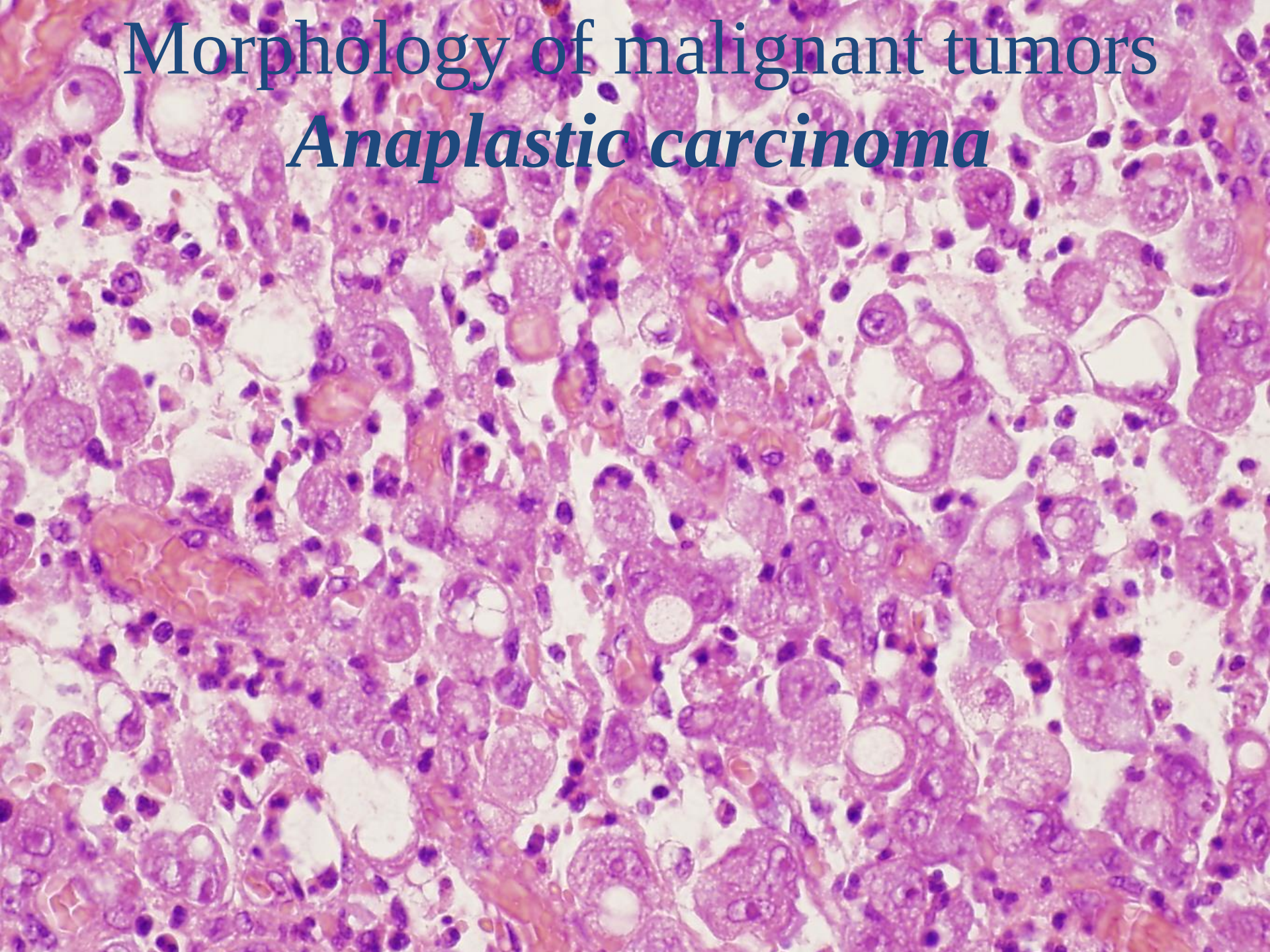
Morphology of malignant tumors

Poorly differentiated adenocc



Morphology of malignant tumors

Anaplastic carcinoma

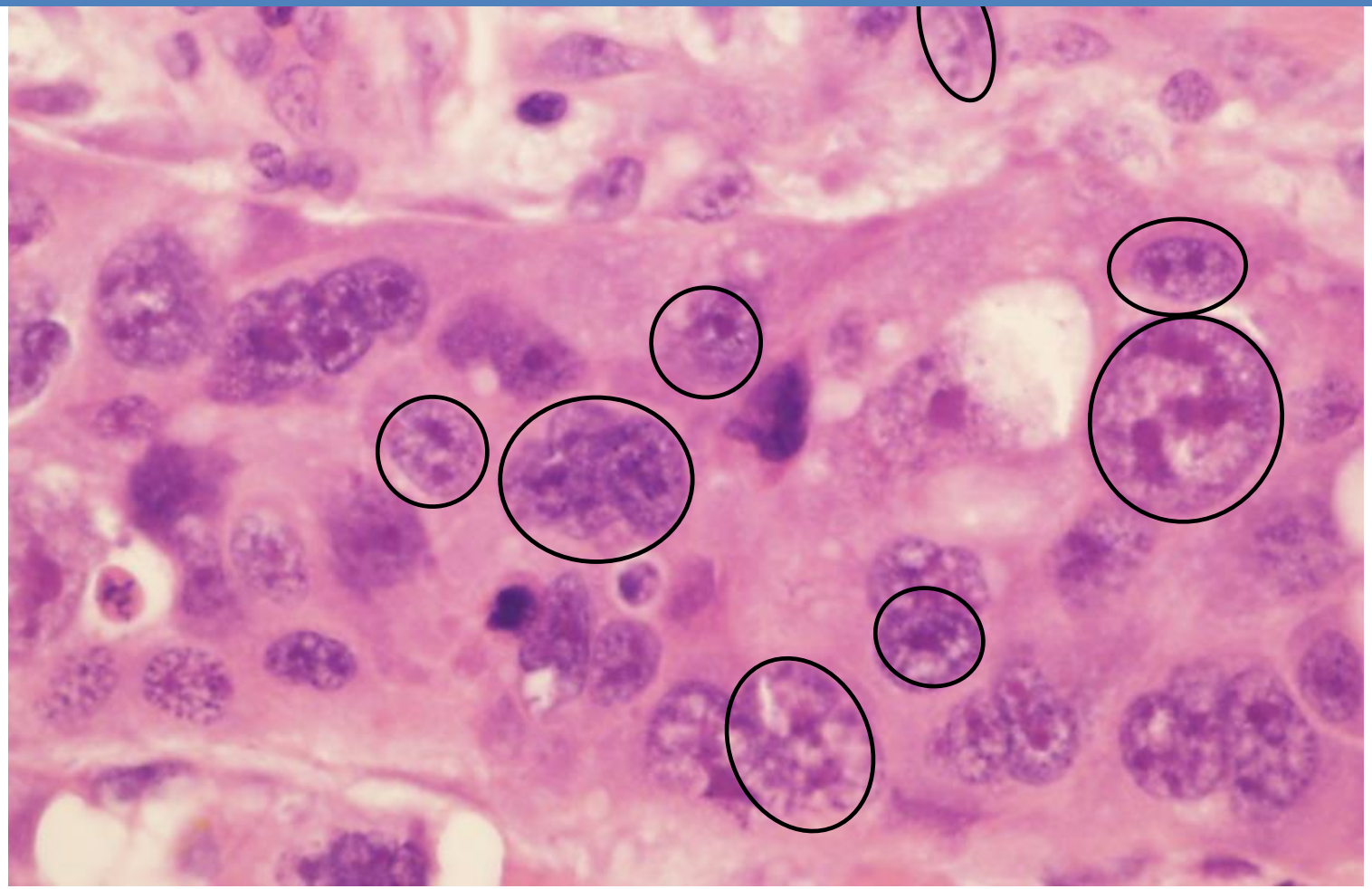


Carcinogenesis-morphology IV.

- Other microscopic features
  - Polymorphism (pleomorphism)
  - Loss of polarity
  - Abnormal nuclear morphology
    - hyperchromatic nuclei
    - large nuclei (nuclear/cytoplasmic ratio increasing)
    - Irregular nuclear shape
    - Large nucleoli
  - Mitoses/atypical mitoses
  - Tumor giant cells

POLYMORPHISM

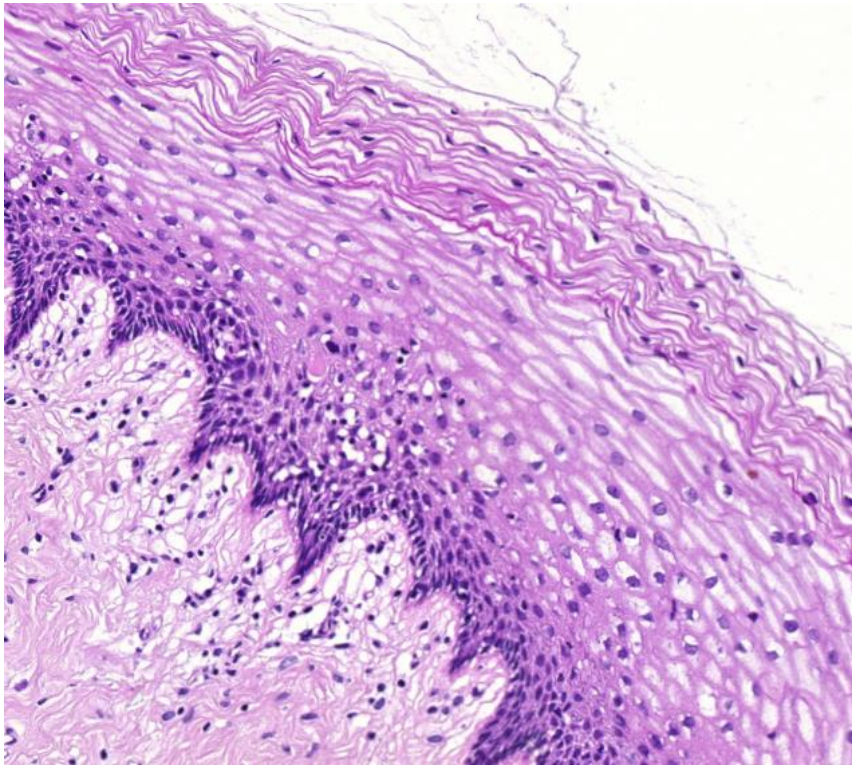
Variable size & shape & nuclear staining properties

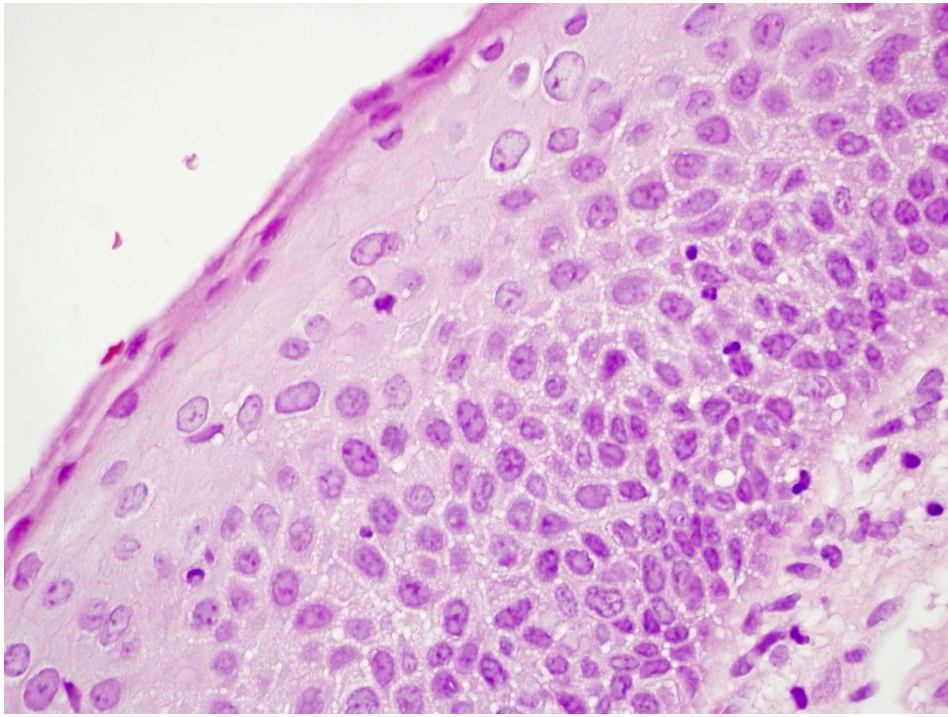


Loss of polarity

Photo Dr Kovács KA

Loss of polarity

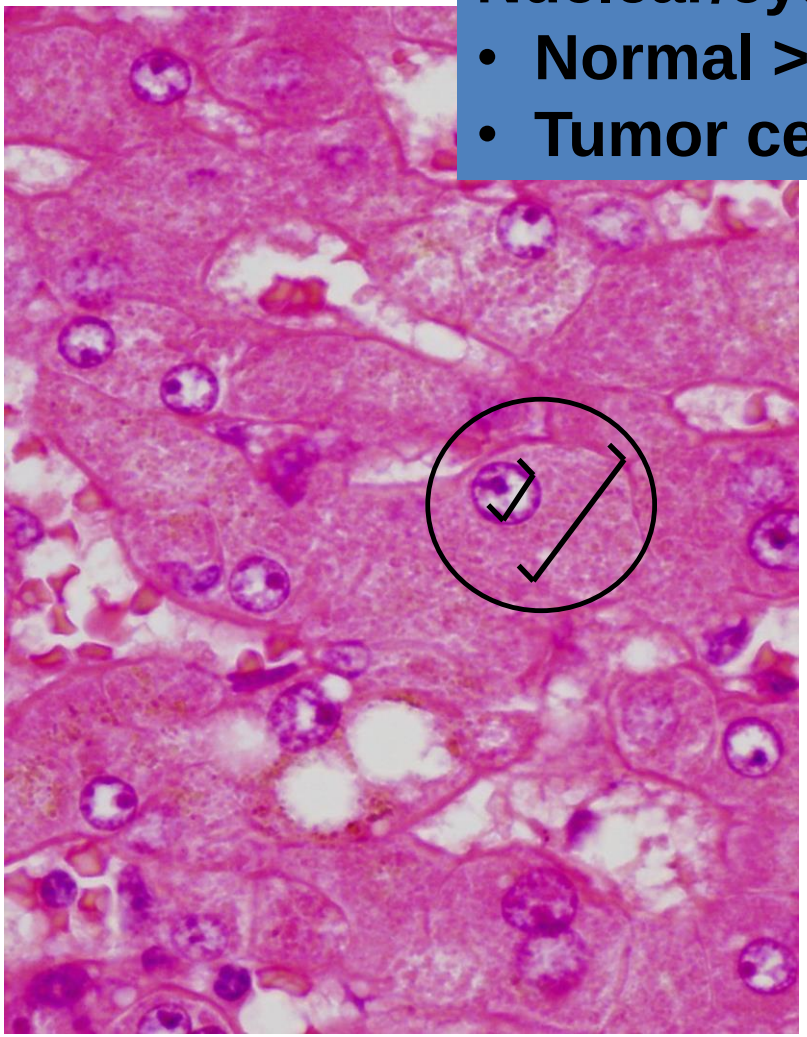


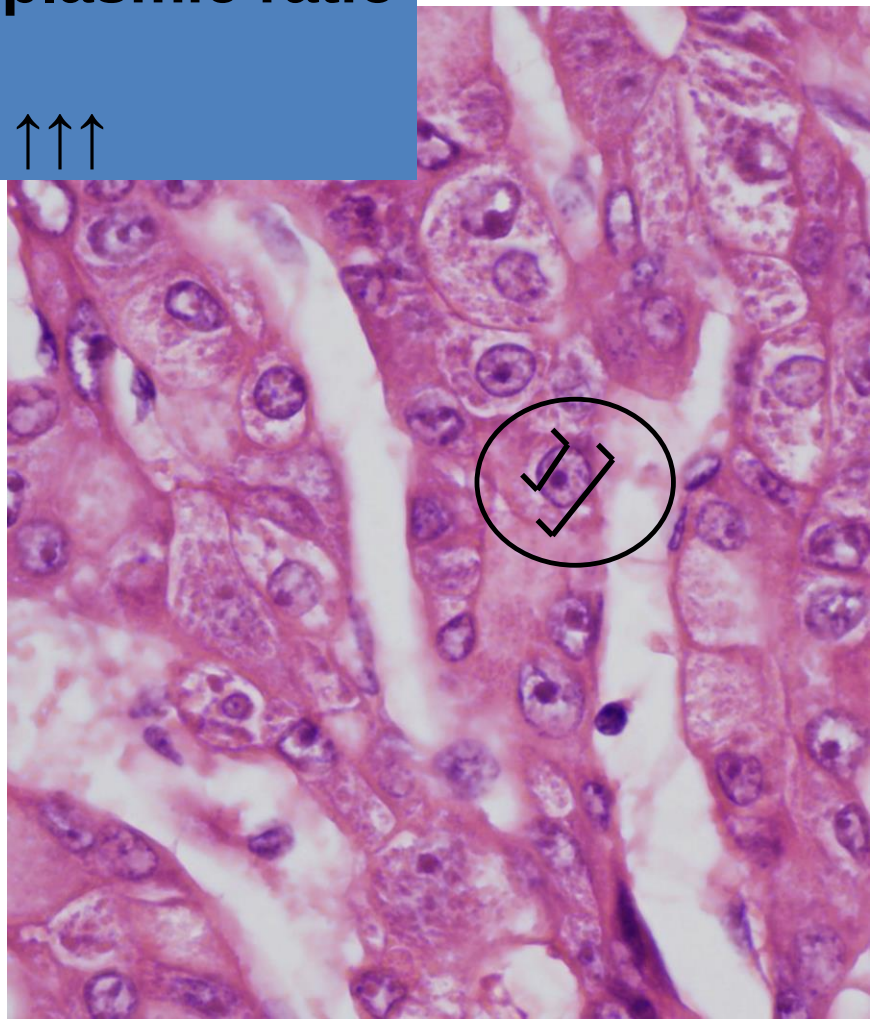


NUCLEAR MORPHOLOGY I.

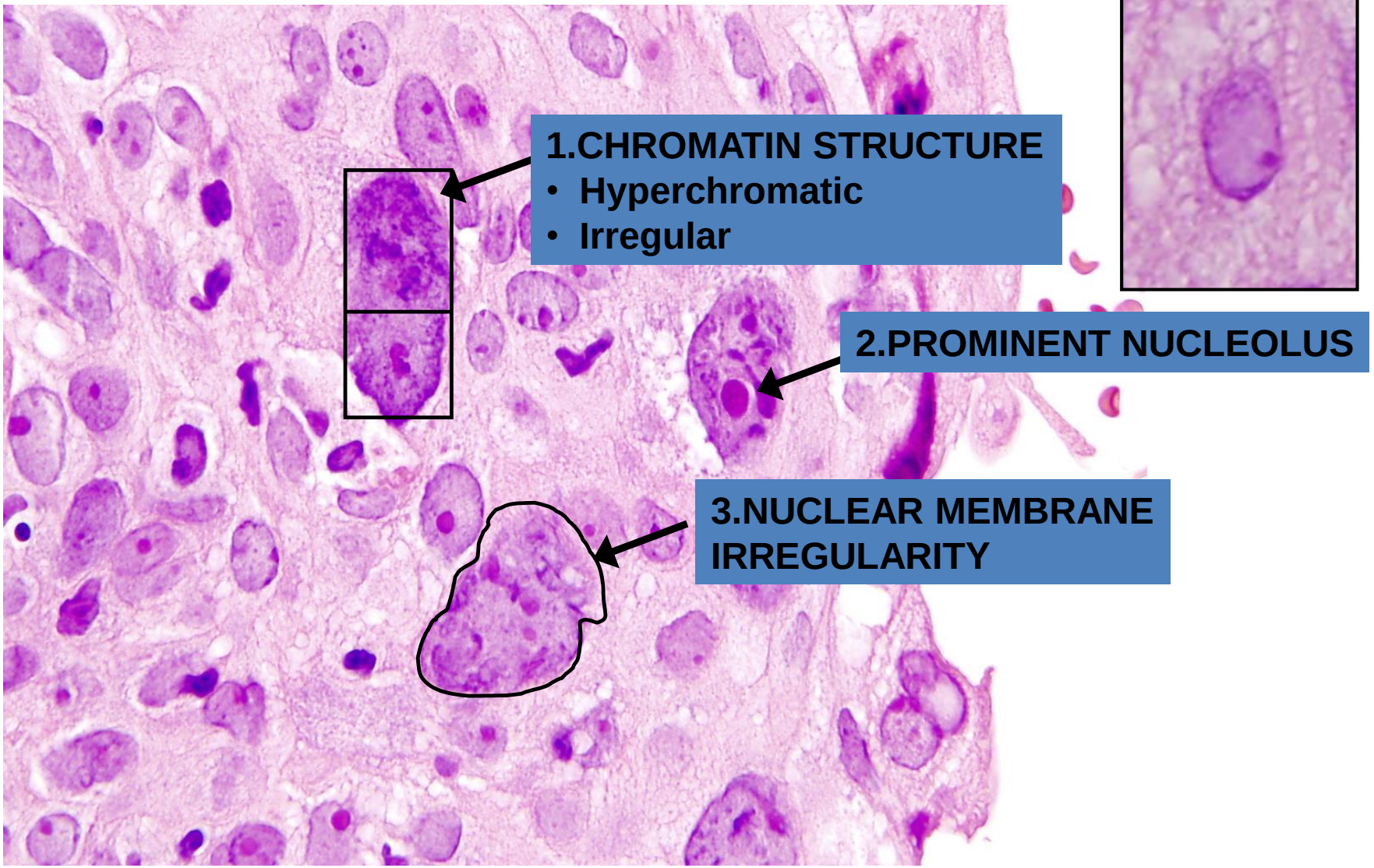
Nuclear/cytoplasmic ratio

- **Normal >1**
- **Tumor cell ↑↑↑**

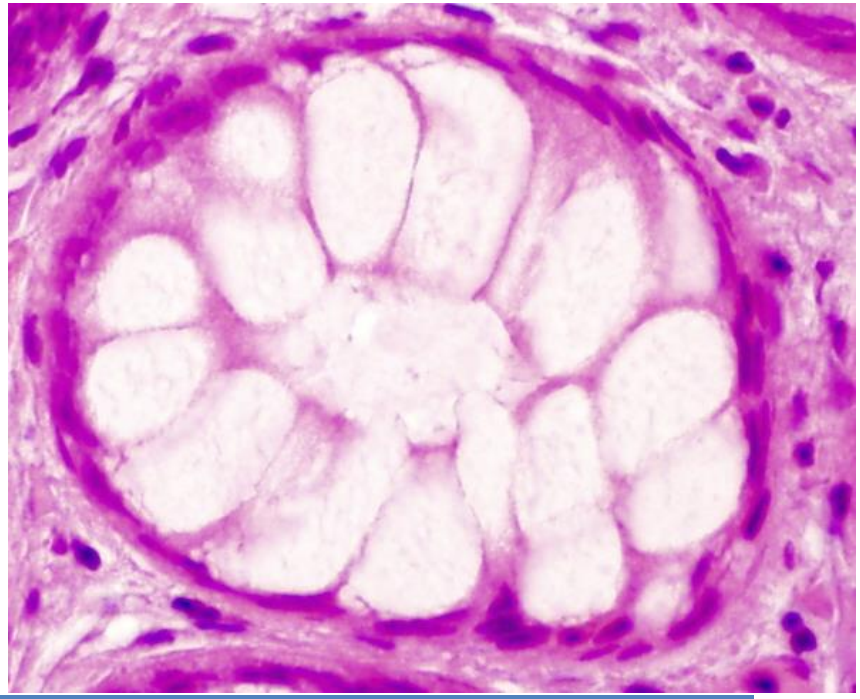




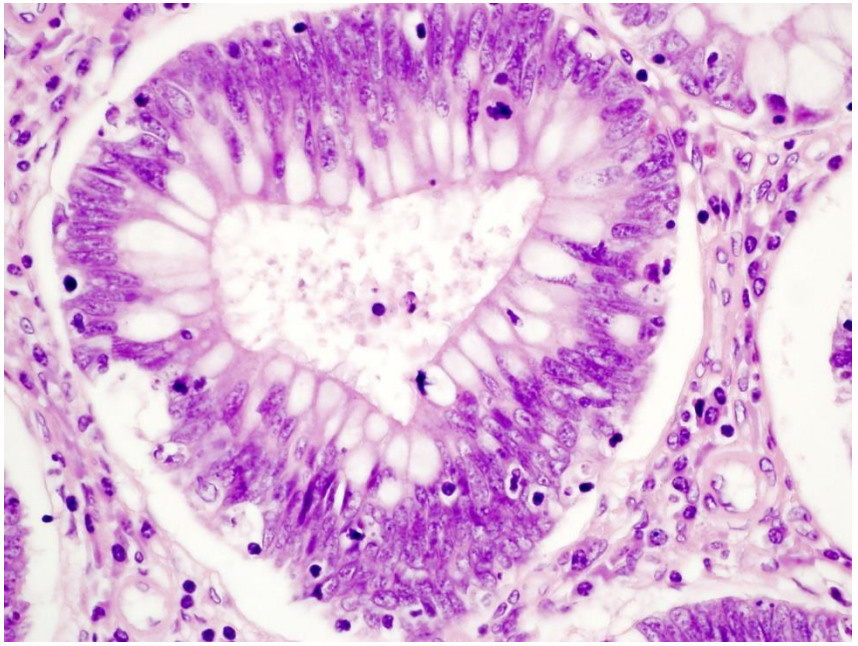
NUCLEAR MORPHOLOGY II.



Abnormal polarisation of nuclei

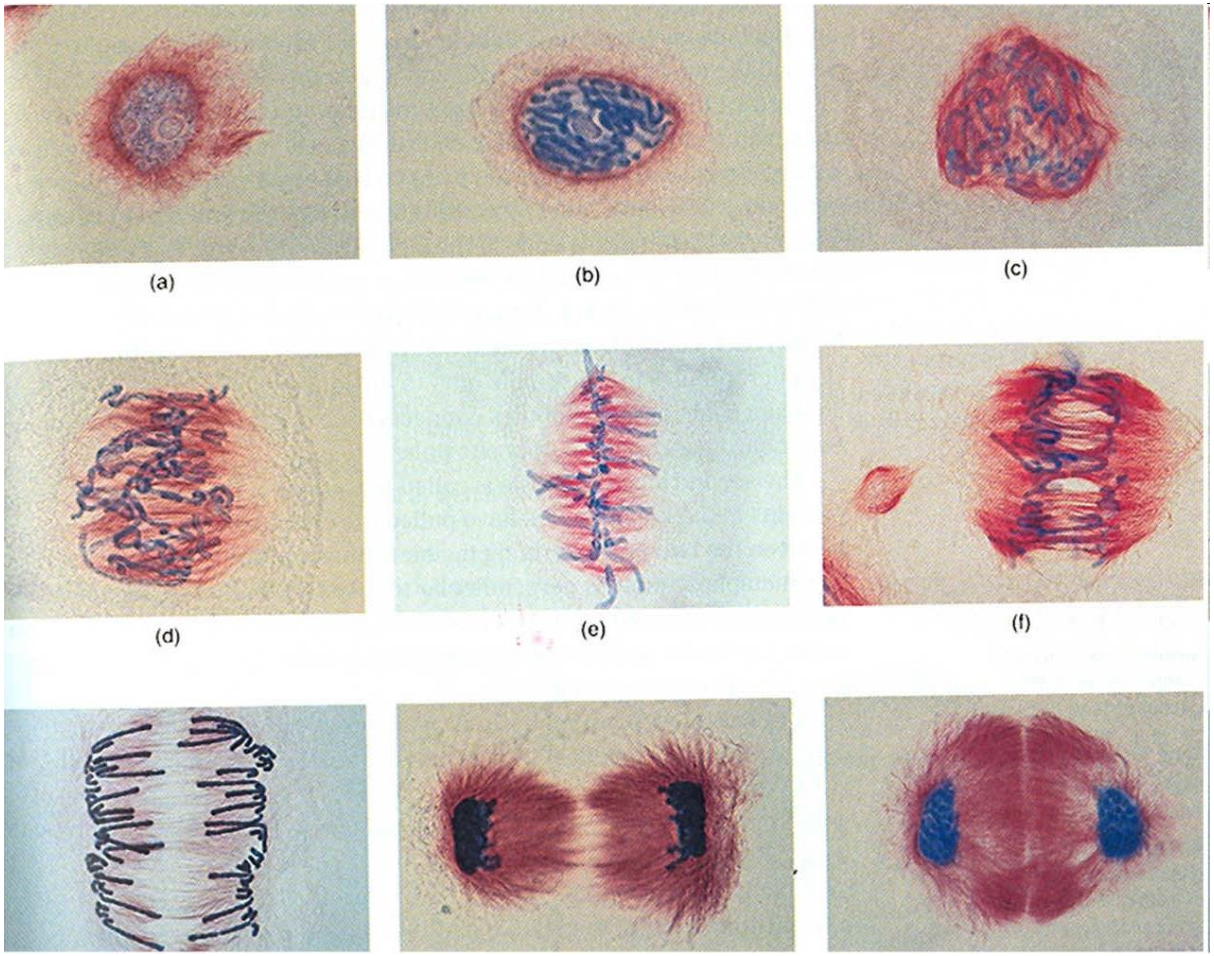


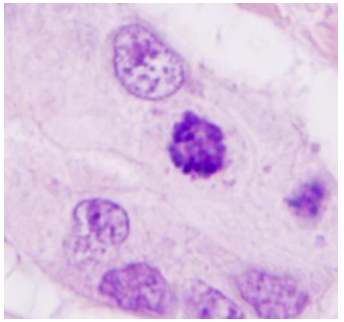
Normal – basally located

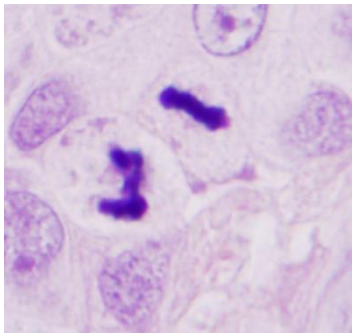


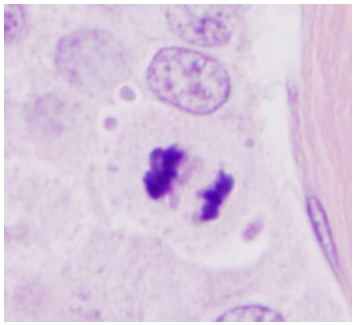
Dysplasia - pseudostratified

MITOSIS
Normal morphology

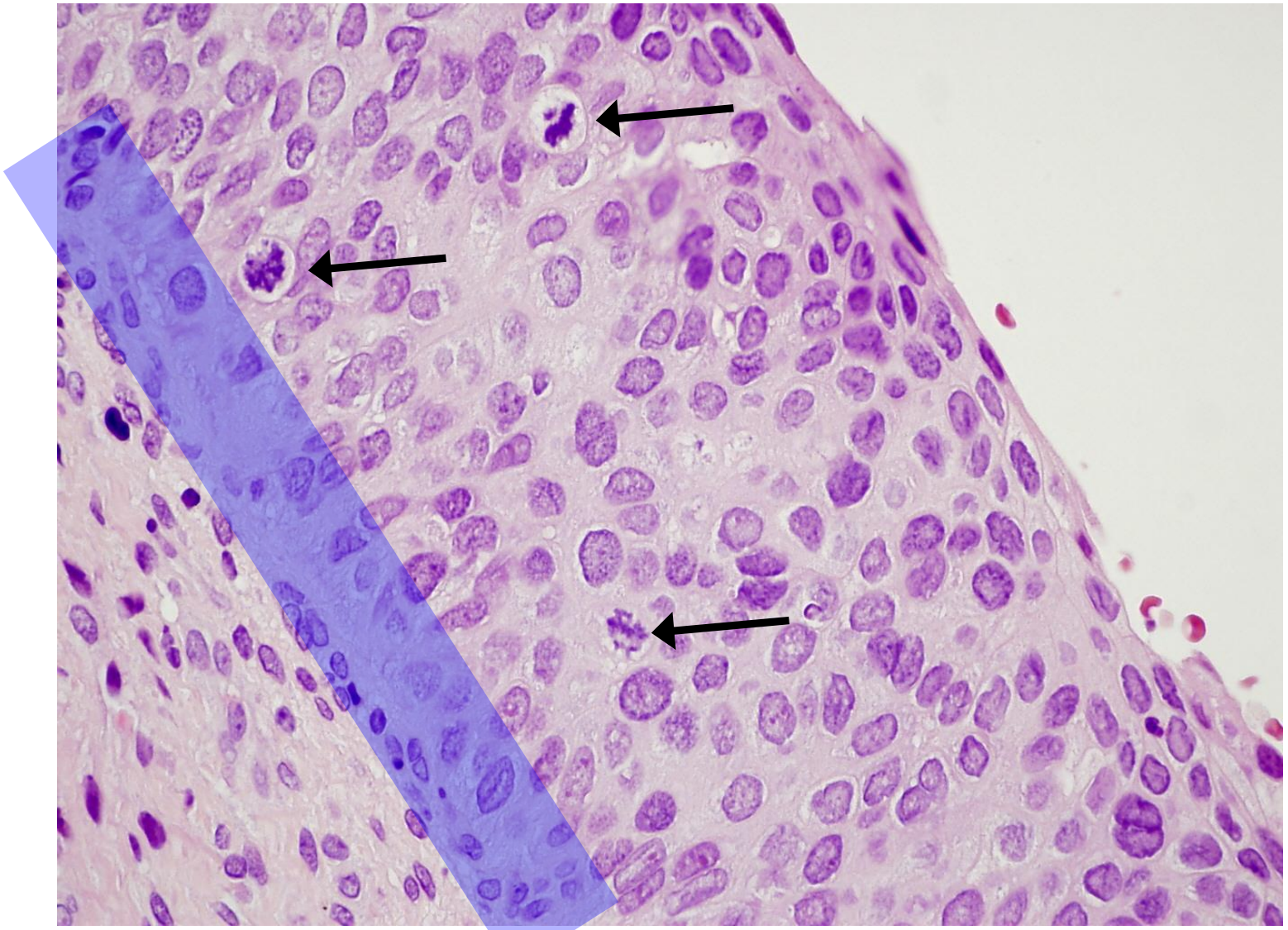




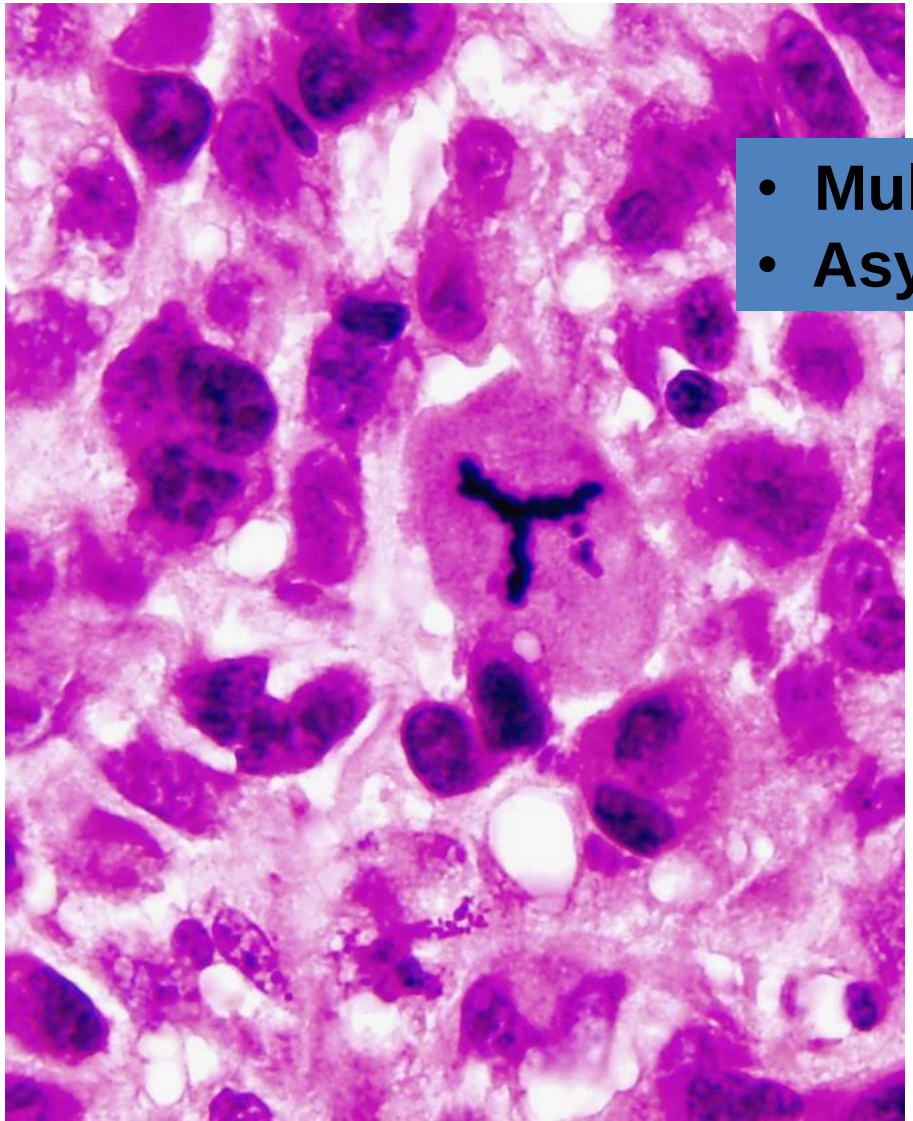




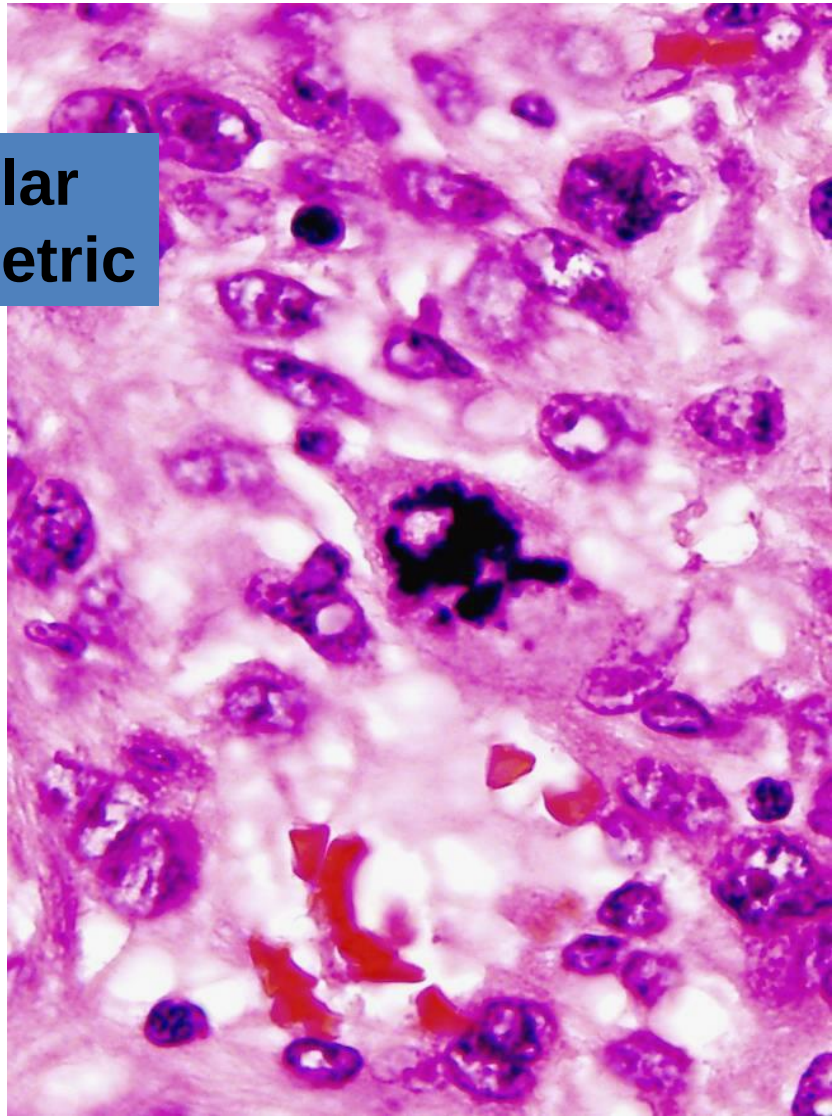
Mitosis in abnormal location



Atypical mitosis



- **Multipolar**
- **Asymmetric**



Benign and malignant tumors- Summary

	BENIGN	MALIGNANT
CIRCUMSCRIPTION	Well (capsule)	Poorly
GROWTH PATTERN	Expansive	Infiltrative
GROWTH RATE	Slow	Fast
DIFFERENTIATION	Well (resembles normal)	Well-moderately-poorly (anaplastic)
METASTATIC POTENTIAL	None	Yes